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DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1970

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HEARINGS

BEFORE A

SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS HOUSE OF REPRESENTATIVES

NINETY-FIRST CONGRESS

FIRST SESSION

SUBCOMMITTEE ON DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE AND RELATED AGENCIES

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ROBERT M. MOYER, *Staff Assistant to the Subcommittee*

PART 4

NATIONAL INSTITUTES OF HEALTH

Printed for the use of the Committee on Appropriations

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1970

TUESDAY, MARCH 25, 1969.

NATIONAL INSTITUTES OF HEALTH

WITNESSES

DR. ROBERT Q. MARSTON, DIRECTOR
DR. JOHN F. SHERMAN, DEPUTY DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT W. BERLINER, DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS, EDUCATION, AND MANPOWER TRAINING
DR. MARTIN M. CUMMINGS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE
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RICHARD L. SEGGEL, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT (BUDGET), NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

Mr. FLOOD. Now we will start our hearings with the National Institutes of Health. We have as the first witness Dr. Robert Q. Marston, the Director. Of course, Dr. Marston, you realize that in the view of the committee you have a very big pair of shoes to fill. Who would know better than you?

Dr. MARSTON. I know it well, sir.

Mr. FLOOD. When I was in the hospital toward the end of Dr. Shannon's term—and, as you know, I prevailed upon him almost on bended knee to stay awhile, which he did, not just because of my request, but for other reasons—but he and I discussed the situation, and there was never any doubt in my mind that you were his choice, and, as usual, Dr. Shannon had good judgment.

BIOGRAPHICAL SKETCH OF DIRECTOR

Now, Dr. Marston, before we proceed with your statement, we will place your biographical sketch in the record.

(Biographical sketch follows:)

BIOGRAPHY OF DR. ROBERT QUARLES MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH

Birthplace and date: Toano, Va., February 12, 1923.

Education: B.S., Virginia Military Institute, 1943; M.D., Medical College of Virginia, 1947; B. Sc., Oxford University, 1949.

Experience: Director, National Institutes of Health, September 1968 to present; Administrator, Health Services and Mental Health Administration, April–September 1968; Associate Director, National Institutes of Health, and Director, Division of Regional Medical Programs, 1966–68; vice chancellor, the University of Mississippi, and dean, School of Medicine, 1965–66; Director of the University of Mississippi Medical Center and dean, School of Medicine, 1961–65; associate professor of medicine and assistant dean in charge of student affairs, Medical College of Virginia, 1959–61; assistant professor of bacteriology and immunology, University of Minnesota, 1958–59; assistant professor of medicine, Medical College of Virginia, 1954–57; assistant resident, Medical College of Virginia, 1953–54; assistant resident, Vanderbilt University Hospital, 1950–51; intern, Johns Hopkins University, 1949–50.

Association memberships: Alpha Omega Alpha; Association of American Medical Colleges (executive council, 1964–67); American Federation for Clinical Research; Society for Experimental Biology and Medicine; Tissue Culture Association; American Society for Cell Biology; American Association for the Advancement of Science; Association of American Rhodes Scholars; American Medical Association; American Public Health Association Fellow.

Special awards, citations, or publications: Rhodes Scholar, 1947–49; Markle Scholar, 1954–59.

Mr. FLOOD. You have a fantastic responsibility and nobody knows it better than this subcommittee.

Would you like to say anything before starting your formal statement?

Dr. MARSTON. Only that I think all of us who started out to work with Dr. Shannon over the years have been impressed with the good order in which he left this very complicated National Institutes of Health. He has continued to be helpful to me when I have needed to seek advice from him.

Other than that, Mr. Chairman, I think the relationship with this committee during the past 3 years when I have had contact with it has been one that leads me to say that I look forward to the committee's sitting by and helping in the future as it has in the past on these very difficult national problems that have to be met through the agency of the National Institutes of Health.

Mr. FLOOD. You have broad shoulders, and you are certainly going to need them.

Do you have any people around the table here, or in the wings, that we do not know? Whom would you especially like to point out to the committee?

Dr. MARSTON. I would like to call attention to Dr. John Sherman, who has been here in other capacities before, but this is his first time as the Deputy Director of the National Institutes of Health. He is on my right.

Dr. Robert W. Berliner, the Deputy Director for Science.

Mr. Richard Seggel, who has been here in previous years, is Associate Director for Administration. Dr. Leonard Fenninger is the Direc-

tor of the Health Profession Education and Manpower Training Bureau.

Mr. FLOOD. Do you have any brandnew men? Dr. Fenninger I guess is the newest, is he not?

Dr. MARSTON. He was before you as head of the Manpower Bureau last year. Dr. Martin Cummings is the Director of the Library of Medicine. Dr. Ronald Lamont-Havers, who took Dr. Sherman's job as Associate Director for Extramural Research and Training, is here. I do not think you have met him before. And Dr. Thomas Kennedy——

Mr. FLOOD. That is a good name, Tom Kennedy. He used to be president of the United Mine Workers. He was from my district. He is Associate Director for Program Planning and Evaluation?

Dr. MARSTON. Yes, Associate Director for Program Planning and Evaluation.

Mr. FLOOD. Dr. Marston, you have a formidable statement here. How do you wish to proceed?

Dr. MARSTON. As you please.

Mr. FLOOD. You are the boss. We will do what you say.

Dr. MARSTON. I would like to present the statement.

Mr. FLOOD. Very well.

GENERAL STATEMENT

Dr. MARSTON. Mr. Chairman and members of the committee:

I am pleased to have the opportunity to appear before you this year in a new role. Although my association with NIH is not new—I first worked there in 1951 and, more recently, served for nearly 3 years as an Associate Director of NIH and as Director of the regional medical programs while that was part of NIH—I have been the Director of NIH for only 6 months which is a very short time for a post that during the past 81 years has had only eight incumbents. However, the newness of my role here today is not due primarily to my own recent appointment but to the fact that I am here to testify about the goals, plans, and needs of what is, in fact, a new organization, operating in a new departmental framework, under a new administration.

Mr. FLOOD. Have you had a chance to talk to President Nixon yourself about this sort of thing?

Dr. MARSTON. I have met him briefly, but not about this sort of thing.

REORGANIZATION OF DEPARTMENT'S HEALTH FUNCTIONS

Dr. MARSTON. As a result of the reorganization of the health functions of the Department that was announced last April, NIH is now not only the mainstay of biomedical research in this country but also has responsibility for Federal support of education in the health professions and for biomedical communications. The new NIH consists of three major components:

The Research Institutes and Divisions—to which we still sometimes refer, collectively, as "the old NIH";

The former Bureau of Health Manpower which has been somewhat reorganized and given a new name—it is now the Bureau of Health Professions Education and Manpower Training; and

The National Library of Medicine.

The three major components of NIH have distinct but complementary functions. The Surgeon General, in his testimony, has already described the considerations that led the Department to bring these activities together. Let me just repeat the principal reason which was succinctly stated in the Department's press release announcing NIH's broadened authority and new role. It said:

> Modern biological science and health professions education are so intimately interrelated that their effective and efficient management within this Department requires that they be the responsibilitiy of a single operational unit. This will now be the NIH.

This intimate relationship is partly due to the fact that biomedical research and health professions education are largely carried out in the same institutions. For the most part, they require the same kind of facilities and depend on people with the same professional qualifications.

Mr. FLOOD. What do you mean by biomedical?

Dr. MARSTON. This is research in the biological fields that have medical and health implications.

Mr. FLOOD. We are not halfwits but the record should show some of these things.

Dr. MARSTON. While the interplay of research and graduate education is helpful to both, it is not equally helpful to both. It is possible to perform first-class research in an institution which has little or no responsibility for formal educaton. In fact, NIH's own intramural research activity at Bethesda is an outstanding example of such an institution. However, it is not possible to provide a first-class professional education for scientists in an institution in which little or no research is conducted. Especially at the more advanced levels of professional education, the methods, techniques, and the intellectual discipline of research are an essential part of the educational process. Progress in most scientific disciplines is now so rapid that a new scientist—and I include physicians in that term—must have a keen awareness of the directions of research in his field. His exposure to the potentials and limitations of research must begin as an integral part of his professional education. In fact, as a well-known physician (Dr. Francis Heed Adler) has pointed out, "the faculties developed by doing research are those most needed in diagnosis."

Mr. FLOOD. Who is he?

Dr. MARSTON. He is an ophthalmologist from Philadelphia.

Our efforts to harmonize effectively the support for biomedical research and education must be undertaken under the crossfire to two fairly common criticisms on which I should like to comment. One of these criticisms is that the support now available for research has unbalanced the academic community and detracted from the performance of its educational function. The truth is that the academic community is out of balance in the same way that a man who has thrown one foot forward is out of balance. If his objective is to take a step forward, he must obviously restore his balance by bringing the other foot forward too.

Mr. FLOOD. Is this the problem of the faculty members who, having been starved all their lives for money to conduct research which is close to their hearts, go into an ivory tower and have ceased to instruct the classes?

Dr. MARSTON. No, sir. I think what has happened is that we have supported research very well but we have done it under conditions in which this was essentially the sole support available to the medical schools. We have not had the necesary support for the educational function.

Mr. FLOOD. We have had the other problem. It was pretty serious, so we hear.

Dr. MARSTON. The problem of the teacher being divorced from his classroom has not been as great a problem in the medical schools as it has been in undergraduate programs. The graduate students in the medical schools often become involved in the research activity as a part of their own educational activity.

Mr. FLOOD. I meant the undergraduate faculty taking Federal largesse and doing what they wanted to do for years, and they can now do it, which is research rather than teaching. You can't blame them for that because they are dedicated men and feel this is where they can make the greatest contribution. But that leaves postgraduate students and seniors teaching in the boots of these learned professors. Don't you know about this problem?

Dr. MARSTON. I have heard it discussed.

Mr. FLOOD. It is a very human failing.

Dr. MARSTON. I think we need to have appropriate support for the educational function. Part of the dilemma has been the lack of that support. It has only been since 1963, with the passage of the Health Education Assistance Act, that it has been possible to give support for the educational function to parallel support for the research activities.

Mr. FLOOD. They are not getting too much fudge, are they?

Dr. MARSTON. No, sir.

Mr. FLOOD. Very well.

Dr. MARSTON. It is true that we have thrown the research foot well forward. The imbalance in the academic community is not due to too much research support but to the unfortunate fact that, until recently, this has been the sole kind of Federal support available. There is a clear and urgent need for comparable educational support. As you know, the Health Professions Act of 1963—and its amendments and supplementary legislation—are designed to provide this sort of support. It is part of the new role of NIH to restore balance by bringing the educational-support programs into line with research support.

RESEARCH VERSUS PRACTICE OF MEDICINE

The other criticism often heard today is that research is enticing physicians from the practice of medicine. Let me counter that with some facts.

In the first place, most of the laboratory research in biomedicine is performed not by M.D.'s but by Ph. D.'s who are not licensed to provide health care. At NIH, for example, nearly half of the professional staff with doctoral degrees hold some degree other than an M.D. Nearly 70 percent of our research grants are for projects on which the principal investigator is not an M.D.

Actually, the number of physicians who are mainly engaged in research is surprisingly small.

Mr. FLOOD. Why is that?

Dr. MARSTON. Because most physicians practice medicine.

Mr. FLOOD. Making too much money.

Dr. MARSTON. I think they go to medical school because they plan to treat sick patients and to restore the health of individuals. This is what most of them do when they come out. The American Medical Association has just published a statistical summary of the major professional activities of medical school graduates who were living on December 31, 1967.

Mr. FLOOD. Does the average doctor as an alumnus on the whole contribute properly to support his medical college?

Dr. MARSTON. I do not think I can answer that question properly, Mr. Chairman.

Mr. FLOOD. What is the scuttlebut?

Dr. MARSTON. There has been a very real move—on the part of the individual medical schools, on the part of the American Medical Association, on the part of the Association of American Medical Colleges—to encourage support from physicians either to the schools from which they graduated or to a general fund to be used for the support of educational purposes.

Mr. FLOOD. Engineers do, lawyers do, AB people do, most do, but there seems to be some—so my spies tells me—dereliction on the part of medics.

Dr. MARSTON. I can say that some of the most useful dollars that came to me while I was in administration, as associate dean or as dean, came from the contributions of the alumni and other physicians who were making regular contributions.

Mr. FLOOD. I am glad to hear it.

Dr. MARSTON. The AMA study shows that of the 296,400 graduates who were still active, 93 percent were engaged in patient care. The other 7 percent was mainly accounted for by 11,400 physicians who were members of medical school faculties and 4,240 who were engaged in administration. The glaring fact is that only 4,726 physicians—or 1.6 percent of the total—had research as their major professional activity.

Mr. FLOOD. Why would that be?

Dr. MARSTON. Why only that amount?

Mr. FLOOD. Yes.

Dr. MARSTON. Again I think it is due to the reason people have for going to medical school. If they plan to go into research, most of them will go for a Ph. D. and not for an M.D. So you have a strong motivation for patient care among those who go into medicine.

Mr. FLOOD. They are practitioners or they "ain't."

Dr. MARSTON. Yes, sir. I think in all schools across the Nation the medical students go to school to become doctors and most of them come out and practice medicine.

Mr. FLOOD. Then it is such a long haul anyhow.

Dr. MARSTON. Yes, sir.

While it is, of course, true that some physicians especially those on medical school faculties, combine research with their other activities, it is noteworthy that of all the physicians who are not primarily engaged in patient care less than a quarter list research as their major activity.

Physicians engaged in research are, with very few exceptions, engaged in clinical research which must involve a physician.

Mr. FLOOD. What is clinical research?

Dr. MARSTON. This is research that involves patients and therefore this type of research must be under the supervision of a physician.

As clinical research is, by its very nature, a combination of research and patient care, the research-physician has not withdrawn from practice. He is probably providing more intensive and higher quality care for his patients than they would receive if he were not engaged in research.

Finally, it is usually true that a physician of the caliber required for successful competition for research-grant funds could make more money if he devoted himself solely to practice in his specialty. He has certainly not been enticed into research because there is money in it. On the contrary, he is in research because he has intellectual curiosity—and, probably, unique talents for research—and because he hopes to make a fresh contribution to the solution of disease problems. A research grant enables him to do this effectively by making the necessary resources available but it provides neither the initiative nor the motivation.

The growing awareness of the problems in health professions education and, especially, of the deficiencies in the provision of health-care services in this country has understandably diverted attention from the importance and needs of biomedical research. In fact, in some quarters the pendulum has swung so far that research is viewed as an expensive hobby that must give way to more urgent needs.

Mr. FLOOD. What does that mean?

Dr. MARSTON. This means, Mr. Chairman, that all of us today are seriously concerned about the health problems in society at large, and each of us wants to do something about these as quickly as possible. Sometimes we forget that, in order to achieve these desirable goals, it is necessary to have the knowledge and the education and the skill. One must have more than good wishes and good desires to achieve the benefits in the health field that one would like to achieve. To deny the needs of research strikes me, Mr. Chairman, as a little like saying that the goose that lays the golden eggs should no longer be fed.

The ultimate purpose of all health activities must be the prevention or cure of disease—and, when neither of these goals is yet attainable, the amelioration of the effect of disease both in terms of extending the useful life of the patient and of minimizing disability and suffering. This is indeed the purpose of all of the programs supported by the NIH appropriations.

Effective action against disease requires, first of all, a knowledge of what is wrong and the availability of some means for doing something about it. In general, the better our understanding of the cause and usual course of disease, the more likely it becomes that we will be able to develop some means of coping with it. That, in essence, is the purpose of biomedical research: The constant expansion of knowledge and its translation into applicable preventive or therapeutic methods.

During the past decade NIH has contributed to the expansion and strengthening of every major health institution in the country. Almost every major medical advance in this country has to some extent depended on research supported by NIH. Almost every citizen has

benefited—and will continue to benefit—directly or indirectly from these research programs.

In fact, research during the past decade or two has completely changed the practice of medicine. Most of the drugs now in common use for the treatment of major diseases were unknown or unrecognized as therapeutic agents when I started medical school in 1943. A whole series of new surgical techniques have been developed that make it possible to intervene in situations in which surgeons used to be unable to help. New and better techniques for monitoring patients and for automating laboratory tests have been developed. Mechanical assistance devices then unknown—such as the pacemaker and the so-called artificial kidney, which is actually an external blood-cleansing device—have already saved thousands of lives. You are well aware of recent dramatic advances in the technology for transplanting human organs. All these radical changes in the practice of medicine—and the certain expectation of even more revolutionary advances—are the direct result of the expansion of research facilities, the enlargement of the corps of research scientists, and the provision of funds to support their work. The greater effectiveness of modern medicine is the tangible payoff for the investment that has been made in medical research.

HEART TRANSPLANTATION

Mr. FLOOD. Have you seen these words of caution about heart transplants and the pendulum swinging the other way in the last few days?

Dr. MARSTON. Yes, sir.

I think there has been concern from the beginning about the major unresolved problems, particularly in the area of immunology and the understanding of tissue reactions in the body.

Mr. FLOOD. The news media have handled heart transplants in such a way that the recent statements I think will come as quite a shock to the average man on the street. It was becoming a pretty prevalent opinion that all you had to do was to transplant a heart, period. Of course, that is not the case.

Dr. MARSTON. I am sure that you know the position that the National Institutes of Health has taken in recent years——

Mr. FLOOD. From the beginning.

Dr. MARSTON. That the answer to the problem is neither to be found by an all-out effort to develop an artificial heart nor an all-out effort to transplant a heart.

Mr. FLOOD. Any good surgical team can transplant a heart. But that is not the trick.

Dr. MARSTON. No, sir. The need to understand the causes of heart disease. With this type of understanding one increases the chance of doing something about heart disease. The thing that we need to remember constantly is that some of these dramatic developmental programs tend to be high-risk programs.

Mr. FLOOD. The mere physical mechanics of a surgeon transplanting a heart is not the primary problem. It is to make it stick that is difficult.

Dr. MARSTON. I agree with you in general, although I must say that the very fact that surgeons can transplant hearts dramatizes the tremendous advances that have been made in anesthiology and blood transfusion and the use of antibiotics and the treatment of shock and

the preservation of organs and the understanding of the immunic process. A whole series of procedures are used to suppress—

Mr. FLOOD. It is much more serious than the average guy knows, the resistance of the body to the new thing.

Dr. MARSTON. Yes, sir.

Mr. FLOOD. Much more than the average person had an idea. They have overplayed the fact of the transplantation and the other business has been ignored. Now we have a problem.

Dr. MARSTON. Yes, sir. I think the point must be made over and over again that when one has the necessary knowledge, then one can move forward quite rapidly.

This is one of the reasons that the developments in genetics and the understanding of DNA, which sometimes seem fairly far removed from such things as treating a patient with heart disease, become so important.

Mr. FLOOD. Could it be that a person might accept an animal heart?

Dr. MARSTON. All our evidence today in immunology would suggest that the more closely related the individuals are, the better the chance of acceptance. I think it would be unlikely that what you suggest would occur.

GERMAN MEASLES VACCINE

This committee has just heard testimony in support of a request for funds to launch a large-scale vaccination program against German measles in order to head off the next epidemic. The last epidemic resulted in the birth of some 30,000 children with serious congenital defects.

Mr. FLOOD. Does this move in cycles?

Dr. MARSTON. Yes, sir.

Mr. FLOOD. Why?

Dr. MARSTON. It is probably a combination of the level of susceptible children in the population and the conditions for spread. In German measles we have a different situation than in influenza where the virus itself is constantly changing and therefore each time one has a new strain——

Mr. FLOOD. This is the same problem which recurs. Why can't you stop that? This is not a new strain. This is the same thing.

Dr. MARSTON. I think we can with the vaccine. What happens is that one has a major epidemic and then a period with a low level of infection. During that time you have more susceptible children growing up.

Mr. FLOOD. Do you have a breakthrough or a target date on the horizon for the vaccine?

Dr. MARSTON. We think, from the standpoint of licensure, that this will be soon now.

Mr. FLOOD. What is soon?

Dr. BERLINER. We think the vaccine will probably be licensed within the next 2 months.

Mr. FLOOD. Whom would you vaccinate?

Dr. BERLINER. The plan generally is to vaccinate children.

Mr. FLOOD. Under 12 months?

Dr. BERLINER. No. It will probably be around the time they start school.

Dr. MARSTON. This would be a school-age program.

Mr. FLOOD. Would you vaccinate a pregnant mother?

Dr. BERLINER. No; very definitely not. That, in fact, would be a great danger, to vaccinate a woman who in fact turns out to be pregnant.

Mr. CASEY. How about the problem of vaccinating a schoolchild? Is there any chance of infection of the mother who is pregnant?

Dr. MARSTON. The experiments that have been carried on to date have not raised this as a problem, Mr. Casey. In answer to your question is there any chance at all, I think we would have to say that all of the information we have at present is that this is not a major risk.

Mr. FLOOD. You have seen that flare up on the vaccination for the old-fashioned red measles.

Dr. MARSTON. Yes, sir. We will have to find out what happened there, whether it was a particular vaccine that was not satisfactory.

Mr. FLOOD. That does not shock you especially. It is just surprising?

Dr. MARSTON. It is the type of thing that one wants to get as much information on as possible, but red measles was once a disease that virtually everybody had. It was a major illness of children. I think the 26 cases have to be looked at in contrast to the large population that has been protected.

Mr. FLOOD. But you are still pretty cocky about having the old red measles licked?

Dr. MARSTON. Yes, sir.

Dr. BERLINER. I believe that most of those children were vaccinated at an age when they did not get the modified measles which the vaccine causes. It has been known for many years that children under 1 year of age very rarely develop measles even when exposed because they carry protective antibodies from their mothers. Eighteen of the 23 children were vaccinated at an age under 1 year which is not a favorable time for vaccination.

Dr. MARSTON. The effect to forestall as a repetition of the rubella tragedy was made possible by a concerted research effort since the last epidemic. Not only did NIH provide a major share of the support for this research but NIH scientists, working in the laboratories at Bethesda, made major contributions to the development of the vaccine.

Mr. FLOOD. Do you have any plans to put on a dramatic extraordinary show like they did with polio—nationwide—PTA's, chambers of commerce, junior chambers of commerce, banks, do you have this in mind?

Dr. MARSTON. CDC will be coordinating this and they plan to work closely with the voluntary health organizations in a cooperative effort to make the vaccine available.

Mr. FLOOD. There is nothing wrong with this sort of thing. It is no stunt.

Dr. MARSTON. No, sir. I participated in the launching of both of the polio vaccines and I think this was a very important performance.

It was a public education. So many people had a sense of pride over doing something about a disease that had been a summer dread of people for years and years.

Mr. FLOOD. In many districts there were more vaccination centers than there were barrooms overnight.

Dr. MARSTON. The Sunday afternoons that those were held were very exciting days.

Mr. FLOOD. Yes, they were.

Dr. MARSTON. I shall leave to the witnesses who will testify for the appropriations of the various research institutes the pleasant task of reporting to you on significant progress in research against some of the major diseases. At this point, it is, I think, more important for me to emphasize the serious and bewildering gaps that exist not only in our knowledge of diseases but in our understanding of the intricacies of normal biological processes.

Despite the impressive—and often dramatic—progress that has been made in the prevention, diagnosis and treatment of many diseases, the art of medicine is still a rather primitive science. In fact——

Mr. FLOOD. The art of medicine?

Dr. MARSTON. Yes, sir.

Mr. FLOOD. The art of medicine. That is a new one.

Dr. MARSTON. No, sir. It is a very old one. Hippocrates spoke of the art of medicine.

BASIC RESEARCH

In fact, a frequent consequence of new advances in knowledge is to raise even more difficult questions or to expose new areas of ignorance. This state of the art lies behind our constant insistence on the importance of what, for want of a better name, is usually called "basic" research.

Basic research is not the opposite of applied research, as so many people seem to think.

Mr. FLOOD. What is basic research vis-a-vis any other kind of research?

Dr. MARSTON. Basic research is the essential first stage in the exploration of a new area. This is when one is trying to understand the basic behavior of biological materials—whether it be in man, whether it be in animals, whether it be in enzymes—to try to understand the basic forces.

Mr. FLOOD. It is not just theoretical, not trying to make gold?

Dr. MARSTON. No, sir, it is trying to find gold, it is not trying to make gold.

Mr. FLOOD. This is not alchemy, you are really looking for something.

Dr. MARSTON. We are really looking for something. Often the basic research is stimulated by disease problems that frustrate the investigator because we do not know the answer about some essential part of the problem. For instance, in the transplantation area, if we knew more about immunology, we would be able to do a better job in the treatment of people.

Mr. FLOOD. That is a good answer.

Dr. MARSTON. It is basic research that makes so-called applied research possible.

Mr. FLOOD. What is applied research?

Dr. MARSTON. It is research after you research that point in the understanding of the basic mechanisms when you can see a possible

application for treatment of people. We were talking about the measles vaccine a moment ago. So-called applied research was not possible until it was found possible to create a strain of virus that had changed its characteristics to the point that it was able to immunize but not to cause a serious disease. The next step was to see how one could use this strain to prevent regular measles from occurring in the population. At this point it became applied research. It still required much additional testing.

The first strains of regular measles were isolated in Dr. Enders' laboratory in tissue culture, and that immediately raised the possibility of the production of a vaccine because the virus had not been grown previously in tissue culture. Moving from that point, the actual development of the vaccine and all that occurred until it was ready to be given to the population at large would be considered applied research.

With rare exceptions, the practical advances of today are the fruit of basic research done over a considerable period of time by a number of different investigators. I am absolutely certain that any slowdown in basic research will be directly reflected in the postponement of solutions to many disease problems. It is particularly important, in an era of restricted budgets, not to lose sight of the indispensable role played by basic research in achieving the objectives of the NIH programs.

I have talked about research at some length but I can sum up my view very briefly. Research is the root on which all other health activities grow. Without that root, no further growth is possible—either in improving the quality of education or the quality of medical service. The old adage that knowledge is power is nowhere more applicable than in the practice of medicine and, as Sir Howard Florey, the developer of penicillin, has said "the lesson of 20th century medical science is * * * that experiment is the most efficient method of acquiring new knowledge".

NIH CLINICAL CENTER

Mr. FLOOD. It is true, is it not, that the National Institutes of Health is not a hospital? You are a research body, are you not?

Dr. MARSTON. That is right. The patients who are admitted to the clinical center at NIH are admitted because of the research programs being carried on. They are there as a part of the research program. They also, I might say, receive some of the best treatment and in some instances it may be the only place——

Mr. FLOOD. Insofar as your facilities are concerned?

Dr. MARSTON. Yes.

Mr. FLOOD. They could not be treated better. However, this is not a hospital, it is a research institution.

Dr. MARSTON. Our facilities are actually quite incomplete in comparison with a normal hospital. We are not fully staffed to take care of all the problems a normal hospital would take care of.

Mr. FLOOD. I would like the record to show that because so many of my colleagues come to me, and the members of this committee, with questions about having Tom, Dick, and Harry and Mrs. Tom, Dick, and Harry admitted to your institution for treatment, and you do not exist for that purpose. It is very difficult for the members to make it clear that this is not just merely another hospital.

Dr. MARSTON. This is quite true. I think that in the areas in which we have research programs we can give some of the best care in the

world, but there are some areas for which we are just not equipped.

Mr. FLOOD. Please continue with your statement.

NEED FOR HEALTH MANPOWER

Dr. MARSTON (continuing). However, knowledge is useless unless it is properly applied. The second requirement for effective action, therefore, is highly trained professional personnel.

I have already touched on the urgent need for a more vigorous attack on the manpower shortage in the health professions. Since the beginning of this century the production of physicians has barely kept pace with our growing population. The number of physicians, in proportion to population, is no better now than it was in 1900.

Mr. FLOOD. What are you short; about 50,000?

Dr. MARSTON. One can take various figures, that is one of the figures.

Mr. FLOOD. That is a lot?

Dr. MARSTON. Yes, sir.

Mr. FLOOD. What about nurses?

Dr. MARSTON. We have something between 600,000 and 700,000 nurses at present. The estimates of additional needs are on the order of a 50-percent increase, but we could get more precise figures for you.

Mr. FLOOD. Give us those figures for the record for doctors, dentists, and nurses.

Dr. MARSTON. All right.

(The information follows:)

ESTIMATED NEED FOR PHYSICIANS, DENTISTS, AND NURSES

	Physicians		Dentists		Nurses	
	1968	1975	1968	1975	1968	1975
Estimated need	363,000	400,000	109,000	137,000	800,000	1,000,000
Estimated supply	311,000	358,000	100,000	109,000	659,000	795,000
Estimated shortage	52,000	42,000	9,000	28,000	141,000	205,000

Dr. MARSTON. At the same time, the need for highly trained physicians and other health personnel has grown sharply as the result of two factors. The first is the greater sophistication of medical practice and the consequent growth of specialization.

Mr. FLOOD. I thought you were supposed to bring back general medical practitioners as the thing now.

Dr. MARSTON. I think that is an add-on, Mr. Chairman, it is not to decrease the need for specialists. Almost without exception, we need more manpower in all areas.

PROPOSALS FOR ADDITIONAL INSTITUTES

Mr. FLOOD. Last year we gave you a National Eye Institute. Does that mean they are coming back for another institute for the left eye, one for the right eye?

Dr. MARSTON. No, sir; I think one Eye Institute is proving to be enough, but there are suggestions for other institutes.

Mr. FLOOD. I know that. Of course, I was exaggerating but that was not my point, there are proposals for more and more institutes.

Dr. MARSTON. I think it brings up some policy problems for the NIH and for this committee which I would like to discuss either now or later.

Mr. FLOOD. You are not overdoing this, are you?

Dr. MARSTON. We are not looking for additional institutes; no, sir.

Mr. MICHEL. I was surprised that they did not combine a little and have an Institute for Eye, Ear, Nose, and Throat.

Mr. FLOOD. I have often thought that. I might be a bit old fashioned, but I am concerned that when we get down to such a narrow field for one new institute that we may be opening the door for many more. Go ahead.

Dr. MARSTON. As a direct result of research, the medical profession is able to deliver care that is infinitely superior to what was possible in 1900 but it takes more—and more diversified—manpower to do it. The second factor is the rise in public aspiration for health care and the consequent rapidly growing demand for high quality professional services. To this we must add, as a third factor for the future, the demand arising from programs designed to bring better health services to the aged and the disadvantaged and to make the best medical care that is technologically possible readily accessible in all parts of the country.

EMPHASIS ON CARE FOR THE AGED

Mr. FLOOD. At that point, is there too much concern about the aged and not enough about the young? Everybody seems to be talking about care for the aged. What about care for the young?

Dr. MARSTON. I think you will hear about this need from the Child Health and Human Development Institute. They feel very strongly that there are major needs for the young in this country and that here again our knowledge is quite incomplete. We do need to know more about family planning, we need to know more about——

Mr. FLOOD. Care for the aged. Everybody is so concerned about the aged. I do not see a comparative concern from you pros about the young. What is the reason?

Dr. MARSTON. I think it is two things. The incidence of illness in the aged is higher and so the requirements for serious care is higher.

The second one is the fact we have just implemented medicare, which is a payment mechanism for health care to the aged, and this has put an emphasis on it.

Mr. MICHEL. If I might add a little political note there, I think it is a fair observation there are many more older people voting.

Dr. MARSTON. I have heard this concern that you are expressing expressed very strongly at the State and local level. There was a meeting of Governors' representatives recently in which they brought up the point that they wanted to be sure that they were not putting all of their resources in the care of the aged at the expense of taking it away from the young.

Mr. FLOOD. Of course, being a statesman instead of a politician, that would never occur to me.

Mr. MICHEL. I know, that is why I wanted to give you that assist.

Mr. FLOOD. That reminds me of the great Senator Taft of Ohio, a great American, a great Senator, and a great man. A controversy arose one day about certain incidents, highly controversial, and when he came back to Washington somebody said to him, "Senator, I thought

you were a statesman." And he said, "Well, to be a statesman you must first get elected."

Mr. MICHEL. He had been elected enough times to be a statesman.

Mr. FLOOD. Go ahead.

Dr. MARSTON. Mr. Chairman, if I might add that the largest single increase in the budgets for the research institutes is for child health activities. This is a $7,611,000 item.

Mr. FLOOD. I know that. I thought somebody should say so.

FEDERAL RESPONSIBILITY FOR MEDICAL EDUCATION

Dr. MARSTON. The need is for a greater number of better trained people in all of the health professions.

We are now in the stage of having to raise our national commitment to medical education to a higher plateau during the 1970's as we raised biomedical research during the late 1950's and early 1960's. The primary burden of doing this will necessarily fall on the Federal Government—especially for training at the doctoral level.

Medical and dental schools are, in a practical sense, national rather than local or even regional institutions. The AMA study to which I have already referred shows that more than 57 percent of the graduates of U.S. medical schools practice in a State other than the one in which they were educated.

Mr. FLOOD. What about the alleged existence in medical schools of quotas against Jews, against Catholics, against Negroes, against women? What about this? This is a very serious charge.

Did you not ever hear of this?

Dr. MARSTON. I think it is very unfortunate if it occurs, Mr. Chairman.

Mr. FLOOD. I agree with you.

Dr. MARSTON. Restrictions that I have had personal contact with have been in the State schools who do give preference to residents of their own States.

Mr. FLOOD. I find no quarrel with that.

Dr. MARSTON. Beyond that, I know of no medical school that would——

Mr. FLOOD. You do not really?

Dr. MARSTON (continuing). Admit to that type of thing.

Mr. FLOOD. Please proceed with your statement.

SHORTAGE OF NURSES

Dr. MARSTON. Questions have been raised about the share of responsibility that the Federal Government must assume for the training of nurses and the allied health professions. It is, of course, true that facilities for training nurses and health technologists are more geographically dispersed than medical or dental schools and that their graduates normally find local employment. It has, therefore, been argued that nurses and technicians constitute a State or regional—rather than a national—core of service personnel and that their training might well be regarded as primarily a State or regional responsibility. However, shortages in these professions are no less acute than the physician shortage and the existence of an adequate number of well-

trained nurses and other supporting personnel is no less a national need.

Mr. FLOOD. What do you think about the program of retreads as we used to call it, bringing back the nurses who quit nursing and got married but the children are now grown, retraining them and putting them back into the practice of nursing?

Dr. MARSTON. I think this is an important effort to make. The Bureau of Professional Education and Manpower Training has had some experience in this.

Mr. FLOOD. What do you think?

Dr. MARSTON. I think we should make serious attempts to utilize this source of already trained man- and woman-power in the health field.

Mr. FLOOD. They know a lot of tricks the kids do not; do they not?

Dr. MARSTON. Yes.

Moreover, new national programs such as medicare, comprehensive health planning, the regional medical programs, and the model cities program are major factors in greatly increasing the demand for auxiliary health personnel.

Mr. FLOOD. Model cities, is that the community health center or what?

Dr. MARSTON. The health components of the model cities program.

Mr. MICHEL. When we are talking about the auxiliary health personnel, do you think the education requirements do inhibit in some respects utilizing to a fuller degree the retreads the chairman talks about, who do not have the academic wherewithal to pass the written examination that is required in so many cases today, but do have the motivation and the just good commonsense of how to help people?

This would certainly not be desirable in the highly professional area, but in the lower level where we see so much need. I have come across a good many people who I think would just fit into this slot very well.

Dr. MARSTON. I think there are many problems here. Until very recently the pay for such people was among the lowest in our society. Status was also a question. This was looked upon as not having a high status and being blocked in terms of advancing.

In the health field, there is a place for a wide range of talent from the most highly trained specialists down to the individuals who have had little or no formal education, but have the ability and the motivation to work with people.

Mr. FLOOD. Why do they not double the salaries of nurses?

Dr. MARSTON. They have been going up recently, Mr. Chairman.

Mr. FLOOD. They are not paid enough, you know that.

Dr. MARSTON. Yes.

Mr. FLOOD. What is the problem? Why can they not double the salaries?

Dr. MARSTON. This is one of the largest costs in a hospital, the nursing costs.

Mr. FLOOD. So what?

Dr. MARSTON. And there is concern about the rising costs of hospitalization.

Mr. FLOOD. Can you stop them from being choked to death by paper. Can you not stop that? Why do you have nurses sitting in some silly room doing paperwork like a clerk?

Dr. MARSTON. There are attempts to substitute people with different training.

Mr. FLOOD. I have reason to admire them and respect them. I just wonder why they do not seem to be properly managed by you fellows or the administrators.

Dr. MARSTON. It is not an uncomplicated question. The whole field of nursing——

Mr. FLOOD. Some old gal down at the end of a hall a quarter of a mile away pushes a button and the nurse must go a half a mile to give her a cup of tea at a quarter of nine. It is silly.

Dr. MARSTON. I think we must find better ways to utilize talent in the nursing field as well as to increase the absolute numbers.

Mr. FLOOD. Just so you know.

Dr. MARSTON. It is therefore both necessary and appropriate for the Federal Government to stimulate and assist the development of suitable training programs for allied health personnel. This is, indeed, the purpose of the institutional and special project grants and the traineeship, scholarship, and loan programs authorized by the Nurse Training Act of 1964 and the Allied Health Professions Personnel Training Act of 1966 and subsequent legislation.

Mr. FLOOD. What do you think of the help the area of nursing has been getting under the 1964 act?

Dr. MARSTON. Mr. Chairman, as you know, there is a report due to the Congress shortly on the whole allied health problem which we will be forwarding.

Mr. FLOOD. What about the nurses under this 1964 act?

Dr. MARSTON. There is the general feeling that there has not been enough support, in terms of dollars, to meet a very critical need. Of course, the discussion that is uppermost in relation to its extension is the question of whether one can bring people into the nursing field who for one reason or another may not have considered the possibility of coming in before. The so-called opportunity loans and scholarships program are designed to encourage people who have not thought of nursing as a profession to think about it as a profession and to come into it.

Mr. FLOOD. Go ahead.

FINANCIAL PROBLEMS OF MEDICAL AND DENTAL SCHOOLS

Dr. MARSTON. A particularly urgent problem, to which the Secretary has already referred in his testimony to this committee, is that a number of our medical and dental schools are having serious financial difficulties. The viability of these schools is a matter for serious concern at a time when we are not only faced with a critical manpower shortage—and are, in fact, in process of establishing additional medical schools—but when urgent social needs are making increasing demands on them.

A more adequate and stable form of institutional support, than now exists, must be provided if the medical, dental, and other professional schools are to rise to the challenge that national societal and manpower needs have placed before them.

Mr. FLOOD. Well, "Societal"; who wrote than one?

Dr. MARSTON. I would have to take credit for that word.

Mr. FLOOD. Really?

Dr. MARSTON. Yes.

Such support should not simply be designed to relieve current financial stresses but should have the more important aim of restoring confidence in the Federal Government's long-term policies in regard to the support of biomedical research and education. This confidence has, unfortunately, been shaken by NIH's inability, for budgetary reasons, to carry out the intentions of the 1966 extension of the Health Research Facilities Construction Act and by the necessity, in order to effect the required reductions in 1969 expenditures, to dilute its long-standing moral commitment policy by renegotiating grant awards that had already been approved.

The close and mutually dependable relationships that have been carefully built up between the principal centers of biomedical research and training and the categorical Institutes are a valuable, if intangible, asset. They have been a major factor in the rise of this country's biomedical research effort to its present preeminence. They are no less important to the smooth evolution of the important health manpower programs that are now in their initial stages.

I am convinced, Mr. Chairman, that the success of the Federal Government's partnership with non-Federal institutions in such national programs depends largely on two conditions:

The predictability and reliability of Federal assistance; and

The feeling of common purpose and professional rapport that exists between the institution and the Federal agency with whose programs it is involved.

I believe that these conditions are, in the long run, more important than the actual funding level.

The immediate purpose of institutional support for medical and dental schools under the health manpower appropriation is to make possible—and provide an incentive for—substantial increases in enrollment. As you know, most of the schools, for quite understandable and legitimate institutional reasons, have in the past resisted moving in this direction. There has, however, been a profound change in attitude and there is no longer any reason to doubt that this program will succeed to the extent that resources for it become available during the next few years.

A longer range purpose of these institutional grants is to facilitate the development of more efficient and effective educational processes in institutions which have diverse aims and capabilities. New approaches in medical education are desirable for three reasons. First, simply in order to accommodate a larger number of students without a proportional enlargement of facilities, faculties, and funds.

Mr. FLOOD. Do you have trouble getting faculties?

Dr. MARSTON. Yes, sir; there is a shortage of faculties for medical schools and for dental schools. These are listed and categorized and published by the Association of American Medical Colleges in summary form each year. We could provide the trend, in terms of faculty deficiencies, for the record if you would like.

Mr. FLOOD. No; I think your answer is enough.

Dr. MARSTON. Secondly, in order to maintain quality standards during a period of fairly rapid expansion—and, if possible, to raise them.

As someone has said, it would be wonderful if we could double the number of schools in the top 25. And, thirdly, in order to prepare students to experiment with changes in the delivery of health services such as the greater use of auxiliary personnel for some of the activities that now absorb too high a proportion of the average practitioner's time but that do not require his extensive—and expensive—training.

Mr. FLOOD. Are there such things as class A schools in medicine, and class B, and class C?

Dr. MARSTON. No, sir; not any more. There used to be prior to World War II. In actual fact, I have known personally only one person who was a graduate of a so-called class B medical school. All of these went out of existence.

COMMUNICATION OF RESEARCH FINDINGS

The third prerequisite for effective action against disease problems is the constant flow and the ready accessibility of the products of research to the people who are in a position to use and apply them. This is largely a question of communication which, as yet, presents many problems. One of the principal functions of the National Library of Medicine is to provide imaginative leadership in the development of new techniques for the storage, retrieval, and dissemination of biomedical information.

Communication of research information is the gateway to its application and it is the most reliable device for constantly enhancing the quality of service to the patient. Communication provides the essential links between research, education, and service. It is is no less important to the maintenance of a high standard of training. It provides the cross-fertilization that greatly increases the yield of research.

The National Library of Medicine, which is now part of NIH, plays a major national role in biomedical communications. Last year the Congress passed a bill authorizing the establishment and construction of the Lister Hill National Center for Biomedical Communications as part of the National Library of Medicine. A request for $900,000 in planning funds for the construction of the Lister Hill Center is included in the budget estimate. The purpose of the Center will be to provide—in the language of the bill—"an urgently required facility for the improvement of communications necessary for health education, research, and practice." It is hoped that the Center will be able to provide leadership for the rapid development and standardization, on a nationwide basis, of the technological aspects of biomedical communication, information systems, and network projects.

JOHN E. FOGARTY CENTER

This committee will be pleased to hear that we are making good progress in creating the John E. Fogarty Center for Advanced Studies in the Health Sciences. A contract for the design of the building was signed last December. The plans are due to be completed by April of next year and we hope that a request for construction funds will be included in the 1971 budget estimates. Meanwhile, the restoration of Stone House is underway and will be completed by July of this year. Stone House, which was the residence of the former owners of part of

the NIH campus, is a substantial and attractive building on the site chosen for the Fogarty Center. It will become a permanent part of the Fogarty Center facilities. Dr. Leavitt, the Director of the Center will report to you later in these hearings on the programs of this memorial to the late Congressman Fogarty.

I have touched briefly on the major responsibilities of the new NIH. All of the wrinkles have not yet been ironed out of the new organization and a number of administrative problems remain to be solved. In developing the new organization we shall strive for the best balance among the various activities always bearing in mind that their ultimate purpose is to achieve the most effective approach to the prevention and cure of disease.

BUDGET REQUEST

Last year when Dr. Shannon made his last appearance before this committee as Director of NIH, he described the budget estimates as "Spartan in character" and as "necessarily limited * * * to the amounts that can be justified as essential if the medical research establishment of the Nation is to be maintained at an effective level and not be threatened with disarray and deterioration." The budget request now before you is no less Spartan and no less limited to the absolute essentials.

The appropriations requested for NIH total $1,484,127,000 which is an increase of $90.1 million over the comparable appropriations for fiscal year 1969.

However, in terms of funds available for obligation—which takes into account carried over funds that remain available for obligation in some of the NIH programs and restrictions on obligations during fiscal year 1969—the net increase for NIH is only $31.7 million or slightly more than 2 percent. The funds requested are distributed as follows among the major activities of NIH:

The $275.6 million requested for direct operations of the Institutes and Research Divisions includes $89.2 million for the conduct of research by the NIH scientific staff and $127.4 million for collaborative projects. The remaining $59 million is for other direct operations, program direction, administrative services, and management of the extramural program.

Of the $634 million requested for research grants, nearly $170 million is for the special research grant programs—including $53.6 million for general research support—and $331 million is for noncompeting research projects which we already have a commitment to support. This leaves $133 million for competing grant applications—an increase of $6.3 million over the amount available for fiscal year 1969 mainly for the new Eye Institute and for family planning research.

The requests for training grants and fellowship total $190 million—a decrease of $7.7 million from the amount available for fiscal year 1969.

A total of $245.5 million is requested for the health manpower programs—an increase of $38.8 million over the comparable figure for fiscal year 1969. A little over half of this amount ($123.9 million) and $30.4 million of the increase is for the institutional support programs.

A total of $11.9 million is requested for dental health activities which is an increase of $1.7 million.

For the construction programs, which are now combined in the Bureau of Health Professions Education and Manpower Training, the budget request is $126.1 million. Together with carryover funds, this will make $149 million available for obligation which is nearly $25 million less than the comparable figure for fiscal year 1969. An increase of $10.8 million is allowed in the construction funds requested for medical schools but this is more than offset by a $10.8 million reduction in construction funds for schools of nursing and by the absence of any request for funds for the construction of health research facilities, medical libraries or allied health professions schools.

A total of $22.2 million is requested for the National Library of Medicine which, with carryover funds, will result in an increase of $2.7 million in the amount available for obligation. The increase is mainly for operating the library and for the activities of the Lister Hill Center. The amount included for grants ($7.6 million) is slightly less than the comparable amount for fiscal year 1969. In addition, $900,000 is included in the budget item for buildings and facilities for architectural planning of the Lister Hill National Center for Biomedical Communications.

These figures admittedly do not make full allowance for everything that could, or should, be done. Health activities—important though they are—must, like other important social programs, continue to be limited by overriding economic constraints. The funds requested do, however, provide for the maintenance of commitments in almost all program areas and allow for modest expansion in some particularly urgent ones. The 1970 budget request is, like the 1969 budget, as lean as is possible without seriously curtailing the activities which it is designed to support. I hope, Mr. Chairman, that circumstances next year will permit resumption of a more vigorous pace for these significant health programs.

Thank you.

Mr. FLOOD. I hope you get your hope. That is an excellent statement.

We will reconvene at 10 o'clock, gentlemen.

WEDNESDAY, MARCH 26, 1969.

FORMULATION OF NIH BUDGET

Mr. FLOOD. The committee will come to order.

As I said when we finished yesterday, Dr. Marston, you had a very fine statement and, because of the importance of your job and your office, the committee examined you rather extensively during your statement.

With two or three significant exceptions, the budgets for the various Institutes fall into an almost mathematical pattern.

Research grant funds are up a bit, just a bit. Fellowship and training funds are down a little. Direct operations are up a little. The percentage of increase and decrease is about the same for all Institutes, with two or three exceptions.

Did you work on this budget, personally?

Dr. MARSTON. Yes. As you know, the budget was put together last spring and last summer. I personally came into the budget picture in the late summer and had a chance to overlap some with Dr. Shannon and his staff.

Mr. FLOOD. Before he left?

Dr. MARSTON. Actually, we had some discussions in August because it had been decided by then. Both of the deputy directors, Dr. Sherman and Dr. Berliner, participated in the budget preparation from the beginning. So we have had a continuity of effort as we have gone through the various phases.

Mr. FLOOD. Actually it is pretty level, the percentage of increases and decreases for the various institutes.

Dr. MARSTON. Yes. We tried, however, to pick out those areas in which we thought it essential either to maintain important programs or to get new programs started. You will notice, in the research areas, for instance, that the two areas where there are real increases for research grants are the population area, the environmental health science area, to a very limited extent, and for the Eye Institute, which is a new institute. We felt that the population studies and the Eye Institute were essential areas in which it is necessary to get a program started.

Mr. FLOOD. This tells me you are treating the research institutes pretty much as one unit.

Dr. MARSTON. We are reviewing centrally in my office——

Mr. FLOOD. Not as nine units, just one unit.

Dr. MARSTON. Yes; we have reviewed it as one unit in my office and for some broad budget categories the changes are roughly the same for all institutes. But we do take account of the relative size of the backlog of unfunded grants in the institutes and of the specific needs of the so-called targeted programs.

Mr. FLOOD. It was not done just across the board?

Mr. MARSTON. No, sir. We have gone through the budget item by item and detail by detail.

Mr. FLOOD. Why not appropriate for one unit?

Dr. MARSTON. You mean for the NIH as a whole?

Mr. FLOOD. Yes; one single appropriation. You have heard this before.

Dr. MARSTON. I think we have the mechanisms, Mr. Flood, for reviewing the needs for the NIH as a whole. I think this budget reflects the same type of thing that you are talking about.

Mr. FLOOD. What about flexibility? What about overhead costs? It seems to me you would have more flexibility and less overhead.

Dr. MARSTON. These are large and complicated programs and I think one has to have available the best judgment of what is going on in the cancer field and its needs, of what is going on in the heart field, and so forth.

Mr. FLOOD. Would you not like flexibility?

Dr. MARSTON. I think we have the flexibility now to make adjustments in the various appropriations in the budget recommendations we make and this is also true of the review mechanism, including the review by this committee.

COST OF ESTABLISHING NEW INSTITUTES

Mr. FLOOD. People are after us day after day for new institutes. They must have new institutes. Of course they do not know what the additional administrative costs will be. These are nice people, sincere, dedicated people.

How much does it cost to set up a new institute, assuming no expansion of what you are doing.

Dr. MARSTON. It depends upon how you do it, but our estimates have been that it takes about $500,000 in additional overhead costs to establish a new institute.

Mr. SEGGEL. That is strictly for the administrative expenses.

Mr. FLOOD. Is that an annual cost?

Dr. MARSTON. It depends on how big an institute it is going to be, but the minimum is around $500,000 every year in terms of the administrative overhead to maintain it.

PROPOSAL FOR LUNG INSTITUTE

Mr. FLOOD. We have a galaxy of bills for new institutes, as you know. An Institute for the Lung seems to be away out in front. And of course I am from the coal fields and I know about miners' asthma. Not this black lung, which is tragic, but the hard coal anthracosillicosis. I was born and raised among people with anthracosillicosis—a horrible thing, progressively worse, and one cannot cure it. It is a killer.

What about that one, tomorrow? And I am prejudiced.

Dr. MARSTON. We have 10 institutes at present and, as you have indicated, there have been suggestions for perhaps as many as six additional institutes. If we get to the point that we have 15 to 20 institutes, it is very clear they will not be institutes as we now define a national research institute.

I think we should look very carefully at how one gets the job done, not at whether it is an institute or not an institute. We already have four institutes that have a commitment to research on diseases of the lung.

The Cancer Institute is concerned with lung cancer, and I would think anyone would agree that that is the appropriate place to work on the problem of lung cancer, not in a separate institute.

The Heart Institute has major programs involving cardiorespiratory research. Now this is an area that we think does need additional emphasis. I have had discussion with Dr. Cooper about how we can——

Mr. FLOOD. Emphasis on what?

Dr. MARSTON. The relationship between the heart and the lungs.

Mr. FLOOD. What is the funding level on that?

Dr. MARSTON. The funding level in the Heart Institute for lung activities is $9 million.

Then we have the Allergy and Infectious Diseases Institute which is concerned with pneumonias and immunological aspects of asthma.

Finally, the Environmental Health Science Institute is concerned with the impact of the environment on the lungs.

What we have done, Mr. Chairman, is to have a series of meetings between the directors of these four institutes over recent months to see what is needed in the area of lung research and to make recommendations in terms of the types of activities that need greater support.

BLACK LUNG

Mr. FLOOD. Black lung is an old story in the coal fields.

Dr. MARSTON. People are appropriately interested in doing everything that is possible to carry out the necessary research in the field of respiratory illness.

What we do propose to do is to have the Heart Institute take responsibility for coordinating those programs that need to be administratively coordinated more effectively to focus on these very important problems. We think this would be a more effective way to meet the needs than establishing a new institute.

Mr. FLOOD. Why did you wait for a disaster in West Virginia to do something on black lung?

Dr. MARSTON. We have not waited for this, Mr. Flood. NIH has long had an interest in doing more in the lung area.

Mr. FLOOD. Isn't that nice. An interest?

Dr. MARSTON. Yes, sir. There have been a number of problems associated with it. There has been the difficulty of recruiting individuals to head up an intramural program, which is one of the areas in which people think we need more activity. There has been a problem in stimulating among the scientists in the type of activities that are needed to get more information about the problem of the lung.

Mr. FLOOD. I am a coal miner. What have you done lately?

Dr. MARSTON. We have brought together the best of our people to look at what can be done to stimulate increased activity in this area and we have initiated activities to try to strengthen the research activity in the whole respiratory area.

Mr. FLOOD. Doctor, you talk like a bureaucrat.

Dr. MARSTON. I have not been in the Government very long.

UNFUNDED RESEARCH GRANT APPLICATIONS

Mr. FLOOD. In 1967 you were able to fund about 90 percent of the total number of research grant applications that were sent to you and approved by the various advisory councils. The number of approved applications that you cannot fund went up in 1968. I see you expect another increase this year. Under your 1970 budget you estimate it will be well over twice the number for 1967. You do not think that is good, I am sure, but some people say, "You are still funding 80 percent and the other 20 percent are low on the totem pole of your priority list. Maybe we should not fund more than 50 percent."

What is the best answer to that point? How do you assess the program impact of the approved but unfunded applications?

Dr. MARSTON. I think it is important to state first that the grant requests approved by the advisory councils represent only 50 percent of the applications that we receive. So we have a very tight review mechanism that begins by eliminating half of the applications for research grants that we receive.

Mr. FLOOD. Perhaps we should, for the benefit of the record, review the process for approval of applications.

Dr. MARSTON. We have a review mechanism in which the best experts in the field review each application and make the decision whether it is for worthwhile research that should be done or not. In this process half of the applications that come to us are eliminated.

Mr. FLOOD. Before you get them?

Dr. MARSTON. Before the question of whether they can be funded or not comes up.

When you say a certain percentage of approved applications has been funded, you are talking about the stage after the review mechanism has already eliminated 50 percent of the applications that were sent into NIH.

Mr. FLOOD. Do you get a lot, many in numbers?

Dr. MARSTON. Yes, sir; thousands.

I think the important point is that we eliminate poor projects on the basis of an expert analysis of whether the application is worthwhile or not. Half of the applications are disapproved and are not considered from that point on. So one could make the case that every application that is approved should be funded because it has already gone through a very stringent review process. Priority scores are only assigned to applications that have already been approved as worthwhile and meriting support. Priority scores would not be necessary if all approved applications could be funded. As all approved applications cannot be funded, the prority scores are designed to establish the order in which approved grants should be paid. They are based on many factors and are not primarily a measure of scientific merit. We should not confuse urgency with quality—in terms of priority scores there is a tenuous relationship between them but they are not the same thing.

Mr. FLOOD. This is really a thorough process.

Dr. MARSTON. Right. Could I continue for one other point?

Mr. FLOOD. Sure.

Dr. MARSTON. This year there are many high-priority applications, particularly in some areas, such as dental research, of which it has been possible to fund very few despite the fact that there is evidence that research is quite productive in that area. In dental research, for example, here is a high probability that dental caries can be eliminated as a major problem during the next 10 years.

Mr. FLOOD. With regard to your training and your fellowship programs, do you have any data to show the percentage of the students that are assisted who have gone to academic careers and research? A round number. I also wondered about that.

Dr. MARSTON. The percentage is high.

This morning I reviewed a preliminary summary of a report that we will be getting in the near future. This is the most recent and most reliable data. It will be available very soon.

Mr. FLOOD. You picked the right morning.

Dr. MARSTON. Yes, sir.

INCREASE IN COSTS OF RESEARCH

Mr. FLOOD. Your total budget is about level from 1968 to 1969 to 1970. Isn't this really a cut, with your increased costs of doing business? How much of a cut is it?

Mr. SEGGEL. We can assume an increase in costs of about 5 or 6 percent. There is a 2-percent overall increase in our appropriations. Of course, the effect of the cut varies from place to place in the various appropriations.

REDUCTIONS IN MORAL COMMITMENTS

Mr. FLOOD. There has been dissatisfaction, to put it midly, among research grantees who must bear a part of this burden of the cut. What are your current problems with the grantees?

Dr. MARSTON. As you know, we had a somewhat traumatic exercise both for us and for the grantees as a result of the expenditure reduction. We renegotiated on a grant-by-grant basis the so-called moral commitments contained in grants. This varied somewhat, but there was an average reduction of about 10 to 15 percent.

Clearly in this type of exercise, Mr. Flood, there was resistance and there was concern, both about the magnitude of the cut also about the problem of planning ahead. This involves institutions with 10-year plans, 20-year plans. It involves individuals who are making career decisions as to whether they will continue to work in a given direction. And then, of course, people just entering the research field—the academic field—are wondering whether they can do better by choosing another career.

I would say the repercussion throughout the academic commuity is one of some confusion and come concern, as I mentioned in my opening statement, about not being able to feel secure in terms of year-by-year support, as well as about the level of support itself.

COST SHARING REQUIREMENTS

Mr. FLOOD. There is a great deal of complaint about the requirement that there be some matching of Federal funds by the grantee. Suppose we go back to where we were on indirect costs and save a lot of paper work and the time of a lot of people. What about handling this problem with a limitation on the amount that could be included in the grants to cover the overhead costs? We did that for years and years. It would certainly save time and administrative cost, would it not?

Dr. MARSTON. I think the problem one runs into there is that somewhere the real costs have to be paid and if the real cost of doing a research project requires a high commitment of decreasing funds from an institution, then I think one eventually gets to the point that the work is not going to be done, cannot be done.

Mr. FLOOD. Just cannot be done.

Dr. MARSTON. It cannot be done if there are not funds available for it to be carried forward.

DUAL COMPENSATION POLICY

Mr. FLOOD. You remember in last year's report we stated expressly our belief that HEW should liberalize its policies on dual compensation to stop this loss of your high-level people in the NIH. A very important paragraph. What about that?

Dr. MARSTON. We feel just as strongly on that this year as we did last year.

Mr. FLOOD. Dr. Shannon and I discussed that at some length last year.

Dr. MARSTON. Yes, sir.

As you recall, at that time there were more than a hundred commissioned officers eligible for retirement.

Mr. FLOOD. That is right.

Dr. MARSTON. We have presented the reasons for needing this. In a limited number of cases we have been able to utilize this mechanism. I think it has been of crucial importance in the limited number of cases in which we have been able to utilize it to retain people.

PERSONNEL RESTRICTIONS

Mr. FLOOD. What are your problems with regard to the Expenditure Control Act?

Dr. MARSTON. I think there are two problems. The personnel restrictions have meant that we have not been able to implement some programs as we would otherwise have done.

We have not been able to open the units in the Clinical Center for the child health and human development clinical research activity. We have not been able to develop the environmental health science activities as rapidly as we would have liked.

Mr. FLOOD. You have real difficulties, have you?

Dr. MARSTON. Yes, sir. We are having difficulty in establishing the Eye Institute properly and of course, as always happens in a case like this, the backup services are the ones that get hit first. We have increasing complaints about some of the mail service, messenger service, groundkeeping, that have taken some of the brunt of the employment limitation.

Mr. FLOOD. Housekeeping?

Dr. MARSTON. Yes, sir. The Clinical Center, with a rapid turnover of people, has been one of the areas with which we have had particular trouble.

SUPPORT FOR MEDICAL EDUCATION

Mr. FLOOD. Mr. Michel?

Mr. MICHEL. Dr. Marston, I was very pleased to note on page 4 of your testimony where you said, "It is part of the new role of NIH to restore balance by bringing the educational support programs into line with research support."

While I say I am glad to hear you make this kind of a statement, I am not altogether sure I understand it. There is no question that our research grant programs, particularly from NIH, have gone out and supported many of our educational institutions.

Can you develop for me a little more in depth what change of emphasis there will be that would implement what you say here?

Dr. MARSTON. As an example, Mr. Michel, we have been able to bring together all of the construction programs, the five construction programs that NIH has responsibility for, into a single administrative unit which will be under the Bureau of Health Professions Education and Manpower Training. You remember that over the years there has been the complaint that if an institution needs a building it had to go to one place for dollars for research facilities and another place for dollars for educational facilities. We are in process of making a more reasonable administrative arrangement for bringing together these activities which basically are institutional support mechanisms.

We have done the same thing in the area of general research support, basic improvement grants, special improvement grants, of bringing these together in a single administrative unit.

Let me go on from the details, unless you want to consider them at greater length, to say that we feel strongly that there is a great social need now, a great need for additional manpower, as this committee knows very well; that the responsibility for making this manpower available is going to fall to a considerable extent on educational institutions throughout the country; and that these educational institutions at present are supported in part by research funds, and more recently also by educational funds. We need to support the environment in which the manpower training is occurring as well as having specific programs earmarked for scholarships or for loans or for a basic improvement grant.

What I meant, specifically, is that we do need to have more resources going into the educational support mechanisms to parallel the dollars and the human resources that are already going into the research area.

Is this responsive to your question?

Mr. MICHEL. Yes.

EXPENDITURE REDUCTIONS

I gather from a good portion of your testimony that it was well tailored for several members of this subcommittee so far as our own individual views are concerned, and the way they have been expressed in the past several years, and may be reflected in the mark-up of this particular bill and underscoring your own burning interest in research and our moving forward with it with all of the resources we have available.

As I recall, last year when we marked up this bill, it was one of my motions that we have a 5-percent cutback in the request for research grants, not in program level, as one means of living within an overall figure, a goal we had to shoot for. This was the first time in my memory on this subcommittee that the curve has not continued to rise, but topped out.

As I recall, in conference with the Senate, we halved the differences between what we thought your shop should have and the individual institutes requests. Then is it not true, under the Expenditure and Revenue Control proposition, you were cut deeper than you would have been by either the House or Senate appropriation bill?

Mr. SEGGEL. Yes, sir; we had to cut another $20 million out of the grants and $4.8 million out of contracts as a consequence of that act.

Mr. MICHEL. Did it hamper you to any great degree to have to live under that kind of restriction this year?

Dr. MARSTON. Things have not been done that would have been done and the sense of uncertainty in the institutions has increased. Some of the things we will never know. We will never know whether dollars that were not expended would have resulted in a finding that would have been important.

But I hear anecdotal statements that people are concerned about the attractiveness of the field of biomedical research for young people at this time. They wonder if this is going to be an area in which the brightest and best can best use their talents.

Mr. MICHEL. Are we in this situation where local and State governments are being so strapped, who in the main are supporting State institutions and the big universities, that the only place to turn to get the money is here, the Federal level, through NIH research grant programs.

That is the way it appears to me.

Dr. MARSTON. I think this is true in some areas. I think it varies.

As you know, in your State there are ambitious programs to expand the medical schools. I know some State funds have already been allocated, and presumably there is a promise of more.

This has varied around the country. I do think that it is hard to take anything away from some of these institutions, such as medical and dental schools, to take any dollars away in any form without rocking the boat.

Training grants came up a moment ago. Fifty percent of our training grant funds go for the support of the faculty and for things that help keep the institution running. When one takes these dollars away, it does not help the people trying to run the institution to say that we did not mean to hurt their efforts to try to increase manpower because it does withdraw resources from the institution as a whole.

EXPANDING OUTPUT OF PHYSICIANS

Mr. MICHEL. But then following closely on that, why does it take so long before we can see an actual expansion then of end product, additional doctors, additional medical people we say we need?

Where do we get the real results from it?

Dr. MARSTON. There has been a very dramatic change in the willingness and perhaps ability of institutions, if they get additional resources, to markedly increase the size of incoming classes. Of course this is not going to produce anything immediately.

Mr. MICHEL. That brings to mind further in your testimony you mentioned new approaches to medical education are desirable for three reasons, and you say the first is simply in order to accommodate a larger number of students without a proportional enlargement of facilities, faculty, and funds. How do we do this?

Dr. MARSTON. You have to have some additional dollars, but not just taken out of another pocket or just shifted around within the same institution. But I think one can have an increased number of medical students without a proportional increase in the total cost of building facilities and of support funds. One can add on additional numbers without the total cost going up proportionately, but one cannot do it without putting more resources in. But I do not think as much as it has cost previously. You ask why can we do it now when we could not do it 10 years ago. I think the answer has to deal with attitudes, it has to deal with the awareness that this period if almost an emergency situation. In fact, I have heard some of the deans and faculty members talking about this time being almost like the wartime emergency we had during World War II, in which we did things on an emergency basis deferring some of the costs until a later date because the urgency was so great.

It is this sense of urgency that I feel pervades many of the in-

stitutions now as they look to the needs of their own communities for additional people.

Mr. MICHEL. As you know, it is not only in this circle here we have raised these questions about so much going into research rather than into actual training of medical people, but I get it more and more among the lay doctors out in the field that have been graduates, for example, of the University of Illinois Medical School. The president of the Illinois State Medical Society in particular recently made a speech and he really laid it on the line. He as much as told the University of Illinois he did not think things had changed very much down there from the time he graduated 30 to 35 years ago, particularly on the strength of numbers of additional doctors they are putting out into the mainstream.

Of course he then took the occasion, knowing I was a member of this subcommittee to send me a copy making the point that you are expanding entirely too much in the field of research out at NIH instead of spreading it around to get additional doctors. So when you get those comments coming actually from doctors out working every day in their chosen field, I do not think we can turn a deaf ear to it. We have to listen to it.

I notice in your testimony you cite, however, some statistics that would tend to disprove some of the allegations that have made made, and I think that is good for a balanced record.

Dr. MARSTON. I think there are two things on that.

There is always a lag, as you know, in communications. The actual fact is that we have not increased either the number of research grants or the number of training grants since about 1964.

People still tend to talk about the earlier period of very rapid growth in research when, as this committee knows, very well, there was a deliberate attempt to mobilize the research capabilities of this country. Dollars were not as tight as they have been in the last 3 or 4 years.

EXAMPLE OF NIH SUPPORTED RESEARCH PROJECT

Mr. MICHEL. I hate to make a personal reference, but this last year I found out, much by accident, that I was the subject of a research project myself.

There had been a research grant from NIH out to the University of Indiana for a blood study. One of the subjects who was found to have this deficiency in the blood turned out to be a cousin of mine working in a VA office out in Kansas or Oklahoma. In tracing back the lineage they found it was not on the mother's side but on the father's side, which then brought me into the act because it was my uncle who has since died. Then after checking out his children they moved to my father and myself and our boys.

The thing that disturbed me a little bit about it was that all we got was a phone call from a young lady who said she would like to come out and take some blood samples. With my knowledge of this thing I was most interested, but with the first call that went to my folks there was a reluctance to participate. There were no advance letters and no advance warnings.

The young lady was a little nervous in taking the sample from me and she missed the vein twice and it got to the point where I said,

"Maybe you'd better try my other arm." It got to be rather comical and I wonder if this happens with other subjects.

I suspect this is all very important somewhere down the line and I suppose in the name of medical research it may have some very profound effect. At least, this was quite a sizable research grant to the University of Indiana to enable this young lady to pursue this line of inquiry.

Dr. MARSTON. It sounds like you had a type of experience one expects in a doctor's family.

I think this brings up an important point from two standpoints.

In my own family, one of my nieces has just had a child with an inherited disease, and this has raised the question of what they need in terms of genetic counseling and the type of testing that may be needed for the rest of the family. There are practical results that will come out of these tests that will tell them what they can expect from the child, whether they should have additional children, how they should plan to channel their own lives. They can be helped because sometime ago there was a study of the type you describe that gave information that now becomes the most important thing to this young couple in how they should plan to live over the next few years. If we did not have that background information, we would have no idea what to tell them.

The second example of great importance is in terms of predicting the chance of having a heart attack. Recently the Heart Institute had studies that classify individuals according to the types of blood they have and this has real implications for advising people that have certain patterns. This is something that Dr. Cooper may talk about later

There is always an early stage before you know enough to be able to say you should change your diet or you should take these drugs or should not have additional children. There is always a stage at which you cannot give a very good explanation or advice of real significance because nobody knows at that stage. And yet 2 or 3 years later, such studies as you describe may make all of the difference in the world in the way somebody lives.

Mrs. REID. Will the gentlman yield?

Mr. MICHEL. Yes.

Mr. REID. I should think the important thing though in a case such as Mr. Michel described would be a little different approach, because I think if someone had approached a person in this way who was not aware of this situation he probably would not have much cooperation.

Dr. MARSTON. I would agree with that.

Mr. MICHEL. I got to inquiring of the young lady if she knew of any broad general guidelines that were laid down from your shop before the grant was even given.

She did say she thought they had attempted previously to write letters to people, but that that proved to be very unsuccessful because people never answered the letters so they received no participation. Probably going out personally and seeing them is better.

I still think the approach could have been better, but that would vary certainly on the person making the inquiry.

Dr. MARSTON. We have spent a lot of time on the development of a policy for clinical investigation and we require a careful review by

our experts, but beyond that we decentralized the responsibility. We require that every institution that is doing any clinical research have a local committee that is broadly representative—and particularly not of the people who are doing the research—and that that committee must review the research protocol in depth, including the possible impact on the family.

Mr. MICHEL. In this case, the University of Indiana Medical School would draw the guidelines under which these investigators would work?

Dr. MARSTON. That is right. They would have had a committee that would have sat down and looked at each part of this project, including the part you are talking about. I think there was a slippage of some type.

NUMBER OF MEDICAL SCHOOLS

Mr. MICHEL. Before we leave that item, what do you mean here by saying "As someone has said, it would be kind of wonderful if we could double the number of schools in the top 25"?

Dr. MARSTON. The problem now is that, in considering various places at which new medical schools, might be started, we want to be very sure that they are going to be absolutely first-rate institutions. We are aiming to get the best institutions in terms of increasing the output, and not to promote institutions that are going to be in trouble, unable to recruit faculty, and have serious financial difficulties. The aim is not just to add a diploma mill of some type, but to add an institution that can meet the needs. The 25 has only to do with being in the upper third.

Mr. MICHEL. How many medical schools do we have in the country?

Dr. MARSTON. It is shifting. We have 101 at present.

Mr. MICHEL. I will not ask you to list those top 25.

Dr. MARSTON. No, sir; I would not know how to do it.

I would have to ask you what you meant by the top 25.

GEOGRAPHICAL MOVEMENT OF MEDICAL SCHOOL GRADUATES

Mr. MICHEL. On this point you made with respect to the AMA study showing 57 percent of the graduates of medical schools practice in a State other than the one in which they were educated, I know we have had a real problem out in the Midwest. As I recall, with regard to the Big Ten schools particularly, many with doctorates have gone to either the west or east coast in the scientific area where the action is, supposedly.

How do you account for this in the medical area? Where are these movements, from where to where?

Incidentally, do each of the land grant universities in the States have a medical school?

Dr. MARSTON. No; I think several answers can be made to this. You have particularly been drained in the Midwest—if that is the right word—by the population shift to the west coast—and particularly to California—which has increased the opportunities for physicians to go into practice there. The movement of physicians is thus a part of the population shift in this country. On the other hand, in the medical field there is another reason. Physicians—I will limit it to that for the moment—are in short supply. This means that there are more

opportunities than there are individuals and, therefore, a physician has almost unlimited opportunity to decide where he might want to practice.

This also means that the competition for services is very keen and people are always trying to recruit physicians and other health workers to come in. It is a very mobile group, as this figure shows. What determines where a physician will practice is not entirely clear. Where he takes his residency and internship tends to relate more closely to his eventual practice place than where he goes to school.

This is complicated because he may have taken his internship and residency in a given area because he planned to practice there.

RESEARCH GRANT "MORAL COMMITMENTS"

Mr. MICHEL. Dr. Marston, develop a little bit more for me this moral commitment policy that you mentioned on page 12 of your testimony relative to the grant awards in light of the reduction in 1969 expenditures. You suggest that some of the grant awards have had to be renegotiated?

Dr. MARSTON. Yes, sir; most research projects take more than a year's time, so what we have done is to require, at the time the application is submitted, an estimate of the cost not only for the first year but for the second year and for the third year. The review system has looked not only at the dollar requests for the first year but the dollar requests for the second year and for the third year.

If we decide that it is worth supporting the project at all, it is also worth being sure it can be completed next year or the year after. Therefore, we remove the funds for the second year and third year from the sort of open competition for new grants and new awards and show them in the budget estimates under the noncompeting category. This does not mean that the investigator automatically gets those dollars when he comes in in the second year. He must need them and justify them in detail on the basis of information that has been developed during the previous year. He does, however, have the assurance that if all is going well and his work is progressing well, and if his dollar estimates are still accurate, then he can recruit individuals and buy equipment and plan to carry on his work over whatever the period of time that the committee said is necessary to carry out that job.

Mr. MICHEL. Who does this reviewing?

Dr. MARSTON. This is done at the staff level in NIH.

Mr. MICHEL. Is it a requirement, when an investigator comes in with an application for a 3-year proposition and is awarded one, that at the beginning of the second and third years he gives you an up-to-date accounting and report of what he has done?

Dr. MARSTON. Yes, sir. We make an actual award each year because we do not have the funds for following through without that. We have always made adjustments on the basis of the need of the project rather than on the basis of lack of funds. We protected, if you will, the funds to be sure there are enough.

Mr. MICHEL. In effect, you are kind of at our mercy from the standpoint of entering into any contract that runs over a year's time?

Dr. MARSTON. Yes, sir. These are not firm commitments. It has been understood that these were "moral commitments." On the other hand,

they are essential to keep from wasting large amounts of dollars. Last year we went back to the investigator not on the basis of whether the dollars were justified or not, but on the basis that we didn't have enough dollars and we would have to renegotiate them down. The alternative was to stop making any new grants.

If we couldn't free up some dollars for that process, we would not be able to maintain the new grant programs, particularly for the younger people coming into the field. Too high a proportion of the dollars would have been tied up in these continuations grants.

Mr. MICHEL. Those contracts are so written that you do have an escape clause?

Dr. MARSTON. We must.

Mr. MICHEL. They are all given to understand that we hope we can do this but we cannot altogether be sure?

Dr. MARSTON. That is right.

Dr. SHERMAN. I think it becomes important, too, to look at the difference in the use of the terms for a good understanding of this situation. You have used the word "contract." In effect, a grant is, in one sense, a contract in that it has a series of terms and conditions recognized by both sides which allow certain options. It is on this basis, as you and Dr. Marston have observed, that this constitutes only a moral commitment, that we could back out of it quickly.

On the other hand, we feel that the moral consideration is probably greater in a grant than it is in the typical contract. Both parties to a contractual arrangement recognize that the circumstances may change drastically—that is part of the game. On the other hand, in the research grants area, the sense of moral commitment is much stronger and therefore much more seriously affected.

Mr. SEGGEL. One reason we had to cut into the moral commitment was that we had to get a maximum effect in the reduction of expenditures. In other words, reducing new awards results in much less of a reduction in expenditures in the current year. Therefore, we had to look at our ongoing operations in order to get the reduction in expenditures that was required under the act.

Dr. MARSTON. Let me say that we received unusual cooperation from the investigators and from the institutions in our primary goal of meeting the requirements. We inconvenienced people but had as little disruption of programs as possible. I don't know whether we could do this again or not. We used up years of good will between the NIH and the academic institutions. I can see a point at which it will be more difficult to do this in the future. These were dollars that the individuals and the institutions, on the basis of all past perfomance, felt they could count on.

Mr. MICHEL. As long as I have been on this committee the curve in this area has constantly been on the rise and this past vear was the first where the curve began to top out so to speak. In this time of budget restraint we may have all we can do to hold our own at this level. I realize that we have to continue to do so many, many things in the area of basic research particularly when, as you say, there are so many things that go awry and end up being dead ends. Hopefully we can get our financial house in order to again accelerate our work in this vital research area.

Dr. MARSTON. This is very reassuring.

FAMILY PLANNING RESEARCH

Mr. MICHEL. One final comment on your testimony, Doctor, on this item of $6.3 million over the amount available for 1969, mainly, you say, for the new eye institute and for family planning research. You touched on it a little bit here in the colloquy we had with respect to that guinea pig operation which I was involved in. What are we talking about in family planning research? What else do we have to know about that?

Dr. MARSTON. Let me speak first to the dollar utilization. There is $3.25 million for research in the area of family planning and human reproduction. This has one major area, the need for more effective contraceptive devices. We have a number that are effective but we don't have any that are ideal. I say ideal both from the standpoint of the family that wants to limit the number of children, but also from the standpoint of the family that may have problems on the other side, lack of fertility. We do need much better knowledge of human reproductive processes and how one can utilize this knowledge both to make it possible to have children, when one wants to have children, and to make it possible to contain the family size. That is what we are talking about here.

Mr. MICHEL. May I ask at that point, I think we have had developed in prior hearings the so-called pills and varieties of them, has there been a long enough experience to determine what the long-range effects of the pill itself are on the woman? Are we at this point far enough along so that we could say that the loop, so-called, is more acceptable?

Dr. MARSTON. No, sir.

Mr. MICHEL. Is it more effective than the pill, for example?

Dr. MARSTON. I think there are two problems with the use of the loop. One, in a number of cases there are side effects enough to cause a discontinuance of its use. Then there is also a significant portion in which the loop just does not stay in. Therefore, it is not effective.

The population problem is, as we all know, one of the major problems that this country, and the world, faces at present. We do not, at this time, have adequate contraceptive control devices to meet the needs though we do have effective advances through the pill and through the loop and through other methods.

Mr. MICHEL. How were the Japanese so effective in meeting their goal of population control?

Dr. MARSTON. I think the main thing was a national determination to meet that goal and then they used all the mechanisms available, including a heavy emphasis on legalized abortion. This still is probably, in terms of overall effect, the single most widely used control mechanism.

RECRUITMENT OF OUTSIDE WITNESSES FOR APPROPRIATION HEARINGS

Mr. MICHEL. One thing I wanted to bring to your attention particularly Dr. Marston. This would not hold only for your shop but there would be others involved, too.

I asked Secretary Finch when he appeared before our committee whether or not he was aware that there were people in his shop who over a period of years have had their own ideas about certain things and might at some future time be at odds with his declared position

and he should at least recognize the possibility of a little covert lobbying for more money than the budget calls for. It has happened in the past.

An example of what happens is this: We hear the Government witnesses, and when we are all through with them we are going to have outside witnesses come in. Generally we tend to think that they present a little different view and a fresh new approach, because they are not in Government and don't have to justify the budget. However, we get some indications that people who have been testifying in behalf of the Government also go out and make an attempt to mold the kind of testimony we get from the outside witnesses.

I am reminded of one letter in particular. I won't quote any names from it but it is dated April 1968. It was from an official in the Department of Health, Education, and Welfare, Public Health Service.

Dr. So-and-so, This is to confirm that the Labor and Health, Education, and Welfare Subcommittee of the House Appropriations Committee would like you to testify as a public witness on April so-and-so, at 10:45 a.m. Dr. So-and-so, and I can meet with you for breakfast at the Marriott Motel, Twin Bridges, U.S. 1, Virginia, at 9:30, such-and-such a room. We look forward to seeing you there.

Sincerely yours.

This committee had not been asked if it would like to hear this witness and certainly had not invited him.

This gives me the distinct impression that there are people, after having testified here and giving us one story, also try to influence the outside witnesses to support their personal position.

What would you do to discourage this kind of activity in your own shop?

Dr. MARSTON. I think the first thing we have to do is to be responsive to the people who want opinions in the substantive area. If somebody calls from the University of Illinois and wants to know what I think about family planning, I think I would have to be as candid in talking to them, not about the details——

Mr. MICHEL. I have no quarrel with that.

Dr. MARSTON. But where we plan to go. I think it is very important that we maintain this type of interchange. That, however, sometimes leads to the reaction: "Gee, I am concerned about this and I want to go down and talk to my Congressman about it." What happens from that point on often becomes very jumbled because he can well say that he talked to me when he talks to you, and that these were my ideas. I know that the Institute Directors have the same problems.

But I hear your message in terms of the other extreme: the attempt to give testimony here and when to organize and design and set up a second set of hearings which really are repetitious.

Mr. MICHEL. I was speaking of an outright recruitment by some of your people to get additional witnesses from the outside to come testify. I realize sometimes there is a pretty fine line of distinction you have to draw here. As a matter of fact, recently on the subject of hospital construction, I made the point that since we put money into gathering this information I hoped it was going to be made available to those out in the hustings or, as the chairman likes to refer to it so many times, out in the provinces where it can really be put to work.

I do not like to see people specially recruiting outside witnesses

because we like to feel that we were getting an objective, independent view from the outside to help us come up with the balanced, best possible decision after getting all the facts.

Dr. MARSTON. You do not want to hear the same opening statement twice.

Mr. MICHEL. It isn't repetition I object to. These employees aren't recruiting public witnesses to come in and support the budget. They are getting them to support the employee's personal views.

Thank you, Doctor.

Dr. MARSTON. Thank you, Mr. Michel.

Mr. FLOOD. Mr. Natcher.

Mr. NATCHER. Mr. Chairman, thank you.

Mr. MICHEL. If you will yield, I am reminded by our good friend, Mr. Moyer here, of an incident about 3 years ago when an outside witness came before this subcommittee and he was not quite ready to testify and had to wait until the NIH messenger brought his testimony to present before the subcommittee.

Enough said.

Mr. FLOOD. He didn't read it very well.

Mr. NATCHER. Couldn't pronounce the words.

PROPORTION OF BUDGET FOR GRANTS

Dr. Marston, in your statement to the committee you have stated that the total amount for NIH is $1,484,127,000 for the fiscal year 1970. Last year the Secretary informed the committee that approximately 94 percent of all of the money appropriated for the Department of Health, Education, and Welfare is for grants.

Can you give the committee some idea of the approximate percentage of your total amount which is for grants? Just approximate.

Dr. MARSTON. It is somewhat different for the three components of NIH.

One has to break out health professions education and manpower training and the Library of Medicine. Almost all of the dollars for health professions education and manpower training are for grants plus just the administrative costs. In the Library of Medicine, on the other hand, only a small proportion is for grants. In fact out of the $22 million for the Library, about $7.5 million is for grants. That is a small part of that program.

The grants portion of the funds for the Institutes and research divisions—I am talking about the research component—is very large. The total figure is $1,107,639,000. Of that, $832 million is for grants. Just about 83 percent for grants.

One has to add to that the dollars that we carry under the so-called intramural programs as "collaborative research." Thus $127 million, in addition to the $832 million, is for work done outside of the NIH by contract. I suspect that when you add these up it would not be too far away from the Secretary's figure of over 90 percent of the dollars going either for grants or for contracts.

Does this answer your question?

Mr. NATCHER. Yes.

Dr. Marston, you state that the amount requested for the new fiscal year is an increase of $90.1 million over comparable appropriations

for fiscal year 1969. Do you take into consideration there the reduction of $6 billion required by the Revenue and Expenditure Control Act?

Mr. SEGGEL. Yes, sir. That does take into account the amount available to us in 1969 which is less the reserves that were taken out as a consequence of that act. This is in terms of new appropriation authority that we are requesting in 1970 over the 1969 base. It is actual.

Mr. NATCHER. Dr. Marston, I certainly want to join with my chairman and other members of the committee in wishing you the best of everything in your new assignment and to say to you quite frankly that you have a lot of outstanding people all around you.

Mr. Chairman thank you.

FUTURE SUPPORT OF MEDICAL SCHOOLS

Mr. FLOOD. Mr. Shriver?

Mr. SHRIVER. Thank you, Mr. Chairman.

Dr. Marston, on pages 12 and 13 of your statement you expressed the desire for a more predictable and stable form of Federal assistance to schools, medical and dental, and other professional schools. It is more important in your judgment than the funding level.

I wondered what you have in mind as to the future programs in connection with the statement.

Dr. MARSTON. Let me say that I could not be more serious about this problem when one is trying to support activities that may take, in some instances, 12 years in the educational areas or as much as a decade in a research area.

I do not think I can give you the answers but I think that I can discuss some of the problems and some of the dilemmas very briefly.

The research activities in this Nation require that one have a mechanism of getting the very best that is available with the best talent.

The project grants mechanism in which a man comes up periodically and says, "This is what I want to do" and you look a year later—and 2 years later and 3 years later—to see what he has accomplished and whether you want to support him further, is one thing. But research has become so complicated now that this is not a mechanism that takes care of all of the research needs. Teams need to be brought together to work on some of the problems today that cannot be resolved by one individual. This requires broad support—support of the environment in which the work must be done.

When one gets to educational support, one is very seldom talking about supporting a given teacher. One is supporting an institution or a department. This can be done through formula support which does not allow for the kind of national review that is very important for maintaining quality but is probably one of the better mechanisms for giving continuity of support.

We have gone that way to a certain extent with the general-purpose research supporting grants and with the basic improvement grants and the special improvement grants under the manpower legislation. I think what we need to do is to give very serious consideration to those activities that require continuing support. This is the place that needs funds this year.

Research institutions must have flexibility. You don't focus on contraceptive devices indefinitely. Maybe this won't be the biggest

problem 5 years from now. Maybe something else in the population problem will be. Making suitable provision for institutional flexibility and institutional stability is this committee's problem as well as our problem. We will be working very hard to try to see how best to achieve these goals. We hope that you will be thinking about it, too.

One more thing. There is much discussion now about the support of education at large and the support for graduate education. This is also going to raise questions that all of us need to be thinking about. How can NIH best achieve its mission—which is to improve the health of the people—in the context of other support mechanisms for general support of science, for general support of health, for general support of education.

That may have been more than you asked for.

Mr. SHRIVER. No, that is exactly what I had in mind.

With the increased expense involved in medical education of all kinds we need to be thinking down the road as to how it can be met. States apparently are not going to be able to do much more than they are doing right now from a financial standpoint.

The answer was very good. There is the possibility of discriminating if it is all done the way it has been done in the past?

Dr. MARSTON. Yes, sir.

Mr. SHRIVER. Against some state or some institution. Maybe a mix of the two.

INCREASES FOR REVIEW AND APPROVAL ACTIVITIES

I notice that each year in the last three in the estimates and actual, there has been about $1 million increase in the cost of review and approval of grants. For instance, in 1968 it was $17,629,000. The 1969 estimate, $18,904,000. The 1970 estimate is $19,914,000. It is about $1 million increase each of those years. Why would that be?

Dr. MARSTON. There are very few things that have not cost more money this year——

Mr. SHRIVER. The amount of grant money that you are spending is about the same.

Mr. SEGGEL. Mr. Shriver, even though the amount of money we are spending is the same, the application load has been rising steadily from year to year. That is one problem. Another problem——

Mr. FLOOD. Your pay costs, too?

Mr. SEGGEL. We have pay costs in here. In addition to that, we have been moving more and more into large types of grants involving more staff work and negotiation, rather than just the small project grants which are usually reviewed strictly through the review process. It requires more staff and more managerial capability to handle the larger types of grants we are getting these days. More complex and larger.

USE OF AUXILIARY PERSONNEL

Mr. SHRIVER. What has been the attitudes of the schools and medical profession generally toward your suggestion to make greater use of auxiliary personnel for some of the activities now performed by more skilled practitioners?

Dr. MARSTON. I think it runs the range from a great deal of enthusiasm—and, indeed, activity, in some areas—to concern about

just how one can do this within the educational setting alone because this is not something that a school decides. It involves licensing boards of States. It involves acceptability in terms of practicing professions. It involves, perhaps, most important of all, acceptability to patients. Experience has been growing in this area and a great deal of discussion has been going on for the last 5 years—papers at major meetings, experimental programs in some institutions, and so forth. The general assumption is that we have to have more manpower but more manpower by itself is not going to do the job. One has to find better utilization and better matching between training and the job to be done.

Mr. SHRIVER. Thank you.

USE OF NEW COMMUNICATIONS TECHNOLOGY

Mr. FLOOD. Mr. Smith?

Mr. SMITH. I assume that you know what that [indicating] is, approximately? The entire Holy Bible is on this slide.

Mr. FLOOD. Suppose you describe it.

Mr. SMITH. It is a little plastic plate about 2½ by 2½ inches. Each dot is a page of the Bible. What happened to all of the enthusiasm that we had 2 or 3 years ago for the possibility that medical research books, and all that, could be put on these little plates and be available to perhaps, if not less skilled doctors, nonspecialists in rural areas; what happened to that idea?

Dr. MARSTON. There is enthusiasm for it. Dr. Cummings, of the Library of Medicine, will tell you that his No. 1 priority is to find ways of using all of the technology that exists now and may be developed over the next few years to help make information available where it is needed. He has had, particularly over the last few months, very serious discussions with the people who will have the responsibility for moving this field forward both in terms of what is available in the technology and what can be developed in the technology.

I think there is a high degree of enthusiasm.

One of the problems, of course, is to decide just what is it that you want; what kind of information is needed and who needs it.

Mr. SMITH. With the electronic devices that are available so that this can be flashed 50 miles to someone's desk on a little screen, why isn't it possible to graduate some doctors with less than 9 or 10 years of education and with the help of a specialist somewhere to be able to deliver some health services not available even by third-rate doctors at the present time in some of these communities?

Dr. MARSTON. My personal response is that it is possible.

Mr. SMITH. I interpreted your comments earlier to indicate that we do not want to move toward any increase in medical personnel that reduces quality of any of them in any way.

Dr. MARSTON. I do not think we want to move in the direction of reducing quality that is delivered to the patient. That would be my concern. I think that——

Mr. SMITH. You didn't necessarily mean that there would not be an inbetween category of doctor?

Dr. MARSTON. No; not in any way.

Mr. SMITH. In other words, you could still get good quality with this kind of a setup even though the personnel that were available in these

communities might not be as skilled or as highly skilled as those in the central office and might even be limited in his practice.

Dr. MARSTON. Yes, sir.

SHORTAGE OF PHYSICIANS

Mr. SMITH. What possibility is there, if the financial support is available, that by 1975 there will be as many doctors per 10,000 per population as we have today?

Dr. MARSTON. I think that it is not probable that we will have all of the doctors available that we would like to have by 1975. I think we will fall short.

Mr. FLOOD. By what?

Dr. MARSTON. I think we will fall short of the goal of having as many doctors as we would like to have for many reasons. For one thing, there is a competition for personnel across the board. That leads me to believe, as I said a moment ago, that we have to make serious and urgent efforts to increase the number of doctors to the extent that we can, but at the same time try to find better ways to utilize their talents.

Mr. SMITH. Per capita will we make any gain?

Dr. FENNINGER. The prediction is that by 1976 the actual shortage will be somewhat reduced so that the number of doctors per 100,000 will be a little greater than it is today.

This is assuming present levels of authorization and increasing capacities of the schools. The number of physicians being graduated by 1976 will reduce slightly the discrepancy between projected needs and actual numbers of physicians.

Mr. SMITH. It is a pretty bleak outlook?

Dr. FENNINGER. We will do slightly better than holding our own in terms of ratio of physicians to population. As Dr. Marston has already pointed out, the problems are much beyond just the question of this ratio. They have to do as you stated, Mr. Smith, with the availability of information to physicians and other kinds of people who are taking care of people in neighborhoods. The pure ratio simply does not answer the question.

Dr. MARSTON. The output will be higher by then so we will more than hold our own on a ratio basis. I think that you are touching on a very important topic. All the estimates that I get from economists and others is that more dollars are going into the health fields between now and the midseventies. A lot more dollars. I am not just talking about Government dollars. The question that concerns all of us is to be sure that in the process of deploying more dollars and more people in the health field we also do a better job. We do not have the assurance right now that that will necessarily occur.

Mr. SMITH. You know this so-called taxpayers' revolt we hear about includes a growing number of people who say, "Why spend all that money for research? I cannot get medical health services."

Dr. MARSTON. National expenditure on health service is $53 billion now and some think it is going toward $100 billion. If you took the $832 million for research grants and put it all in major cities in this country for health services, I don't think you would be able to notice the difference. But you would assure that 5 years and 10 years from now you would not have anything to put into that health service system

such as better ways of treating people. Health services and research are different orders of magnitude in terms of dollars needed.

Mr. SMITH. The really basic problem with these people is that when they get sick they want somebody to give them a pill that will help them. If there is no doctor available without taking a day off from work that they cannot afford to do, to sit in an office for a whole day to wait for the doctor—as far as they are concerned, the health services are not available to them.

Dr. MARSTON. Right.

EXPANSION OF MEDICAL SCHOOLS

Mr. SMITH. I think it is a very serious problem. Maybe you could enlarge on this. You said for qu'te understandable and legitimate institutional reasons the schools have refused to expand in the past. What are these understandable and ligitimate reasons?

Dr. MARSTON. The biggest one is a lack of resources, a lack of dollars in the past. The schools, particularly private institutions, were in a financial bind. There was a dropoff in dollars available from foundations. The only source of dollars from the Federal Government was for research—I am talking about prior to the passage of the health manpower legislation. The question was: How can we expand if we do not have the resources w'th which to expand?

Mr. SMITH. I think that you are right from my conversations with people. There has been a change of attitude only in the last year or two.

Dr. MARSTON. Right.

Mr. SMITH. My experience and interest in this has indicated to me that when you give them more dollars (at least up until the last year) they didn't spend them to increase the number of personnel anyway. Many took any amount of money to increase the quality of personnel being turned out. They were not as interested in quantity.

Do you think if we gave more money that they will have a sustained interest in quantity as well as quality?

Dr. MARSTON. I think, Mr. Smith, this is something that one can say is a condition of the mind.

Mr. SMITH. It has just about got to be that way.

Dr. MARSTON. We have done it in terms of research grants and other grants.

Let me turn it the other way around. The increase in this budget of $11 million for institutional support has as a high priority preventing schools from going under. As a secondary priority, the expansion of numbers.

If one comes back 2 years from now and finds that out of that $11 million there was not a marked increase in numbers, one has to go back and read what the conditions of making the dollars available were. If there was a high emphasis, it was a high emphasis on schools in great trouble.

EFFECT OF REVENUE AND EXPENDITURE CONTROL ACT

Mr. SMITH. What effect did the Revenue Expenditure and Control Act have on your program of project grants?

Dr. MARSTON. It is about the same. It is about the same as regular grants in terms of renegotiations. Specific figures are——

Mr. SMITH. Did it reduce the number of grants or the amount to each grantee?

Mr. SEGGEL. We did both, Mr. Smith.

Mr. SMITH. Please summarize what happened in terms of numbers?

Mr. SEGGEL. We had to reduce our total grants by $20 million as a consequence of the act. Part of this was done by renegotiating existing grants and trying to reduce the costs. These were so-called noncompeting grants with moral commitments. Some of this took effect by virtue of the fact we were not able to pay as many new grants as we would otherwise have paid.

Mr. SMITH. With regard to those you renegotiated, did it reduce the amount of research they were doing or can they absorb it some other way?

Dr. SHERMAN. Mr. Smith, we took a calculated risk in our strategy for this. Indeed, it was a strategy, because it represented a change in the way we have been doing business for about 20 years. That risk was to assume that both in the interests of our program and in the maintenance of the institutions carrying out the program, we would probably be better off to keep the highest possible number of grants active and cut back on the dollar value even though we recognized that this well could, and apparently in many instances did, either reduce the amount of research productivity or stretch it out for a much longer period of time than had been planned.

Mr. SMITH. Did you say 20 fewer grants?

Mr. SEGGEL. $20 million was the reduction we made in 1969 under the act.

Mr. SMITH. What was the number of grants that you did not fund?

Mr. SEGGEL. I do not know that.

Dr. LAMONT-HAVER. We have 800 less grants this year than last. That is less than we had last year.

Mr. MICHEL. Would you yield?

How many new ones would you have in 1968? How many new ones did you enter into in 1968 as against 1969, and then what is that total number of continuing ones in both those years? That will give us a little basis of comparison.

Dr. LAMONT-HAVER. In 1968 we had a total of about 11,000 grants altogether.

Mr. MICHEL. Put the precise figures in the record.

Dr. LAMONT-HAVER. Yes, sir.

(The information follows:)

A total of 11,099 regular research program grants of all types were awarded by the NIH during fiscal year 1968.

Dr. LAMONT-HAVER. This year we will be down closer to about 10,000 grants altogether.

As far as the new grants are concerned, each year we fund approximately 3,000. That is competing grants, new and competing continuations.

I would have to check that.

Mr. MICHEL. Would you give us an estimate of the new competing ones in 1968 and 1969?

Dr. LAMONT-HAVER. Yes, sir.

(The information follows:)

REVIEW AND AWARD ACTIONS ON NIH COMPETING RESEARCH GRANTS BY PROGRAM,[1] FISCAL YEARS 1967-69

Program and actions	Number			Dollars in thousands		
	Fiscal year			Fiscal year		
	1967	1968	1969	1967	1968	1969
Research project grants:[2]						
Reviewed	8,517	8,465	7,740	$272,942	$297,552	$288,218
Approved	5,398	5,261	5,023	146,657	151,835	160,420
Awarded (dollars, direct costs)	4,591	3,326	[3] 3,170	129,220	98,703	[3] 93,400
Awarded (dollars, total costs)				152,691	121,303	[3] 116,500
Program projects and categorical clinical research centers:						
Reviewed	307	317	294	79,295	88,868	68,998
Approved	230	234	225	43,104	45,793	38,722
Awarded (dollars, direct costs)	197	166	[3] 160	37,362	30,718	[3] 26,500
Awarded (dollars, total costs)				44,015	37,330	[3] 32,000
All other programs (general clinical research centers):						
Reviewed	41	31	30	18,066	15,745	14,999
Approved	36	31	28	12,691	12,624	11,941
Awarded (dollars, direct costs)	11	17	[4] 19	2,938	8,077	[4] 7,839
Awarded (dollars, total costs)				3,053	8,501	[4] 8,207

[1] Dollars shown for reviewed and approved applications reflect direct costs only. Term "competing" includes "new" and "competing renewal" grant actions.
[2] Includes 5 "SO2" applications reviewed and 30 awarded in 1967, and 2 reviewed and not awarded in 1968.
[3] Estimate.
[4] Awards as of Apr. 1, 1969.

Note: "Reviewed" and "approved" refer to corresponding June, November, and March cycles.

Mr. MICHEL. Give us up-to-date information on that.

Dr. MARSTON. We can give you the dollar change. The new competing ones had $145,800,000 in 1968 and this went down to $126 million in 1969. There was a drop there.

Mr. SMITH. That is all.

Mr. FLOOD. Mrs. Reid?

EMERGING AREAS OF RESEARCH

Mrs. REID. Thank you, Mr. Chairman.

Dr. Marston, in your excellent statement you referred to the long-term policies of our Government in support of biomedical research and education. Although I was not a member of this subcommittee last year, Dr. Shannon discussed with the subcommittee a number of areas where more rapid development was desirable in science operations. Do you have definite conditions or changes which you are contemplating or making?

Dr. MARSTON. I think we have got—and I have perhaps talked about it enough—a very real need to keep pressing for a much better understanding of many, many medical problems. We have got much further to go in biology, in 1969, and than we had in physics, say 50 years ago, in terms of having any type of generalized idea of how living organisms functions. As I have said, biology and medicine are still rather primitive sciences.

Then we have got the very real responsibility in NIH of choosing when a field is ripe to have an effect on people—when it is ready for a so-called developmental phase. This tends to be a high-cost and a high-risk phase. This is part of what Dr. Shannon was talking about last year, how do you know when you have got to the point that it is worth a sizable investment to try to produce a vaccine or to try to develop an artificial heart, that type of thing.

We have done two things: Last September I and my top staff visited every Institute, and talked, not about budget, but about programs and what they saw over the next year and over the next 2 or 3 or 4 years in terms of activities in their general areas of responsibility. We followed this up with more recent meetings partly to do just the type of thing you are talking about: to be sure, regardless of how tight the dollars may be, that we are not missing investments in some very important areas. I could pick some of these out. I think the Environmental Health Science Institute, which is just getting started, is going to be very important. Population research and the problems of childhood have emerged as important national concerns. A subject that this committee has heard about now for a number of years, the relationship of viruses to cancer, is one that I think deserves very serious support.

For many years the neurological diseases did not show much movement. Mostly it was a matter of training people to recognize symptoms. Right now, the delayed effect of the so-called slow viruses is giving us a new view of what may be causing damage in the brain. This has a high priority.

The answer to your question is that, "Yes, we have been giving serious thought to special areas that need special support, whether it be in further basic research or in terms of application."

Does that answer your question?

Mrs. REID. Yes; thank you.

Dr. MARSTON. I must say, one of the most exciting things that I have ever done is to go around and talk to each of the institutes along these lines. There was not one that didn't come up with some lines of research that had a real potential for changing the way we live in the future.

RATIO OF PHYSICIANS TO POPULATION IN FOREIGN COUNTRIES

Mrs. REID. You discussed at some length today the dearth of physicians and doctors, and the fact that Russia has more doctors graduated than we do here. How does the number of physicians we have compare in proportion to the population with that of other nations of the world?

Dr. MARSTON. Let me comment first on Russia. This was set as a high national priority. In addition, the decision was made, following the war and the resulting shortage of males, that ladies would be included, as a national policy, in the health field and trained as physicians. I do not know what the figures are for comparisons. I could find this for you.

Mrs. REID. If you have some of them, I would like a few of the countries listed. It would be interesting to compare those.

Dr. MARSTON. Yes, ma'am.

(The information follows:)

THE FOLLOWING TABLE IS BASED ON DATA GATHERED BY THE STATISTICAL OFFICE OF THE UNITED NATIONS

Country	Year	Population (in thousands)	Number of physicians	Physicians per 100,000 population
Israel	1965	2,563	6,720	262.2
U.S.S.R.	1965	230,600	485,000	210.3
Czechoslovakia	1965	14,159	26,252	185.4
Austria	1966	7,290	13,108	179.8
Italy	1967	51,962	91,519	176.1
Bulgaria	1965	8,200	13,593	165.8
Hungary	1965	10,148	16,162	159.3
New Zealand	1964	2,594	[1] 3,873	149.3
Argentina	1962	21,399	[1] 31,831	148.7
United States	1965	194,572	288,671	148.4
Germany (West)	1965	59,041	87,310	147.9
Greece	1965	8,551	12,573	147.0
Belgium	1965	9,464	13,793	145.7
Australia	1965	11,360	15,739	138.5
Denmark	1964	4,720	6,335	134.2
Switzerland	1965	5,945	7,778	130.8
Poland	1965	31,496	[1] 39,613	125.8
Spain	1965	31,604	[1] 39,709	125.6
Germany (East)	1966	17,067	21,365	125.2
Norway	1964	3,694	4,556	123.3
Canada	1966	20,050	23,990	119.7
Netherlands	1965	12,292	14,362	116.8
Japan	1965	97,960	[1] 109,000	111.3
France	1965	48,922	54,181	110.7
Sweden	1965	7,734	8,520	110.2

[1] Registered personnel.

ADMINISTRATION OF GRANT PROGRAMS

Mrs. REID. We have also discussed at some length today the administration of grants. Of course, I know that you are aware there has been criticism of NIH administration of grants. In reviewing last year's hearings, there was considerable discussion about this matter. Steps were outlined to tighten up this situation. Do you feel that this has been done?

Dr. MARSTON. Yes. A number of things have occurred and are occurring on a continuing basis as far as tightening up the administration of grant programs. The overall departmental team, that was mentioned, to look at the grant policies across the Department is meeting very activley and has been a focal point for improving management of the whole review and approval process. Dr. Sherman was at a meeting of this committee 2 weeks ago and perhaps he would like to comment on the progress that is being made there.

Dr. SHERMAN. I think, Mrs. Reid, two things have developed just in the space of the 12 months that give evidence that steps of a positive sort have taken place. The first is, as Dr. Marston mentioned, the establishment of a system within the Department to look at grants administration generally and on which all elements of the Department's granting components have been represented and actively engaged. We have both an inside group, as it were, and a group composed partly of staff and partly of experts from the outside.

This group has had very active discussions about improving procedures both within the governmental agencies having the responsibility for the administration of these programs and steps to improve the quality of the administration of Federal and non-Federal funds

in the Institutions, mostly academic but not limited to that, where the work is carried out.

In addition to that, each of the agencies—including NIH—has taken active steps to improve the quality of management—again, in both settings: our activities and those of the Institutions where the money is expended. We at NIH have concentrated particularly on the latter. We feel that with any program as large, as complex and as important as ours, we could never hope, nor should we wish, to build a staff large enough to manage it solely from the central headquarters.

I hope this is responsive to your question.

Mrs. REID. Yes, thank you.

I would like to say, Doctor, I, too, want to thank you for your statement and your responses to the questions. This has been most enlightening to me.

Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Hull?

SMOKING AND HEALTH

Mr. HULL. Thank you, Mr. Chiarman.

Dr. Marston, I know you have been in your post at NIH only about 7 months now. But I wonder if that has been long enough to find out why each of your Institutes seems to take a different stand on the cause or causes or emphysema and whether or not the cigarette has been established as causal. Do you know that in the special material submitted to us at last year's hearings, the NIAID reports in at least three places that the cause or causes are unknown, with no clear-cut leads. What is now the Institute for Environmental Health Sciences speaks of the association of prolonged cigarette smoking with increased risk of chronic, obstructive, and degenerative pulmonary disease. The NIAID says the exact causes are largely unknown.

Meanwhile, material issuing from the Clearinghouse for Smoking and Health is citing lung cancer, emphysema, chronic bronchitis and coronary heart disease as the principal cause of death attributable to cigarette smoking.

Whom are we to believe, Doctor? And are we to understand that all the Institutes continue to ask for more money each year to find the causes of diseases that some of them say have been proved to be caused by cigarettes?

Dr. MARSTON. I can speak only to the NIH part at present. I do not know that I will be able to give you a satisfactory response to your question, as I understand it. It does include the total problem with the lung, cancer of the lung, chronic respiratory problems, and emphysema. I think that perhaps one needs to separate these. The evidence of past and recent years of the deleterious effects of cigarettes in terms of lung cancer remain compatible with the information that we got. I am sure that Dr. Endicott will speak more to the details of what has occurred in the last year.

The need for additional research in terms of chronic lung disease is a point that I had talked about earlier in the discussion of the need for the Lung Institute, including not only the effects of cigarettes but of other environmental hazards and the cause of chronic lung disease.

Mr. HULL. Are we to understand, Doctor, that all of the Institutes

continue to ask for more money each year to find the causes of diseases that some of them say have been proved to be caused by cigarettes?

Dr. MARSTON. We are not asking for much more money for the Institutes this year, Mr. Hull.

Yes, I would think, if I could again stick with something such as cancer, that clearly we are continuing to try to understand how it is that cancer comes about, what the multiple causes might be, and then again with the realization that as the Surgeon General said when he was here, that the word "cause" itself has become a more complicated word than it used to be sometime ago. We speak in terms of 'causally related' rather than as a specific cause such as a tuberculosis bacillus causing TB or pneumococcus being the causal agent for pneumonia. Certainly there are many agents, activities, conditions going all the way from genetic effects through viruses to specific drugs that have an impact on the causation of a given lesion that occurs.

SLOAN-KETTERING "SINGLE INSTRUMENT" GRANT

Mr. HULL. Dr. Marston, I believe you were in a different part of HEW when the Fountain Committee was so critical of NIH granting policies and when we discussed this last year with Dr. Shannon. The Fountain Committee singled out for criticism a large general grant to Sloan-Kettering. It didn't question the legality of the grant, but took the view that the Surgeon General "acted unwisely in using the broad discretion" given him under the Public Health Service Act.

We asked Dr. Shannon last year if NIH intended to make any more such grants in the future and he said he had no specific plans to do so.

But in the NIH justification material this year, Dr. Marston, I see a very small asterisk and the notation "includes Sloan-Kettering single instrument grant."

How much of the $11,811,000 earmarked for "basic research and other," will go to Sloan-Kettering?

Dr. MARSTON. This is the same grant. Let me respond in this fashion: We will be getting a report on the experience with this grant. As you recall, this was an attempt to meet some of the needs that we had talked about earlier in terms of institutional support. It was set up on a trial basis with the requirement that there be a detailed report which we would study to get guidance as far as future policy is concerned.

We are just about at the time of receiving that report——

Dr. BERLINER. The grant is for roughly $4 million. The grant was negotiated downward.

Dr. MARSTON. This is not a new grant to Sloan-Kettering. It is the same one.

Mr. HULL. What did they accomplish in the past year with NIH funds? Supply that for the record.

Dr. MARSTON. Yes, sir.

(The information follows:)

HIGHLIGHTS OF RESEARCH PROGRESS, 1966–68

GRANT CA–08748

(Sloan-Kettering Institute for Cancer Research)

Over the first 3 years of this grant, noteworthy progress in both laboratory and clinical research has been achieved at the Sloan-Kettering Institute. In a retrospective consideration of the achievements, it is possible to relate this progress

to the current state of cancer research in general and to make some prospective judgments for the future.

Immunological studies with Burkitt's lymphoma (a leukemia-like cancer indigenous to certain areas in Africa) have shown that immunological components (antibodies) to a common antigen exist in the sera of patients with Burkitt's lymphoma, carcinoma of the postnasal space, lymphosarcoma, and chronic lymphocytic leukemia. These findings raise the possibility of an etiological connection among these four neoplastic diseases. This is of particular significance in view of the fact that a viral etiology has been implied for Burkitt's lymphoma.

Continuing investigations with transfer factor as an adjunct to cancer therapy in patients with inflammatory breast cancer has resulted in a preparation (from pooled leukocytes of healthy donors) that has caused a partial tumor regression of 5 months' duration in one patient. As the system for obtaining leukocytes from healthy donors is expanded, an increased number of clinical trials will be possible with this potentially important preparation.

Further studies with immunological systems of experimental animals have resulted in the development of new information (and concepts) and technical procedures so that the use of animal model systems can be fully exploited with respect to leukemia and mammary tumors. Specific mouse and guinea pig systems, in conjunction with electron microscopic observations, should permit a deeper probe into the relationship of antigenic manifestations and virus-like particles in leukemic cells and their precursors.

The application of biomathematical concepts and procedures has progressed satisfactorily with special emphasis on models for the spread of contagious disease and medical diagnosis, protocols for clinical trials designed to choose the best method of treating cancer, assessments of the effects of contraceptive methods on the incidence of cervical cancer, and on computations necessary for the preliminary assessment of the effects of an autogenous irradiated experimental vaccine in human osteogenic sarcoma. And, in addition, studies have continued with respect to cell kinetics (i.e., rate of growth and reproduction), an important base on which chemotherapy dosages are predicated.

Biochemical activities continue to cover a wide range of investigations from the molecular level to the biochemical events occurring in patients following chemotherapy. The matter of DNA and RNA synthesis and the differences that exist between normal and tumor cells in this regard are of intense interest, and knowledge on this matter is completely essential to understand the reasons cancer cells come into existence and for the development of chemotherapeutic drugs designed to take advantage of the phases in synthesis during cell cycles. While many thoughtful and highly technical experiments have been performed and reported in the technical literature, perhaps one of the most significant observations recently made is the passage of mouse tumor DNA from mouse tumor cells to healthy hamster cells when the two cell types were grown together under laboratory conditions. As a result, the hamster cells manufactured specific mouse antigenic material (i.e., DNA), and in some instances produced tumors when implanted into living hamsters.

With respect to chemotherapeutic drugs, new compounds have been synthesized at SKI and, after sufficient animal testing, have been put into clinical trials. Among the more interesting compounds are the arabinopyrimidine nucleosides such as arabinosyl-5-flurocytosine (ara-FC) and several of its analogs. In addition, the effects of 1-β-D-arabinofuranosylcytosine (ara-C) have been studied. Ara-FC has produced remissions in children with leukemia, but not in adults with nonleukemic malignant tumors. Ara-C produced remissions in acute leukemia in children and adults and in adults with a variety of non-leukemic malignant tumors. Ara-C in combination with thioguanine was of value in acute myeloblastic leukemia (i.e., more than 50 percent of the patients developed remissions). Another drug, Daunomycin, produced remissions in 45 percent of the cases, but when combined with predmisone, resulted in a 51-percent remission rate in children with acute leukemia. Combination therapy of these and other drugs is continuing.

One of the most significant breakthroughs in chemotherapeutic management of leukemia patients began in 1967 with the first controlled administration of the enzyme preparation L-asparaginase. Prior preclinical workup of this drug by the combined efforts of professional and supporting staff from at least nine laboratory areas within SKI served to bring this important preparation to clinical trials in Memorial Hospital in record time. Trials in both children and adults with acute leukemia have yielded a high percentage of remissions, some of which have persisted more than a year. In association with the extensive work on this compound, a laboratory test has been developed to indicate

asparagine-dependence of human leukemia cells in culture. This has provided an effective procedure for the selection of patients suitable for clinical trials with L-asparaginase.

An offshoot from the general field of chemotherapy has been the studies at SKI on the cancer-causing effects of compounds closely related to the purine compounds that have been effectively used as cancer chemotherapeutic agents. These new compounds, called N-purine oxides, are powerful cancer-causing substances and are highly useful in studying the fine line of difference between growth inhibition and growth stimulation. It is believed that N-purine oxides can occur naturally. In addition to these carcinogenesis studies, substantial progress has been made in identifying the tumor-promoting substances in tobacco that seem to be produced in part during the fermentation process, and particularly during flue-curing.

Growth promotion in a different respect has been studied with considerable success, using a preparation derived from the enzymatic digestion of bovine growth hormone. Such a preparation has produced controlled growth in human pituitary dwarfs. The biochemical manipulations now in progress offer considerable speculation regarding the ultimate clinical application of this and other similar preparations.

Research in biophysics at SKI has many ramifications, but essentially it is concerned with the pathways of the effects of radiation on biological systems. Consequently the ongoing research program covers, as in the case of biochemistry, many areas from the molecular level in individual cells to the application of radiation for the diagnosis of the presence or absence of a cancer. Of primary concern at the cellular level are the environmental circumstances affecting a cell's response to radiation effects. Substantial and practical results have been obtained on the effects of antimetabolites, sensitizers, inhibitors, etc., in conjunction with X-radiation, ultraviolet radiation, and pulsed high energy radiation. Such results may have practical application in radiotherapy in cancer patient management and in the use of radiation in diagnostic procedures. Of considerable importance, also, is the use of radioactive substances (i.e., fluorine-18, calcium-47, etc.) in metabolic studies, as well as in radiotherapy and radiodiagnostic procedures. Within the past 18 months, a new cyclotron has gone into operation at the Sloan-Kettering Institute, from which there is now produced a variety of radioactive substances, tailor made for specific research situations. Also during the past 2 years, quantitative scanning devices (gamma camera) with computer linkup have been developed and improved so that more accurate diagnosis can be made of deep-seated cancers.

In the general area of clinical medicine research, studies of life-threatening biochemical determinations and fluid imbalance in cancer patients have continued, resulting in improving the clinical procedures for maintaining proper fluid and salt (electrolyte) balance in such patients on various drug therapy regimens. Similar studies in other abnormal situations that develop in association with cancer have led to improved clinical management procedures. Work on the development and use of new analgesic drugs during the past 2 years has led to the use of pentazocine, an effective and clinically useful oral analgesic, and it has been found that pentazocine-morphine combinations produce more analgesia and fewer side effects than either drug alone. During the past year, in parallel to the clinical medicine work, considerable emphasis has been placed on complete organ transplantation as a clinical management procedure. Consequently surgical and immunological procedures appropriate for complete resection and total replacement of the liver have been developed in dogs. And within the past 2 months such a transplant has been made in a human patient, replacing a cancerous liver with a healthy liver.

The above-discussed highlights of research progress is only a small portion of the tremendous amount of research that has been reported during the past 3 years in approximately 1,300 publications in the leading scientific journals in this country and elsewhere. These particular items were pointed out, for they are examples of research results that are both basic in concept and applied in utilization and that contribute significantly to the continuing prosecution of research on the cancer problem. For the most part the research projects in these highlights are illustrative of original thought; however, the L-asparaginase work is a perfect example of the final culmination of the ideas and efforts of a number of investigators in several other institutions besides SKI, all working toward a common goal—the control of cancer in man.

Mr. HULL. Has administration of the grant been set up in such a way as to meet the criticisms of the Fountain committee?

Dr. MARSTON. I think I would want to see the report on their experience with it. If I could ask Dr. Endicott to respond to that——

Dr. ENDICOTT. We have had a report from the committee, a special committee established solely to follow this grant which we regard as experimental. We have now had the first report from that committee which was presented at the advisory council meeting in March. Their recommendations were that the period of moral commitment be extended for a period of 2 additional years to permit the committee to have a full 5-year period to observe the effectiveness of this type of support. The committee's preliminary report was highly favorable both in terms of the quantity of research and its quality. Interestingly enough, without waiting the full 5 years of experience, the committee recommended that we give serious consideration to extending this type of support to additional institutions.

SMOKING AND HEALTH

Mr. HULL. Doctor, Secretary Finch told the Senate Commerce's Public Health and Welfare Subcommittee earlier this month that HEW accounts for more than 70 percent of Federal expenditures in biomedical research. I know that the Government accounts for almost that same percentage of all money that's spent by public or private institutions on health research.

Doctor, with scientists and medical researchers and their institutions so very dependent on HEW funds how can they be objective about smoking and health?

Dr. MARSTON. Mr. Hull, the evidence on smoking and health has come from a variety of sources not only in this country but in other countries. The answer to this would be the one one would expect. If it were a bias limited to recipients of American grants, the conclusions might be different that came from other countries.

Mr. HULL. Are not HEW grantees and contractors liable to come up with answers they know will be consistent with the HEW stands on the smoking controversy if they are ever to get moneys from you again?

Dr. MARSTON. I would hope not.

Mr. HULL. I would hope not, too.

SHARING OF FEDERAL LABORATORIES AND EQUIPMENT

Doctor, the current issue of Science magazine reports that expensive research equipment and facilities in Federal labs are expected to be more readily available now to university scientists working on their own projects. A directive from President Nixon allows Federal agencies to pay research costs at the Government facility when a university invstigator's project is consistent with the goals of Federal labs. This directive supposedly follows the 2-year study which shows, I suppose, that the possibilities have been considered for some time.

Can you tell me if this will strengthen your research programs into the causes of such disease as cancer, arteriosclerosis, and emphysema?

Dr. MARSTON. We have had, over the years, some experience in close working relationships with other institutions and, indeed, in the utilization of Federal laboratories. For instance, NIH has worked rather closely with some of the Oak Ridge programs because they had complex, expensive equipment which we did not have. Our experience

to date has been that this type of sharing of expensive equipment has been productive. I agree with Dr. Dubridge and the President that it should be expanded.

Mr. HULL. Dr. Shannon said that of a $100,000 grant to an institution for medical research, perhaps two-thirds goes for professional and technical salaries, including payments to medical students. Is this new arrangement likely to save any money?

Dr. MARSTON. The one of sharing the expenses?

Mr. HULL. Yes.

Dr. MARSTON. I do not think it will save any money. It will do two things. It will remove any doubt about the appropriateness of using Federal equipment by non-Federal personnel to carry out projects that could require expensive duplication. I think, in terms of a large savings, it would be in the sense of not having duplication of expensive equipment.

Mr. HULL. In other words, would NIH be able to, in basic research, to get what Mr. McNamara used to call "more bang for the buck?"

Dr. MARSTON. In terms of picking up loose dollars, I do not think we will find many as a result of this. I think that its impact will be to give positive encouragement to sharing expensive equipment.

Dr. BERLINER. In the area of biological research, we don't ordinarily have very many expensive items of equipment such as you might find in physics where they have an accelerator that may cost $20 or $30 million.

Mr. FLOOD. Palo Alto?

Dr. SHERMAN. Stanford linear accelerator.

Dr. BERLINER. The one built by the University of Illinois is even more expensive. That sort of thing does not often come into biological research. Although we consider our facilities and other Government labs available for this sort of collaboration, I do not think it is likely to have the same impact it would have on the other institution.

Mr. HULL. I see that it is to be left to the directors of the local facilities to decide which university's proposals would be accepted and whether or not the research fits into the lab goals.

How will you keep track of this in the various NIH facilities?

Mr. MARSTON. I do not think this will raise a problem for us. Where there has been a need to share equipment, I think we have already been able to do this in a number of instances. Administratively, I see no additional problems.

Mr. HULL. Have you outlined goals for each of the NIH labs?

Dr. MARSTON. No, sir.

Mr. HULL. What are those goals?

Dr. MARSTON. You mean in this?

Mr. HULL. Yes.

Dr. MARSTON. As far as sharing of equipment?

Mr. HULL. Yes.

Dr. MARSTON. No, I have not. This was recently announced.

DUAL COMPENSATION POLICY

Mr. HULL. Dr. Marston, I'm sure you've read our committee report for last year, especially the section in which we said we were quite disturbed by the extent of recent and immediately prospective losses in top positions in the NIH, and the impact they might have in the future. We said the committee believed the Department should give

immediate consideration to liberalizing its policies on dual compensation appointments under existing law.

Can you tell us, Dr. Marston, what has been done about this, or what your plans are?

Dr. MARSTON. We have had three key instances in which the dual compensation allowance has been the most important and, indeed, essential element in maintaining top talent. We feel that we have a long way to go and need additional opportunities to utilize this mechanism.

SUPPORT OF NEW RESEARCH

Mr. HULL. We hope there are no more immediate resignations scheduled for the near future about which we have not heard.

In that committee report of last year, we also expressed concern about undesirable long-term consequences of restrictions on support of new projects and on new research talent. We were worried about this because of the cutbacks on grant money at the various institutes for fiscal 1969.

Do you know, Doctor, if, as we suggested, renegotiation of large, long-term grants was possible to support new work by new investigators? And what about the plans for this year, with cutbacks again in the research budgets of many of our institutes? Will you be able to fund new blood and new work?

Dr. MARSTON. We did do this. We have so far been able to assure that the new investigator has a fair share of the grant funds. It is becoming increasingly difficult to give this type of assurance. Not just from the standpoint of what we do, Mr. Hull, but it is what people believe is happening. Many of the young people have questions in their minds as to whether there will be adequate long-term support to justify a career commitment.

Mr. HULL. What about the plans for this year to cut back again in the research budget submitted by your Institutes?

Dr. MARSTON. The negotiations in the noncompeting continuations have included negotiations for 1970, on the same basis as 1969. This has been accomplished for the same purpose.

Mr. HULL. Will you be able to fund new blood and new work?

Dr. MARSTON. We hope so. Yes, sir.

MONITORING EQUIPMENT USE

Mr. HULL. Dr. Marston, in line with the economies that we have all been talking about, I feel I must compliment you and your predecessor, Dr. Shannon. I saw a squib in the paper here just the other day that NIH officials were about to stage their annual "walk-through" of the NIH campus and buildings, looking for idle equipment. In a practice begun by our friend, Dr. Shannon, and so wisely continued under your administration, unused equipment is reissued to other NIH components and agencies. I understand Dr. Shannon's men last year redistributed almost $300,000 worth of equipment, thus saving the Government a good deal in new equipment purchasing.

Mr. FLOOD. Dr. Shannon was that kind of a worker.

Mr. HULL. Would you care to tell us how it went this year?

Mr. SEGGEL. Mr. Hull, this is actually now in process so we do not have any new results to present at this point. We are doing the same thing this year.

Mr. HULL. I hope that you do.

Doctor, in the Howard S. Diel lecture you gave last November in Detroit, you called for new ways to give broad institutional support to maintain the environments in which education can proceed.

Would you elaborate on that now, Doctor?

Dr. MARSTON. I think this is in keeping with the discussions that we had earlier. It is how one does several things; that is, carry out the Federal stewardship and the prudent use of dollars at the same time that one allows the flexibility for the institutions to meet their needs, realizing that institutions do differ one from another.

Secondly, the proper mix between the national quality standards that one can achieve perhaps best through the project mechanism versus the recognition of some aspects of the research and educational activity must be determined by local needs. Some institutions need construction in order to do the job. Some need scholarships. Some need operating funds. I think we need to examine very carefully, this committee and the NIH, the best mix of the various mechanisms of supplying support for research and education.

PARTNERSHIP WITH INDUSTRY

Mr. HULL. Would you tell us how you feel about enlisting industry support and perhaps even money in helping to solve what has been called environmental health problems?

Dr. MARSTON. I think that it is important to try to work with industry. One of the advantages of our Environmental Health Sciences Institute is that it is not a regulatory agency and therefore its ability to work closely with industry has been augmented. Indeed, Dr. Kotin, when I recently visited his shop, pointed out the effectiveness of his communications with industry and the desire on the part of industry to work closely with his Institute on these problems. I would say that we feel it is very important to work closely with industry on the environmental problems.

Mr. HULL. I see that at least one page of the NIH justification material this year makes mention of industry partnership, in the general statement of Dr. Davis' National Institute of Allergy and Infectious Disease. Tell us, Dr. Marston, please, about any work the NIH is doing now or plans to do in partnership with industry.

Dr. MARSTON. Would you like for me to give some examples now or supply it for the record?

Mr. HULL. All right.

Dr. MARSTON. There are a number. I would say most of the Institutes in one way or another do work with industry.

(The information follows:)

COLLABORATIVE RESEARCH CONTRACTS WITH PROFITMAKING INDUSTRY

Although by far the largest part of NIH resources are devoted to the support of biomedical research carried out under the auspices of nonprofit educational institutions, foundations, and research institutes, and another substantial portion of funding is devoted to in-house intramural research, a small but significant segment of the annual budget, particularly in some of the highly directed research and development programs of several of the Institutes and research divisions, is dedicated to fruitful collaborative contractual agreements with profitmaking industries.

Some examples follow (these exclude strictly procurement contracts):

Institute	Program	Type of business	Number of contracts	Fiscal year 1969 current funding level
Division of Biologics Standards	Determination of safety of components of new vaccines	Research and development, independent research laboratories, chemical testing services.	8	$114,000
National Institute of Arthritis and Metabolic Diseases.	Artificial kidney	Industrial engineering, manufacturers of chemicals and plastics, custom machinery, instrumentation and design.	13	1,808,717
National Institute of Allergy and Infectious Diseases.	Production and testing of microbiological reference reagents, vaccines, serums.	Research and development, independent testing laboratories, pharmaceutical manufacturers.	27	3,046,093
National Heart Institute	Artificial heart and myocardial infarction	Research and development, medical instrumentation and equipment, plastics manufatcuring.	51	4,750,879
National Cancer Institute	Chemotherapy and etiology	Testing laboratories, pharmaceutical manufacturers, data processing, animal production, chemical industries.	129	24,152,974

Mr. HULL. In your Diehl lecture, Dr. Marston, you mentioned the dangers of asbestos and uranium as cancer-producing agents. I am sure, under the circumstances, that you will want to correct an impression put forward by a Washington Post writer late last year, that the U.S. Government is ignoring the dangers of asbestos.

The article said that three Federal departments, including the Public Health Service, had failed publicly to acknowledge the warnings of investigators at New York's Mount Sinai Hospital of the serious occupational hazards of asbestos.

Dr. Kotin told us last year that, when he had more room for animal studies, he would be doing asbestos inhalation work with mice. Is there any other work being done on asbestos within NIH?

Dr. MARSTON. The only person that I have talked to about this is Dr. Kotin. I talked to him in some detail.

Dr. Berliner, do you know?

Dr. BERLINER. I am not aware of that.

Dr. MARSTON. That is one that he feels is very important.

Mr. HULL. Dr. Kotin told us last year when he had more room for animal studies he would be doing asbestos inhalation studies with mice. Is there any other work being done on that in NIH?

Dr. MARSTON. I know that there is work other than the inhalation on mice. There are supported studies not only on the asbestos fiber itself, but the reaction of tissues to the fibers. There are surveys being carried out in terms of studies of lungs to see what the incidence of asbestos fibers is. I believe there is a registry recently——

Dr. BERLINER. A particular type of tumor associated with asbestos.

Mr. FLOOD. There is no doubt about it, is there?

Dr. BERLINER. About the relationship between the asbestos and this particular tumor?

Mr. FLOOD. Yes.

Dr. BERLINER. No; I don't believe so.

Mr. HULL. And while we're discussing asbestos, Doctor, are you familiar with some preliminary research reported last year from London that asbestos fibers have been found in beer? Is there any investigation of that in this country?

Dr. MARSTON. No, sir.

Mr. HULL. Dr. Marston, Dr. Howard Rusk posed an interesting thought in a recent magazine column. About the use of counterpart funds available abroad from sale of our surplus agricultural products. Did you see it?

Dr. MARSTON. I have had discussions about it. I didn't see the article.

Mr. HULL. Dr. Rusk mentioned cutbacks in health programs for emerging countries from our Agency for International Development. He said that counterpart funds are now used "in modest degree"—primarily by the Rehabilitation Services Administration and the NIH—for what he called valuable research projects. And he suggested that counterpart money might also go for training greatly needed health workers in these countries. Just like the United States, these countries have health manpower problems.

What is your feeling on this, Doctor?

Dr. MARSTON. I do not think, Mr. Hull, that I know enough about this subject at this time, but I would be glad to look into it and let you have an opinion.

Mr. HULL. Fine. I would appreciate that very much.

Dr. MARSTON. All right.

(The information follows:)

USE OF FOREIGN CURRENCIES FOR TRAINING

There are undeniably urgent and limitless needs in foreign countries for training of health workers. Utilization of counterpart funds for such a purpose opens the doors for U.S. assistance when requested. There are, however, other ramifications which preclude immediate favorable reaction. As you stated, Mr. Hull, "just like the United States, these countries have health manpower problems." The unfortunate fact is, the United States itself doesn't have sufficient manpower to send to other countries to train their health workers. In addition, while foreign currencies can be utilized in the country of origin, there is also a substantial requirement for U.S. dollars with which to pay American salaries, purchase equipment and supplies and to meet many other expenses of an effective operation. Inasmuch as the question has been asked of NIH, I should point out that neither the Public Health Service Act nor the delegated portion of Public Law 480 contain the necessary authority to permit the NIH to engage in this type of training activity.

NATIONAL COUNCIL ON RESEARCH POLICY

Mr. HULL. Dr. Marston, the name of your eminent predecessor, Dr. Shannon, who appeared before us for so many years keeps popping up. I wonder if you saw any reports on a lecture he gave in Dallas early this year for the American Association for the Advancement of Science.

Dr. Shannon said the United States needs an executive body comparable to the National Security Council to make policy decisions for research programs in the biomedical and other sciences. He said such a group might lessen what he called the chaotic competition for funds in the major science areas and between research and education, which as you probably know, was a major concern of his.

Most important, he said that such a high-level policymaking body would consider fund allocation in relation to broad social goals and national purposes. He admitted—and as the head of NIH for so very long I guess he should know—that there are many central mechanisms for program review and policy counsel in the sciences now. But he said these, individually, or in combination, are not adequate for the Nation's future.

Dr. Marston, as the new head of an organization that spends most of the Nation's health research funds, what do you think of this idea of Dr. Shannon's?

Dr. MARSTON. I have talked to Dr. Shannon off and on over the years.

Mr. FLOOD. A very Shannon-like statement.

Dr. MARSTON. Yes, sir. I have talked to Dr. Shannon and others about this. I think, Mr. Hull, that we are at a point where we do need, at a very high level of government, some additional mechanisms to make the very broad decisions of how fast and under what conditions we are going to explore the whole nature of man in terms of getting additional information. We do need to avoid the type of thing that has been implicit in some of the discussions here, that somehow you

can solve major social problems by taking a million dollars here and putting it into another spot.

Part of Dr. Shannon's point at that meeting, I am sure, was that we need to be able to take a broader view of national policy and to be able to then make the commitment of resources that allows one to get the job done rather than doing it in a piecemeal fashion and with the possibility of a little bit up one year and a little bit down the next year. I am in complete sympathy with these goals. I think the question of the specific mechanisms that one uses to achieve this requires public debate and analysis of the details. That was a good speech that Dr. Shannon made in Houston. He brought up some of the key issues that all of us will be facing over the next few years. They do require that we give serious consideration to them.

Mr. HULL. Thank you very much. My very best to you.

Mr. FLOOD. Mr. Casey?

COST OF MEDICAL EDUCATION

Mr. CASEY. Thank you, Mr. Chairman.

How many medical schools are there in the country?

Dr. MARSTON. One hundred one.

Mr. CASEY. What does it cost to run those 101 medical schools, do you know? Total.

Dr. MARSTON. No, sir. I can get estimates but the problem that one runs into immediately is, do you want it to include the cost of the teaching hospitals; how much of the affiliated hospital costs does one want to include?

Dr. KENNEDY. There are some 2-year schools in that. There are a couple more on the drawingboards.

Dr. MARSTON. We can get several answers to your question, depending on what one includes.

Mr. CASEY. How do they arrive at what is the cost of training a medical student?

Dr. MARSTON. It depends on how you want to define the cost. If you want to say that to train a medical student requires a 500-bed teaching hospital and include in that cost the total cost of running the hospital, you have one answer. If you say that to train a medical school student requires a research environment and you include the cost of the research environment, it is very hard to get a simple figure that says X number of dollars will each year cover that.

Mr. CASEY. Let us limit it to the school itself. They do not take into consideration the cost of operating the hospital in their budget and operating cost of the school, do they?

Dr. MARSTON. You have just about every pattern or any pattern that you want. Most of the institutions in recent years have been moving toward what is called a medical center, in which the cost of everything that goes on in the center has some type of central control.

Mr. CASEY. Don't the medical schools, as a rule, if they have a contract with, say, a county hospital for staffing that hospital, don't they get something in return from that hospital?

Dr. MARSTON. Some of them do and some of them get very little.

Mr. CASEY. Some of them have a contract so they know they have the hospital for their teaching facilities?

Dr. MARSTON. Right. Some of them own their own hospital and run it.

Mr. CASEY. They do not pay the hospital to use it, as I understand it. In other words, the hospital is glad to have them there, as a rule.

Dr. MARSTON. What happens under some circumstances is that the faculty and student services to the hospital are not paid for in full by the hospital.

PLANNING OF NEW MEDICAL SCHOOLS

Mr. CASEY. Dr. Kennedy just mentioned there are some on the drawingboards, some medical schools on the drawingboards. There were a couple of them, I believe. What participation are you having in the creation of these two new medical schools, wherever they may be?

Dr. MARSTON. We have participation in several ways. Usually we become involved in the planning at a very early stage, whether it is an expansion of an existing medical school or the creation of a new one.

Mr. CASEY. Let us keep it on that. I know about your expansion.

Dr. MARSTON. We are usually involved in the construction, frequently from several standpoints through the manpower legislation, through the research construction funds, and through the library construction funds. Of course, if it is dental, then it is through the dental and nursing areas. We become involved——

Mr. CASEY. You become involved in it from the time the first architectural line is drawn?

Dr. MARSTON. That is right.

Mr. CASEY. You say if you are going to ask us for participating funds, we want to be in on the planning?

Dr. MARSTON. Yes, sir.

Mr. CASEY. What will your ultimate goal be; how many students?

Dr. MARSTON. Yes, sir.

Mr. CASEY. Whether it is a State or private institution?

Dr. MARSTON. Right.

Mr. CASEY. After the brick and mortar are up and the labs are in, you participate in what way?

Dr. MARSTON. We participate in basic improvement grants through the manpower legislation.

Mr. FLOOD. Through what?

Dr. MARSTON. Through the Health Manpower Assistance Act. If they have $100,000 of research activity, they would also get a general research support grant from the research funds. They can apply for special improvement funds. Students are eligible for scholarship and loans under the activities we have there. If they have——

Mr. FLOOD. What?

Dr. MARSTON. The scholarship and loans under—again—under the Health Manpower legislation.

And they can apply for research grants, too.

Mr. FLOOD. Who do you mean by "they"?

Dr. MARSTON. The medical school.

Mr. CASEY. Medical School X would apply for a research grant.

Mr. FLOOD. The school itself?

Dr. MARSTON. Or the individual faculty members.

Mr. FLOOD. They usually apply, the school with one of the faculty members named as the investigator, is that right?

Dr. MARSTON. Yes. There is one key point on this.

Before we can legally supply construction funds, we must have a letter of reasonable assurance from the accrediting body that at the time they admit their first class they will have a reasonable chance of being accredited.

Mr. FLOOD. Does that include a new wing to a nurses' school?

Dr. MARSTON. If the nursing school is already accredited, no. This would not require the additional assurance we are talking about if we have a completely new one. In other words, we do not want——

Mr. CASEY. You mean accredited by——

Dr. MARSTON. The Joint Accrediting Committee of the AMA and AAMC.

Mr. CASEY. Do you require any assurance from them they have money to run it the first year?

Dr. MARSTON. This is part of the review process. Before I came into the Government I served on a number of the site visits. That was the question that was asked more often than any others, What financial resources do you have available to run the school?

Mr. CASEY. They come around and ask you the same thing, do they not?

Dr. MARSTON. The Federal resources for the operation of a medical school are not adequate to justify building a medical school if these are the only dollars.

ASSURANCE OF FUTURE FEDERAL ASSISTANCE

Mr. CASEY. What I want to know is what assurance do you give them as to what assistance they can get to operate the school.

Dr. MARSTON. I think we have the problem that we spoke about earlier, that we do have a year-by-year appropriation and we can not promise them firmly what they can get.

Mr. CASEY. You made one statement here on page 13 which I think is the whole crux of this turmoil of where we are going on the doctor supply, and that is the predictability and reliability of Federal assistance and the feeling of common purpose of professional rapport that exists between the institutions and the Federal agency with whose program it is involved.

Mr. FLOOD. Do you have a medical school in your district?

Mr. CASEY. Do I have one?

Mr. FLOOD. Yes.

Mr. CASEY. Yes, sir; right smack in the middle of my district.

Dr. MARSTON. I could not agree with you more.

Mr. CASEY. And they are talking about putting in another one, State school. And there is a little jealousy developing here. That is why I asked Dr. Stewart the other day whether he thought it should be considered.

His opinion was that Houston can support another medical school and probably another one in the next 15 years.

Mr. FLOOD. Two or three, do you mean?

Mr. CASEY. Three.

What is your opinion on a metropolitan area like Houston? Of course he qualified it by saying as long as it did not detract from the State school that was in existence at Galveston.

Dr. MARSTON. That is right; yes. I think I would agree with Dr. Stewart.

Mr. CASEY. That the State did not siphon money away from the Galveston school to go into this one?

Dr. MARSTON. One of the problems in schools and States that have had multiple-State schools is the failure to recognize that they are going to have to put up considerably more money in order to have a second, third or fourth school.

Mr. CASEY. Let's get back to the statement here now: How are we going to meet this observation you make that we need to have a predictability and reliability of Federal assistance?

Dr. MARSTON. I do not think there is an easy answer to that one because you know there is nothing sure.

BASIC SUPPORT FOR MEDICAL SCHOOLS

Mr. CASEY. Is there any basic per pupil support that the schools could depend on? Even with only $10 a year they would know they had a thousand dollars coming in if they had a hundred students. Right now they do not know whether they are going to get a nickel or not other than the moral commitment.

Dr. MARSTON. The basic improvement grant is the per student one, but it is too small in terms of dollars.

Mr. CASEY. Does each school know it is going to get it?

Dr. MARSTON. I was until 92 additional institutions were made eligible at the extension of the law.

Yes; in general the answer is that each school does know what it is going to get in terms of basic improvement grant.

Dr. FENNINGER. This would not be absolutely true under the new legislation where the medical school receives a fixed sum, then of the remaining appropriation 75 percent is for enrollment and increases in enrollment, with a double factor for increase in enrollment, and the remaining 25 percent for the number of graduates.

Mr. CASEY. That sounds like the guy that figures out the income tax returns.

Dr. FENNINGER. It is not predictable in an absolute sense.

Dr. MARSTON. I think you get predictability in two ways.

There are ways other than by formula. One is by performance and by priority. If the schools knew that there was going to be a high priority on the maintenance at least of the dollars that are going into the things that they require to run—the dollars that go into research, training, education of physicians, education of nurses, education of allied health professionals. If they knew this was going to have a high priority at every level of Government, this would be one type of predictability. They would recognize that if you had a major national change, this might have to be modified.

I do not think it is reasonable to expect an absolute assurance. But I think the concern now, Mr. Casey, is that this year it might be the production of increased numbers of physicians and next year it might be some other urgent social problem, and that to get the dollars to do the latter you are going to take it from the former.

Mr. CASEY. It depends on what the Congress might do with the appropriation.

Dr. MARSTON. Congress, the executive branch, NIH, all of us.

Mr. CASEY. We have a formula for impacted areas, as they call it, in the public school system where it is a per pupil deal. The executive has been trying to cut that back for the last 2 years.

Mr. CARDWELL. Longer than that.

Mr. CASEY. Yes, longer than that.

That comes under the jurisdiction of this committee, and we try to follow the executive and we go up there and get our head knocked off because it has now been put in and the school districts are dependent upon it, they expect it, and a majority of the Members of the House have not favored taking any part of it away from them. Somebody is going to have to come up with some good idea of how we can give some basic support to these medical schools instead of this idea of "Well, we make these grants on the basis of the appropriations available."

Here you have some of your research men saying, I'll come to your school if you will guarantee me $100,000 a year for the next 5 years, something like that. You know what goes on.

Dr. MARSTON. Yes. The problem is that the schools are very different and their needs are different, and to put it purely on a per capita basis alone as the only mechanism is not right.

Mr. CASEY. But for your basic medical education you are going to have to support these schools with a definite figure they can depend on?

Dr. MARSTON. Yes, sir.

Mr. CASEY. Then they can get their specialization or preeminence in a particular field through the talent of the people they have at their institutions and then you can give your specialization grants.

Dr. MARSTON. I agree.

Mr. CASEY. I wish you would think up something. Nobody else has. And we have this problem. I think the public is willing to back it.

You mentioned here that the Federal Government has got to be looked to and you consider it a Federal problem because these doctors go all over the country. You could carry it one step further and say this is of as much importance to the welfare of this Nation as defense, and we train our officers in Federal schools. Do not charge them a dime.

The Navy has their school for officers. Of course, I do not want to see that for medical schools myself. You do have some competition between these three military institutions, but I do not think that is comparable with what we are talking about. But I do think that we need to work up a formula whereby each school has something definite they can plan on. Then if Joe Blow dies and leaves them another building or operating room for their hospital or whatever it is, that is all right too, but you cannot depend on Joe Blow dying at the right time to keep the school running.

Dr. MARSTON. Right.

Mr. CASEY. Or you might find the widow will break the will, too.

Those sort of things are unpredictable and they have to have something definite to depend on.

Dr. MARSTON. Yes.

I would hope this can be pursued even further, Mr. Casey, when Dr. Fenninger is giving the report on the progress that has been achieved so far, and on the problems that he has encountered in the very brief history of the health manpower assistance legislation.

Mr. CASEY. I know you are interested in it.

Dr. MARSTON. Yes, sir.

Mr. CASEY. And of course you say the emphasis now is on increasing the capacity or enrollment of existing schools. Is that what your money this year is primarily aimed toward; that is, as far as producing new doctors is concerned?

Dr. MARSTON. The situation can best be summarized this way: We have a number of new medical schools that will either come into existence or are under consideration. Generally, they tend to be somewhat more expensive than the expansion of existing schools, but here I think one has to be more specific than that—one has to talk about a specific existing school versus a new school. The change of climate that has occurred over the last year or two and the very real problems, that you have outlined so well, that we face in this Nation have led all of the schools to try to see what they can do to increase their number of students.

It is important to capitalize on this climate. Over time we are not only going to have to expand existing schools, but also to build new schools. We are not going to get it either way. It is quicker to do it by expanding an existing school because——

FUNDS AVAILABLE FOR NEW MEDICAL SCHOOLS

Mr. CASEY. How much money do you have in this budget that you can use for expansion or creation of new medical schools?

Dr. MARSTON. We have construction funds which is a total—and this is for everything, this is all of the dollars that are available for construction of medical, dental, the whole group of schools, the research needs that they must have in order to get started—we have $149 million for that purpose.

In the special improvement grants, we have the authority to assist schools that are in trouble and might lose their accreditation and go out of existence, or to stimulate schools to increase numbers, or to stimulate schools to change their curriculum.

In that area we have $12.5 million which goes to schools of pharmacy and schools of veterinary medicine, and we have $11.1 million to do all of these other things. That is to stabilize the weak schools and to offer an inducement for enlarging classes and all of the rest.

Mr. CASEY. You say $12.5 million could be used for the same purpose?

Dr. MARSTON. No, sir; that one was added on for the purpose of including schools of veterinary medicine and schools of pharmacy under the basic improvement grant. So for all intents and purposes we have $11.1 million increase for grants to——

Mr. CASEY. Existing schools?

Dr. MARSTON. Existing schools.

Mr. CASEY. Or new schools?

Dr. MARSTON. The new schools probably in 1970 really would not be involved in this.

Mr. CASEY. You say they would not?

Dr. MARSTON. These are operating funds. So the new schools that come in would get a basic improvement grant.

Mr. CASEY. What about the $149 million for construction? That is available to new schools?

Dr. MARSTON. That is available to new schools.

Mr. CASEY. For buildings and hardware?

Dr. MARSTON. Yes, sir.

Mr. CASEY. I wish you lots of luck, Doctor. I still have great confidence in NIH.

Dr. MARSTON. Thank you, sir.

Mr. CASEY. I hope I can be helpful to you.

Dr. MARSTON. Thank you very much.

Mr. CASEY. We will place in the record the updated statistical data and statements that you have prepared for the record at our request.

(The material referred to follows:)

HISTORY OF CONGRESSIONAL ACTION ON BUDGET REQUESTS FOR NIH INSTITUTES AND DIVISIONS

Year	Budget request			Appropriation		
	Obligational cash	Liquidating cash	Contract authority	Obligational cash	Liquidating cash	Contract authority
1932	$48,000			$48,000		
1933	48,000			48,000		
1934	54,775			54,775		
1935	50,000			50,000		
1936	64,000			64,000		
1937	64,000			64,000		
1938	464,000			464,000		
1939	515,000			515,000		
1940	587,750			707,000		
1941	712,120			711,000		
1942	705,000			700,000		
1943	1,278,270			1,278,270		
1944	1,291,000			2,555,020		
1945	2,835,000			2,835,000		
1946	2,078,000			3,414,700		
1947	10,799,500			8,125,448[1]		
1948	22,403,000			28,876,000		
1949	45,701,460		$2,300,000	37,668,000		$10,300,000
1950	40,567,000	$3,900,000	3,595,000	50,167,000[3]	$4,925,000[2]	15,425,000
1951	49,845,000	12,725,000		47,334,750[3]	12,725,000	
1952	53,386,000	5,648,000		52,477,291	5,198,000	
1953	55,005,000			59,030,750		
1954[4]	56,340,000			71,153,000		
1955[5][6]	71,128,000			81,268,000		
1956[5][6]	90,023,000[7]			98,458,000		
1957[5]	126,725,000[7]			183,007,000		
1958	190,183,000			211,183,000		
1959	211,814,000			294,383,000		
1960	294,279,000			400,000,000[8]		
1961	400,000,000			560,000,000[9]		
1962	583,000,000			738,335,000[9]		
1963	780,400,000			880,800,000		
1964	930,454,000			918,454,000		
1965[10]	956,492,000			965,992,000		
1966[10]	1,105,006,000			1,138,406,000		
1967[11]	1,231,764,000			1,306,983,000[12]		
1968[11]	1,152,250,000			1,143,424,000		
1969	1,188,293,000[13]			1,100,092,000		
1970	1,099,776,000					

1/ Includes $386,500 transfers.
2/ Not less than $3,000,000 was earmarked for liquidating cash; an additional $1,175,000 was used for that purpose.
3/ Excludes $3,216,250 rescinded.
4/ Excludes $131,000 for Gorgas Memorial Laboratory.
5/ Excludes $147,000 for Gorgas Memorial Laboratory.
6/ Includes $90,000 transfer.
7/ Includes $200,000 transfer from other appropriations.
8/ Includes $12,139,000 for construction of mental health-neurology research facility.
9/ Includes $1,000,000 for planning for a gerontological research facility; and $750,000 for modernization at the Rocky Mountain Laboratory, Hamilton, Montana.
10/ Includes $25,000,000 for Regional Medical Programs, $19,700,000 for Mental Health Staffing, and $20,250,000 for Heart Disease, Cancer and Stroke Program.
11/ Excludes $246,741,000 for National Institute of Mental Health. Includes $20,615,000 for Environmental Health Sciences.
12/ Excludes $21,000,000 unobligated balance available, start of year, for Regional Medical Programs.
13/ Excludes $30,928,000 unobligated balance available, start of year, for Regional Medical Programs.

NOTE: --Not all amounts on this table are comparable from year to year because of inconsistencies in the content of the appropriations. Prior to 1938 they exclude all salaries. Prior to 1943 they exclude all salaries other than those of employees of the National Cancer Institute. Prior to 1949 they exclude pay of regular corps officers. For 1948, 1949, and 1950 they include funds for support of narcotic hospitals at Fort Worth and Lexington which were subsequently transferred.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

SUMMARY--NATIONAL INSTITUTES OF HEALTH
(Institutes and Divisions)

Total, operating accounts:	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$278,848,000	$255,130,000	$241,895,000	$283,870,000	$400,618,000	$331,910,000	$322,807,000 1/
1961--------	368,139,600	336,463,600	332,437,000	375,137,000	553,200,000	459,100,000	448,425,000 1/
1962--------	570,875,000	548,818,000	494,676,000	548,818,000	710,100,000	629,459,000	530,441,000
1963--------	746,662,000	719,200,000	653,501,000	707,201,000	752,201,000	737,201,000	612,156,000
1964--------	853,673,000 2/	764,759,000 2/	742,333,000	736,326,000	741,518,000	736,326,000	710,187,000
1965--------	861,055,000 2/	832,277,000 2/	778,327,000	773,349,000	787,949,000	787,099,000	781,670,000
1966--------	936,295,000	907,905,000	867,270,000	878,970,000	902,320,000	896,720,000	907,772,000
1967--------	1,093,273,000	1,045,221,000	957,937,000	992,158,000	1,027,158,000	1,022,158,000	992,262,000
1968--------	1,200,156,000	1,168,511,000	1,087,936,000	1,084,610,000	1,137,186,000	1,084,610,000	1,143,415,000
1969--------	1,231,878,765	1,211,727,765	1,119,371,000	1,080,813,000	1,129,913,000	1,100,092,000	----------
1970--------	1,218,293,000	1,136,127,000	1,099,776,000	----------	----------	----------	----------

1 Includes $7,000,000 transferred to "Construction of Mental Health-Neurology Research Facility".

2 Includes $30,000,000 for "Special Cancer Research".

NOTE:--
Excludes the "National Institutes of Mental Health" established as a bureau in 1967.
Includes the "Division of Environmental Health Sciences" established as a part of "NIH" in 1967.
Excludes the "Division of Regional Medical Programs", transferred to HS&MHA in 1970.
Includes the "National Eye Institute" established as a separate appropriation in 1970.
Includes the "Salaries and expenses, Office of the Director" established as a separate appropriation in 1970.

"Obligations", on all tables, include rental payments made to GSA by transfer.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

BIOLOGICS STANDARDS

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1964--------	$4,868,000	$4,868,000	$4,817,000	$4,787,000	$4,787,000	$4,787,000	$4,273,000
1965--------	5,075,000	5,075,000	4,969,000	4,969,000	4,969,000	4,969,000	4,433,000
1966--------	7,894,000	7,864,000	6,406,000	6,406,000	7,206,000	6,806,000	5,256,000
1967--------	8,597,000	8,524,000	7,905,000	7,904,000	7,904,000	7,904,000	6,979,000
1968--------	9,280,000	9,280,000	8,649,000	8,649,000	8,649,000	8,649,000	7,699,000
1969--------	8,942,760	8,910,760	8,499,000	8,499,000	8,499,000	8,499,000	----------
1970--------	9,078,000	8,836,000	8,338,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL CANCER INSTITUTE

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$81,864,000	$80,232,000	$75,218,000	$83,308,000	$110,203,000	$91,257,000	$85,030,000
1961--------	95,995,400	88,785,400	88,869,000	102,469,000	126,375,000	111,000,000	106,262,000
1962--------	129,519,000	125,672,000	117,167,000	125,672,000	160,000,000	142,836,000	110,352,000
1963--------	158,901,000	155,700,000	139,109,000	150,409,000	158,409,000	155,742,000	122,424,000
1964--------	154,999,000	145,706,000	145,114,000	144,340,000	145,114,000	144,340,000	131,349,000
1965--------	147,504,000	145,664,000	139,714,000	138,970,000	138,970,000	138,970,000	139,041,000
1966[1]------	170,974,000	160,950,000	153,968,000	157,618,000	163,768,000	163,768,000	161,374,000
1967--------	188,134,000	176,594,000	163,957,000	170,656,000	175,656,000	175,656,000	173,283,000
1968--------	198,580,000	193,058,000	183,356,000	183,356,000	192,356,000	183,356,000	177,010,000
1969--------	207,348,030	201,413,030	187,707,000	182,592,000	191,592,000	185,149,500	----------
1970--------	203,741,000	190,352,000	184,402,000	----------	----------	----------	----------

[1] Includes $10,000,000 transferred from "Special Cancer Research" appropriation in 1966.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

SPECIAL CANCER RESEARCH

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1965--------	$30,000,000	$30,000,000	----------	----------	$10,000,000	$10,000,000	$10,000,000

NOTE:--Transferred to "National Cancer Institute" appropriation in 1966.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL HEART INSTITUTE

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$52,911,000	$47,671,000	$45,594,000	$52,744,000	$89,500,000	$62,237,000	$61,565,000
1961--------	69,798,700	65,047,700	63,162,000	71,762,000	125,166,000	86,900,000	86,239,000
1962--------	110,205,000	105,723,000	97,073,000	105,723,000	160,100,000	132,912,000	91,053,000
1963--------	155,712,000	148,000,000	126,898,000	143,398,000	149,398,000	147,398,000	104,343,000
1964--------	148,884,000	132,784,000	130,108,000	129,325,000	130,545,000	129,325,000	117,405,000
1965--------	132,489,000	129,156,000	125,640,000	124,521,000	125,171,000	125,171,000	124,061,000
1966--------	146,821,000	146,575,000	141,412,000	146,212,000	143,462,000	141,462,000	141,167,000
1967--------	171,226,000	172,766,000	148,407,000	154,770,000	169,770,000	164,770,000	164,333,000
1968--------	194,796,000	190,385,000	167,954,000	167,954,000	177,954,000	167,954,000	161,863,000
1969--------	190,515,000	189,148,000	169,735,000	164,120,000	172,120,000	166,927,500	----------
1970--------	186,708,000	168,984,000	163,141,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF DENTAL RESEARCH

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$9,907,000	$7,715,000	$7,420,000	$9,725,000	$10,164,000	$10,019,000	$9,968,000
1961--------	13,803,300	11,996,300	11,204,000	12,604,000	16,710,000	15,500,000	14,616,000
1962--------	15,265,000	14,681,000	13,933,000	14,681,000	20,000,000	17,340,000	12,963,000
1963--------	20,017,000	19,700,000	17,199,000	19,199,000	22,199,000	21,199,000	17,451,000
1964--------	23,314,000	20,212,000	19,809,000	19,689,000	19,809,000	19,689,000	19,151,000
1965--------	21,055,000	20,402,000	20,209,000	20,090,000	20,190,000	20,190,000	20,001,000
1966--------	22,460,000	22,658,000	22,177,000	22,177,000	23,677,000	23,677,000	23,482,000
1967--------	29,600,000	26,208,000	24,884,000	28,308,000	28,308,000	28,308,000	28,067,000
1968--------	32,388,000	31,926,000	30,307,000	30,307,000	32,307,000	30,307,000	29,283,000
1969--------	34,121,391	33,676,391	30,414,000	29,553,000	30,414,000	29,983,500	----------
1970--------	32,989,000	30,595,000	30,062,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$37,014,000	$32,564,000	$31,215,000	$37,790,000	$51,200,000	$46,862,000	$46,182,000
1961--------	52,949,900	47,519,900	47,541,000	52,841,000	70,760,000	61,200,000	58,608,000
1962--------	77,783,000	73,661,000	68,740,000	73,661,000	90,000,000	81,831,000	78,559,000
1963--------	103,761,000	101,560,000	91,921,000	98,721,000	105,721,000	103,388,000	95,110,000
1964--------	124,579,000	115,759,000	114,717,000	113,679,000	114,717,000	113,679,000	104,970,000
1965--------	121,908,000	117,432,000	113,369,000	112,344,000	113,544,000	113,344,000	112,592,000
1966--------	121,502,000	121,818,000	119,203,000	121,203,000	123,203,000	123,203,000	121,622,000
1967--------	142,265,000	137,506,000	129,908,000	133,687,000	135,687,000	135,687,000	133,508,000
1968--------	156,889,000	153,157,000	143,954,000	143,954,000	147,204,000	143,954,000	139,321,000
1969--------	157,239,000	154,089,000	146,489,000	141,287,000	147,287,000	143,888,000	----------
1970--------	155,479,000	141,491,000	139,968,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960	$32,727,000	$30,803,000	$29,403,000	$33,613,000	$48,966,000	$41,487,000	$40,248,000
1961	44,404,100	40,386,100	39,662,000	44,362,000	61,550,000	56,600,000	55,348,000[1]
1962	60,587,000	57,624,000	54,100,000	57,624,000	80,000,000	70,812,000	61,208,000
1963	82,158,000	79,785,000	71,206,000	77,506,000	86,506,000	83,506,000	70,794,000
1964	95,379,000	89,270,000	88,407,000	87,675,000	88,407,000	87,675,000	81,970,000
1965	94,532,000	91,491,000	88,608,000	87,889,000	88,089,000	88,089,000	87,751,000
1966	104,489,000	100,294,000	96,403,000	96,403,000	102,153,000	101,153,000	100,250,000
1967	118,868,000	113,386,000	106,418,000	111,296,000	116,296,000	116,296,000	113,067,000
1968	134,540,000	134,359,000	128,633,000	128,633,000	135,633,000	128,633,000	121,916,000
1969	146,438,726	149,019,726	131,195,000	126,674,000	132,674,000	128,934,500	----------
1970[2]	107,884,000	104,869,000	103,485,000	----------	----------	----------	----------

1 Includes $7,000,000 transferred to "Construction of mental health-neurology research facility".

2 Excludes funds for blindness, established as a separate appropriation the "National Eye Institute" in 1970.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960	$29,126,000	$25,379,000	$24,071,000	$30,286,000	$41,000,000	$34,054,000	$34,025,000
1961	38,477,100	35,462,100	34,739,000	38,439,000	48,234,000	44,000,000	43,780,000
1962	54,833,000	52,182,000	48,322,000	52,182,000	60,000,000	56,091,000	53,303,000
1963	64,262,000	64,155,000	59,342,000	62,142,000	68,142,000	66,142,000	62,387,000
1964	79,569,000	69,765,000	69,226,000	68,723,000	69,226,000	68,723,000	66,213,000
1965	70,995,000	69,256,000	68,600,000	70,100,000	70,400,000	70,100,000	69,742,000
1966	76,558,000	77,003,000	74,987,000	74,987,000	77,987,000	77,987,000	77,710,000
1967	98,186,000	94,684,000	85,702,000	88,670,000	90,670,000	90,670,000	89,598,000
1968	96,668,000	96,086,000	94,422,000	94,422,000	98,922,000	94,422,000	90,883,000
1969	105,471,598	106,653,598	98,562,000	95,119,000	99,119,000	96,840,500	----------
1970	115,278,000	106,044,000	103,922,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1966--------	$146,306,000	$137,753,000	$124,538,000	$124,538,000	$129,388,000	$127,188,000	$127,064,000
1967--------	155,528,000	146,854,000	137,175,000	142,613,000	145,113,000	145,113,000	144,805,000
1968--------	167,113,000	163,485,000	160,284,000	160,284,000	164,284,000	160,284,000	155,750,000
1969--------	186,193,000	175,481,000	165,777,000	161,250,000	166,250,000	163,513,500	----------
1970--------	175,899,000	161,786,000	157,803,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1964--------	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000) [1/]	$30,450,000
1965--------	49,147,000	44,487,000	43,152,000	42,696,000	42,696,000	42,696,000	41,320,000
1966--------	60,220,000	55,860,000	53,524,000	53,524,000	55,024,000	55,024,000	53,615,000
1967--------	68,560,000	68,349,000	61,448,000	61,422,000	64,922,000	64,922,000	62,237,000
1968--------	80,292,000	76,211,000	68,621,000	68,621,000	74,621,000	68,621,000	66,824,000
1969--------	80,569,100	77,975,100	75,394,000	70,859,000	76,359,000	73,126,500	----------
1970--------	85,065,000	80,965,000	78,411,000	----------	----------	----------	----------

[1] Congress authorized the transfer of $34,000,000 from other NIH appropriations to establish the National Institute of Child Health and Human Development.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

NATIONAL EYE INSTITUTE

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1970--------	$35,124,000	$35,279,000	$25,778,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

ENVIRONMENTAL HEALTH SCIENCES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1964--------	$10,180,000	$7,029,000	$5,461,000	$4,239,000	$4,239,000	$4,239,000	$4,209,000
1965--------	10,993,000	10,993,000	10,920,000	9,380,000	9,730,000	9,380,000	9,227,000
1966--------	18,367,000	18,049,000	15,933,000	15,933,000	15,983,000	15,983,000	15,735,000
1967--------	32,153,000	26,516,000	24,312,000	24,298,000	24,298,000	24,298,000	11,917,000
1968--------	28,059,000	21,994,000	20,615,000	17,289,000	20,615,000	17,289,000	16,709,000
1969--------	24,559,666	24,319,666	18,099,000	17,541,000	18,099,000	17,820,000	----------
1970--------	19,593,000	19,539,000	19,004,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

GENERAL RESEARCH AND SERVICES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1960--------	$35,299,000	$30,766,000	$28,974,000	$36,404,000	$49,585,000	$45,994,000	$45,789,000
1961--------	52,711,100	47,266,100	47,260,000	52,660,000	104,405,000	83,900,000	83,572,000
1962--------	122,683,000	119,275,000	95,341,000	119,275,000	140,000,000	127,637,000	119,966,000
1963--------	161,851,000	150,300,000	147,826,000	155,826,000	161,826,000	159,826,000	136,126,000
1964--------	211,901,000	179,366,000	164,674,000	163,869,000	164,674,000	163,869,000	150,197,000
1965[1]------	177,357,000	168,321,000	163,146,000	162,390,000	164,190,000	164,190,000	163,502,000
1966[1]------	60,704,000	59,081,000	58,719,000	59,969,000	60,469,000	60,469,000	58,563,000
1967--------	80,156,000	73,834,000	67,821,000	68,534,000	68,534,000	68,534,000	64,468,000
1968--------	101,551,000	98,570,000	81,141,000	81,141,000	84,641,000	81,141,000	76,157,000
1969[2]------	89,880,494	90,441,494	86,900,000	82,719,000	86,900,000	84,809,500	----------
1970[2]------	80,087,000	76,527,000	74,809,000	----------	----------	----------	----------

[1] Excludes the "National Institute of General Medical Sciences" established as a separate appropriation in 1966.

[2] Excludes the "Office of International Operations", transferred to the"National Institute of Allergy and Infectious Diseases" and "Fogarty International Center" in 1970.

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

JOHN E. FOGARTY INTERNATIONAL CENTER
FOR ADVANCED STUDY IN THE HEALTH SCIENCES

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1969--------	$600,000	$600,000	$600,000	$600,000	$600,000	$600,000	----------
1970--------	4,175,000	3,667,000	3,460,000	----------	----------	----------	----------

APPROPRIATION HISTORY AND OBLIGATIONS, 1960-70

SALARIES AND EXPENSES, OFFICE OF THE DIRECTOR

	NIH estimate to Department	Department estimate to Bureau of the Budget	Bureau of the Budget allowance	House allowance	Senate allowance	Appropriation	Obligations
1970--------	$7,193,000	$7,193,000	$7,193,000	----------	----------	----------	----------

HISTORY OF THE 1970 BUDGET

SUMMARY

NATIONAL INSTITUTES OF HEALTH INSTITUTES AND DIVISIONS

(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$704,767	-$55,099	$649,668	-$15,502	$634,166
Fellowships	59,623	-3,214	56,409	-2,827	53,582
Training	149,690	-6,472	143,218	-6,800	136,418
Total grants	914,080	-64,785	849,295	-25,129	824,166
Direct operations:					
Laboratory and clinical research	95,270	-2,215	93,055	-3,894	89,161
Collaborative research and development	146,665	-14,646	132,019	-4,619	127,400
Biometry, epidemiology, and field studies	10,662	84	10,746	-788	9,958
International center	1,864	17	1,881	-141	1,740
Computer research and technology	5,114	-164	4,950	-197	4,753
Biologics standards	9,078	-242	8,836	-498	8,338
Training activities	1,029	-57	972	-119	853
Review and approval of grants	20,107	448	20,555	-641	19,914
Program direction	7,231	-606	6,625	-325	6,300
Management and central services	7,193	.....	7,193	.....	7,193
Total direct operations	304,213	-17,381	286,832	-11,222	275,610
Total obligations	1,218,293	-82,166	1,136,127	-36,351	1,099,776

BIOLOGICS STANDARDS

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Direct operations:					
Biologics standards	$9,078	-$242	$8,836	-$498	$8,338
Total obligations	9,078	-242	8,836	-498	8,338

NATIONAL CANCER INSTITUTE

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$89,944	-$7,546	$82,398	-$1,910	$80,488
Fellowships	4,422	-48	4,374	-173	4,201
Training	12,270	-629	11,641	-455	11,186
Total grants	106,636	-8,223	98,413	-2,538	95,875
Direct operations:					
Laboratory and clinical research	17,155	44	17,199	-21	17,178
Collaborative research and development	74,512	-5,123	69,389	-3,287	66,102
Biometry, epidemiology, and field studies	1,606	33	1,639	-74	1,565
Review and approval of grants	2,626	-1	2,625	-27	2,598
Program direction	1,206	-119	1,087	-3	1,084
Total direct operations	97,105	-5,166	91,939	-3,412	88,527
Total obligations	203,741	-13,389	190,352	-5,950	184,402

NATIONAL HEART INSTITUTE

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$115,552	-$11,023	$104,529	-$3,222	$101,307
Fellowships	7,922	-318	7,604	-295	7,309
Training	18,840	-690	18,150	-708	17,442
Total grants	142,314	-12,031	130,283	-4,225	126,058
Direct operations:					
Laboratory and clinical research	14,405	78	14,483	-842	13,641
Collaborative research and development	24,576	-5,810	18,766	-618	18,148
Biometry, epidemiology, and field studies	1,852	.....	1,852	-128	1,724
Training activities	163	44	207	-3	204
Review and approval of grants	2,561	228	2,789	-16	2,723
Program direction	837	-233	604	39	643
Total direct operations	44,394	-5,693	38,701	-1,618	37,083
Total obligations	186,708	-17,724	168,984	-5,843	163,141

NATIONAL INSTITUTE OF DENTAL RESEARCH

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$17,585	-$1,989	$15,596	-$37	$15,559
Fellowships	1,800	-35	1,765	-71	1,694
Training	5,875	-266	5,609	-219	5,390
Total grants	25,260	-2,290	22,970	-327	22,643
Direct operations:					
Laboratory and clinical research	5,092	-4	5,088	-141	4,947
Collaborative research and development	1,019	-77	942	.....	942
Biometry, epidemiology, and field studies	508	20	528	-92	436
Review and approval of grants	739	-14	725	38	763
Program direction	371	-29	342	-11	331
Total direct operations	7,729	-104	7,625	-206	7,419
Total obligations	32,989	-2,394	30,595	-533	30,062

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$104,086	-$11,464	$92,622	-$333	$92,289
Fellowships	7,037	-300	6,737	-262	6,475
Training	16,703	-594	16,109	-629	15,480
Total grants	127,826	-12,358	115,468	-1,224	114,244
Direct operations:					
Laboratory and clinical research	15,815	-115	15,700	-36	15,664
Collaborative research and development	8,285	-1,491	6,794	-124	6,670
Biometry, epidemiology, and field studies	869	-23	846	-134	712
Review and approval of grants	2,324	43	2,367	6	2,373
Program direction	360	-44	316	-11	305
Total direct operations	27,653	-1,630	26,023	-299	25,724
Total obligations	155,479	-13,988	141,491	-1,523	139,968

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$60,695	-$1,189	$59,506	.....	$59,506
Fellowships	3,347	-134	3,213	-$128	3,085
Training	17,495	-1,836	15,659	-612	15,047
Total grants	81,537	-3,159	78,378	-740	77,638
Direct operations:					
Laboratory and clinical research	10,920	-101	10,819	-719	10,100
Collaborative research and development	10,215	-306	9,909	183	10,092
Biometry, epidemiology, and field studies	2,970	148	3,118	-90	3,028
Training activities	80	-7	73	-1	72
Review and approval of grants	1,813	307	2,120	-6	2,114
Program direction	194	258	452	-11	441
Total direct operations	26,192	299	26,491	-644	25,847
Total obligations	107,729	-2,860	104,869	-1,384	103,485

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$67,827	-$6,942	$60,885	-$303	$60,582
Fellowships	4,754	-392	4,362	-171	4,191
Training	9,640	-152	9,488	-370	9,118
Total grants	82,221	-7,486	74,735	-844	73,891
Direct operations:					
Laboratory and clinical research	16,580	-286	16,294	-1,112	15,182
Collaborative research and development	14,334	-1,401	12,933	-78	12,855
Training activities	196	-38	158	-3	155
Review and approval of grants	1,586	27	1,613	-82	1,531
Program direction	361	-50	311	-3	308
Total direct operations	33,057	-1,748	31,309	-1,278	30,031
Total obligations	115,278	-9,234	106,044	-2,122	103,922

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$95,626	-$10,584	$85,042	-$779	$84,263
Fellowships	22,700	-1,327	21,373	-1,333	20,040
Training	48,667	-1,766	46,901	-1,333	45,568
Total grants	166,993	-13,677	153,316	-3,445	149,871
Direct operations:					
Collaborative research and development	3,946	-257	3,689	-401	3,288
Training activities	498	-52	446	-109	337
Review and approval of grants	3,298	-33	3,265	-14	3,251
Program direction	1,164	-94	1,070	-14	1,056
Total direct operations	8,906	-436	8,470	-538	7,932
Total obligations	175,899	-14,113	161,786	-3,983	157,803

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$51,069	-$3,299	$47,770	-$1,206	$46,564
Fellowships	4,330	-137	4,193	-166	4,027
Training	10,433	-421	10,012	-391	9,621
Total grants	65,832	-3,857	61,975	-1,763	60,212
Direct operations:					
Laboratory and clinical research	7,875	-848	7,027	-654	6,373
Collaborative research and development	6,044	824	6,868	-147	6,721
Biometry, epidemiology, and field studies	2,249	-94	2,155	21	2,176
Training activities	92	-4	88	-3	85
Review and approval of grants	2,031	9	2,040	-3	2,037
Program direction	942	-130	812	-5	807
Total direct operations	19,233	-243	18,990	-791	18,199
Total obligations	85,065	-4,100	80,965	-2,554	78,411

NATIONAL EYE INSTITUTE

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$26,052	.....	$26,052	-$6,392	$19,660
Fellowships	798	.....	798	-148	650
Training	5,381	.....	5,381	-1,919	3,462
Total grants	32,231	.....	32,231	-8,459	23,772
Direct operations:					
Laboratory and clinical research	759	.....	759	-5	754
Collaborative research and development	498	.....	498	-149	349
Biometry, epidemiology, and field studies	608	.....	608	-291	317
Review and approval of grants	856	.....	856	-390	466
Program direction	327	.....	327	-207	120
Total direct operations	3,048	.....	3,048	-1,042	2,006
Total obligations	35,279	.....	35,279	-9,501	25,778

ENVIRONMENTAL HEALTH SCIENCES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$7,868	$1,083	$8,951	$16	$8,967
Fellowships	200	.....	200	-6	194
Training	4,047	-155	3,892	-152	3,740
Total grants	12,115	928	13,043	-142	12,901
Direct operations:					
Laboratory and clinical research	6,669	-983	5,686	-364	5,322
Review and approval of grants	455	-3	452	-9	443
Program direction	354	4	358	-20	338
Total direct operations	7,478	-982	6,496	-393	6,103
Total obligations	19,593	-54	19,539	-535	19,004

GENERAL RESEARCH AND SERVICES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$68,253	-$2,086	$66,167	-$1,336	$64,831
Fellowships	162	-8	154	-8	146
Training	389	-13	376	-12	364
Total grants	68,804	-2,107	66,697	-1,356	65,341
Direct operations:					
Collaborative research and development	3,236	-1,005	2,231	2	2,233
Computer research and technology	5,114	-164	4,950	-197	4,753
Review and approval of grants	1,818	-115	1,703	-88	1,615
Program direction	1,115	-169	946	-79	867
Total direct operations	11,283	-1,453	9,830	-362	9,468
Total obligations	80,087	-3,560	76,527	-1,718	74,809

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Grants:					
Research	$210	-$60	$150	.....	$150
Fellowships	2,101	-465	1,636	-$66	1,570
Total grants	2,311	-525	1,786	-66	1,720
Direct operations:					
International center	1,864	17	1,881	-141	1,740
Total obligations	4,175	-508	3,667	-207	3,460

SALARIES AND EXPENSES, OFFICE OF THE DIRECTOR

Development of 1970 budget estimates
(In thousands)

Obligations by activity	National Institutes of Health to Department of Health, Education and Welfare	Change	Department of Health, Education and Welfare to Bureau of the Budget	Change	President's Budget
Direct operations:					
Management and central services	$7,193	.....	$7,193	.....	$7,193
Total obligations	7,193	.....	7,193	.....	7,193

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

History of 1970 Budget

Summary
(In thousands)

Obligations by activity	National Institute of Mental Health to Health Services and Mental Health Administration	Change	Preliminary estimate to Department of Health, Education, and Welfare	Change	Department of Health, Education, and Welfare to Bureau of the Budget	Change	President's budget
Support and conduct of research:							
Grants:							
Research	$111,190	-$17,913	$93,277	-$5,741	$87,536	-$5,263	$82,273
Hospital improvement	13,110	-1,000	12,110	-10	12,100	-4,100	8,000
Early child care demonstrations	14,500	-14,500	---	+5,000	5,000	-4,000	1,000
Direct operations:							
Intramural Research	20,688	-2,354	18,334	---	18,334	-75	18,259
Planning, development and administration	9,464	-2,266	7,198	-1,241	5,957	-182	5,775
Manpower development:							
Grants:							
Training	131,030	-16,050	114,980	+654	115,634	-3,134	112,500
Fellowships	14,385	-3,519	10,866	---	10,866	---	10,866
Direct operations	5,384	-600	4,784	-30	4,754	-171	4,583
Support of State and community programs:							
Grants:							
Construction of community mental health centers	60,000	-14,500	45,500	-6,000	39,500	-9,000	30,500
Staffing of community mental health centers	79,914	-5,714	74,200	-8,400	65,800	-14,500	51,300

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

History of 1970 Budget (continued)

Summary
(In thousands)

Obligations by activity	National Institute of Mental Health to Health Services and Mental Health Administration	Change	Preliminary estimate to Department of Health, Education, and Welfare	Change	Department of Health, Education, and Welfare to Bureau of the Budget	Change	President's budget
Support of State and community programs: (cont'd)							
Grants:							
Narcotic addiction and alcoholism community assistance.....	25,000	-17,000	8,000	+4,000	12,000	---	12,000
Direct operations.....	4,559	-2,137	2,422	-43	2,379	---	2,379
Service activities:							
Narcotic addiction and drug abuse treatment and research	25,772	-6,903	18,868	-538	18,330	-874	17,456
Regional and field activities.....	2,436	-90	2,346	---	2,346	---	2,346
Scientific communication and public education.....	4,131	-1,360	2,771	---	2,771	---	2,771
Program direction and management services	7,281	-1,847	5,434	-99	5,335	-214	5,121
Total estimate.....	528,844	-107,753	421,090	-12,448	408,642	-41,513	367,129

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION - NATIONAL INSTITUTE OF MENTAL HEALTH

Saint Elizabeths Hospital

History of 1970 Budget

Summary
(In thousands)

Obligations by activity	Saint Elizabeth's Hospital to Health Services and Mental Health Administration	Change	Preliminary estimate to Department of Health, Education, and Welfare	Change	Department of Health, Education, and Welfare to Bureau of the Budget	Change	President's budget
Salaries and Expenses.....	$41,511	-$1,630	$39,881	---	$39,881	-$1,005	$38,876
Less Reimbursements.....	28,513	-658	29,171	---	29,171	-700	28,471
Direct Appropriation.....	$12,998	-2,278	10,710	---	10,710	-305	10,405

NATIONAL INSTITUTES OF HEALTH

YEAR END STATUS OF EXTRAMURAL PROGRAMS

RESEARCH GRANTS-REGULAR PROGRAM [1]

(Dollar amounts in thousands)

	1967		1968		1969 estimate		1970 estimate	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Cancer:								
Funded	1,210	$57,267	1,153	$58,274	1,113	$58,613	1,108	$59,056
Unfunded	148	4,583	128	4,537	170	7,357	209	9,542
Heart:								
Funded	2,032	88,473	1,783	86,007	1,500	80,833	1,386	81,474
Unfunded	100	4,220	261	8,786	197	9,792	206	11,581
Dental:								
Funded	314	10,792	297	10,872	224	10,419	270	10,502
Unfunded	54	1,482	26	871	104	4,738	60	3,373
Arthritis:								
Funded	2,490	81,408	2,316	83,132	2,137	80,762	2,100	81,360
Unfunded	246	6,240	316	8,995	363	12,800	280	10,560
Neurology:								
Funded	1,641	60,169	1,638	61,909	1,599	63,755	1,735	67,281
Unfunded	31	722	110	3,410	266	11,577	241	12,279
Allergy:								
Funded	1,281	42,776	1,335	49,029	1,205	50,346	1,289	50,761
Unfunded	155	4,613	215	6,815	286	10,267	324	13,149
NIGMS:								
Funded	1,620	63,388	1,432	69,291	1,407	69,653	1,418	70,206
Unfunded	450	17,282	528	17,505	372	17,598	459	19,705
NICHD:								
Funded	1,072	36,674	969	37,655	909	34,997	964	38,495
Unfunded	104	3,863	130	3,861	154	7,554	236	10,790
DEHS:								
Funded	81	3,699	82	4,949	73	4,855	100	4,900
Unfunded					15	507	14	455
Fogarty:								
Funded	138	364	94	209	55	130	55	130
Unfunded								
Subtotal:								
Funded	11,879	445,010	11,099	461,327	10,222	454,363	10,425	464,165
Unfunded	1,288	43,005	1,714	54,780	1,927	82,190	2,029	91,434
NLM:								
Funded	31	597	54	1,261	47	1,321	55	1,480
Unfunded	1	338	3	186	4	112	5	140
BHPEMT:								
Funded	84	3,239	105	4,242	94	4,754	88	5,066
Unfunded	19	847	16	828	22	1,206	30	1,745
Total NIH:								
Funded	11,994	448,846	11,258	466,830	10,363	460,438	10,568	470,711
Unfunded	1,308	44,190	1,733	55,794	1,953	83,508	2,064	93,319

[1] Excludes special research grant programs with unfunded applications totaling $8,780 in 1967, $12,825 in 1968, $28,887 in 1969, and $53,759 in 1970.

YEAR END STATUS OF EXTRAMURAL PROGRAMS-Continued

FELLOWSHIPS

(Dollar amounts in thousands)

	1967		1968		1969 estimate		1970 estimate	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Cancer:								
Funded	248	$3,171	305	$4,019	299	$4,374	285	$4,201
Unfunded			1	11	98	982	114	1,424
Heart:								
Funded	395	6,508	390	6,769	418	7,604	365	7,309
Unfunded							55	661
Dental:								
Funded	113	1,552	123	1,722	121	1,765	113	1,694
Unfunded					13	154	26	252
Arthritis:								
Funded	433	6,077	446	6,574	467	6,737	430	6,475
Unfunded			106	1,028	25	261	30	275
Neurology:								
Funded	237	3,434	242	3,757	233	3,889	203	3,735
Unfunded	9	70	1	20	44	562	82	885
Allergy:								
Funded	251	3,447	262	3,912	274	4,362	240	4,191
Unfunded			9	83	15	120	25	362
NIGMS:								
Funded	2,395	19,400	2,357	20,207	2,333	21,373	1,991	20,040
Unfunded	984	6,572	1,058	7,616	924	7,096	1,269	8,460
NICHD:								
Funded	262	3,724	234	3,664	252	4,193	207	4,027
Unfunded			3	29	5	72	57	577
DEHS:								
Funded	15	99	5	42	20	200	18	194
Unfunded								
GkS-DRFR:								
Funded	5	41	16	148	15	154	15	146
Unfunded					5	55	8	84
Fogarty:								
Funded	165	1,200	159	1,378	196	1,636	183	1,570
Unfunded	25	223	37	233	22	236	37	355
Subtotal:								
Funded	4,519	48,653	4,539	52,192	4,628	56,287	4,050	53,582
Unfunded	1,018	6,865	1,215	9,020	1,151	9,538	1,703	13,335
BHPEMT:								
Funded	108	501	123	620	143	800	140	800
Unfunded	3	17	3	15	5	28	38	228
Total NIH:								
Funded	4,627	49,154	4,662	52,812	4,771	57,087	4,190	54,382
Unfunded	1,021	6,882	1,218	9,035	1,156	9,566	1,741	13,563

YEAR END STATUS OF EXTRAMURAL PROGRAMS-Continued

TRAINING GRANTS

(Dollar amounts in thousands)

	1967		1968		1969 estimate		1970 estimate	
	Number	Amount	Number	Amount	Number	Amount	Number	Amount
Cancer:								
Funded	180	$12,015	199	$11,050	191	$11,641	182	$11,186
Unfunded	5	135	5	323	11	660	20	1,731
Heart:								
Funded	396	17,752	395	17,267	397	18,150	378	17,442
Unfunded	12	376	8	343	6	205	25	1,306
Dental:								
Funded	108	5,398	102	5,280	98	5,609	91	5,390
Unfunded	4	86	3	104	1	57	13	746
Arthritis:								
Funded	309	14,855	311	15,383	304	16,109	286	15,480
Unfunded	10	367	6	360	----	----	----	----
Neurology:								
Funded	469	18,515	505	18,508	509	19,262	485	18,509
Unfunded	----	----	24	2,316	62	4,444	120	7,627
Allergy:								
Funded	189	8,916	182	8,855	174	9,488	156	9,118
Unfunded	4	204	7	297	4	157	14	1,016
NIGMS:								
Funded	674	43,735	637	44,729	588	46,901	525	45,568
Unfunded	122	5,126	91	4,151	66	5,420	82	7,996
NICHD:								
Funded	143	9,279	151	9,747	150	10,012	127	9,621
Unfunded	----	----	9	1,116	17	2,153	42	3,649
DEHS:								
Funded	47	3,693	50	3,763	44	3,892	47	3,740
Unfunded	----	----	----	----	3	143	5	292
GRS-DRFR:								
Funded	6	245	8	368	7	376	9	364
Unfunded	----	----	2	108	3	180	3	235
Subtotal:								
Funded	2,521	134,403	2,540	134,951	2,462	141,440	2,286	136,418
Unfunded	157	6,294	155	9,118	173	13,419	324	24,598
NLM:								
Funded	17	812	18	922	18	1,137	15	1,021
Unfunded	5	331	5	198	2	132	7	467
BHPEMT:								
Funded	886	26,087	889	27,257	819	29,287	819	30,711
Unfunded	28	1,112	73	2,731	89	5,025	109	8,880
Total NIH:								
Funded	3,424	161,302	3,447	163,130	3,299	171,864	3,120	168,150
Unfunded	190	7,737	233	12,047	264	18,576	440	33,945

DESCRIPTION OF EACH NIH GRANT PROGRAM

The data presented below include data from the National Institute of Mental Health through 1966, NIMH became a separate Bureau in 1967. The data includes the Division of Environmental Health Sciences beginning with 1967 when it became an NIH component. It does not include data for the Bureau of Health Manpower and the National Library of Medicine, although they became components of NIH in 1970.

REGULAR RESEARCH GRANTS

1. Purpose of program

To provide grant support of research in health, medicine, and allied fields with the major objectives (1) of continuing existing programs of research, (2) of expanding medical and biological research activities in universities, hospitals, laboratories, and other public or private institutions and (3) of stimulating new investigations in fields needing exploration. The grants range from support of smaller, discrete, and circumscribed projects, which are defined as project grants, to support of broad programs which integrate the research interests of several investigators, and which are called program project grants.

2. Funds

1959 obligations	$139,629,000
1960 obligations	185,474,000
1961 obligations	240,607,000
1962 obligations	305,527,000
1963 obligations	353,102,000
1964 obligations	401,868,000
1965 obligations	425,516,000
1966 obligations	461,756,000
1967 obligations	448,431,000
1968 obligations	461,327,000
1969 estimates	454,363,000
1970 estimates	464,165,000

3. Present stage of development

The modest cancer grants program of 1938-1945 of less than $100,000 annually changed in 1946 to a health, medicine, and related sciences program of $780,000. Steady annual increases since 1946 have produced the 1969 program of about $617,000,000 in regular and special research grant programs. This will support about 10,800 research projects conducted in over 1,600 institutions throughout this country and abroad, and covering the full range of biological and related research. While the program continues in major part to support the ideas of investigators in the grantee institutions, a significant part of the grants provide support of programs reflecting initiative of NIH staff, such as cancer chemotherapy and psychopharmacology.

4. Plans for the future

The NIH believes that medical research should continue to expand as long as this country is faced with major crippling and killing diseases and conditions. Further, it believes that a number of factors contribute together to provide full assurance that substantial expansion can be effected. These factors include (1) a sharp expansion in the population base from which new M.D.'s and PH.D's will be drawn, (2) a steadily rising college enrollment, (3) significant percentage increase in graduate enrollment, and (4) improving educational opportunities for the more talented students, including both new medical schools and strengthened graduate and professional schools.

GENERAL RESEARCH SUPPORT GRANTS

1. Purpose of program

To provide funds for the general support of the medical research and research training programs of institutions under conditions enabling the recipients to meet needs which could not be effectively met by other forms of support. The grants can be utilized for such purposes as capitalizing on emerging research opportunities, exploring new and unorthodox ideas, or stimulating and developing an over-all research or research training program. The broad type of support made possible through these grants can enable an institution to achieve a better balance of their total research and training programs, and permit the recipient institutions to strengthen their overall biomedical research capabilities under conditions and in directions of their own choice.

2. Funds

The amount available for distribution to this program constitutes "such uniform percentage, not to exceed 15 per centum, as the Surgeon General may determine, of the amounts provided for grants for research projects for any fiscal year through the appropriations for the National Institutes of Health..." (Public Law 86-798).

1962 obligations	$20,000,000
1963 obligations	30,000,000
1964 obligations	35,000,000
1965 obligations	45,000,000
1966 obligations	45,200,000
1967 obligations	1/ 51,700,000
1968 obligations	1/ 59,674,445
1969 estimates	1/ 60,700,000
1970 estimates	1/ 61,500,000

1/ An amount for NIMH is included here (1967--$6,434,000; 1968--$5,483,000; 1969--$7,755,000; 1970--$7,863,000) inasmuch as the total is obligated through NIH.

3. Present stage of development

In 1969 general research support grants will provide support for 330 health professional schools, hospitals, research institutes, laboratories, centers and certain other nonprofit research organizations heavily engaged in health related research. In addition approximately 108 academic institutions other than health professional schools will be supported. Approximately 12 institutional advancement awards will also be made. These awards are intended to encourage the recipient institutions to enter the health research field for the first time or to expand and improve their present biomedical research activities.

4. Plans for the future

The 1970 President's budget continues this program with an increased level of support, including support for 344 institutions or organizations under the basic program 115 biomedical sciences support grants to academic institutions and 12 Health-Sciences Advancement Awards.

INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING

1. Purpose of program

Research grants are awarded in this program to American universities to enable these universities to establish centers within both their own organizations, and in affiliate centers within foreign institutions to broaden collaborative research and research training in the biomedical fields.

2. Funds

In 1961, this program was administered by the National Institute of Allergy and Infectious Diseases and supported by six of the Institutes plus the Division of General Medical Sciences. This same situation existed in 1962 except for the absorption by Allergy of the support of Heart and Arthritis Institutes. In 1963, the program was administered by the Office of International Research, OIR, part of the Office of the Director, NIH. In 1964, OIR was incorporated into the GRS appropriation. In 1969 this activity was transferred to the NIAID and in 1970 will become the responsibility of the National Institute of Allergy and Infectious Diseases.

1962 obligations	$2,093,000
1963 obligations	2,483,000
1964 obligations	2,484,000
1965 obligations	2,511,000
1966 obligations	2,473,000
1967 obligations	2,360,000
1968 obligations	2,314,000
1969 estimates	2,300,000
1970 estimates	2,300,000

3. Present stage of development

The initial phase of the program devoted to the administratively complex task of developing foreign research resources in collaboration with selected foreign universities and research institutions has been completed in each of the centers. All centers are now actively engaged in specific research projects.

A substantial portion of current research is focused upon the demography, epidemiology, and ecology of disease states which are of concern to the United States and the host nation. A multidisciplinary approach is being developed within the several centers to study more effectively the complex biomedical problems which prevail at the foreign sites. As a consequence, professional staffs are being developed and trained to investigate, through a selective amalgamation of basic science, clinical and public health research methods, not only tropical diseases, but a wide variety of other disease states which exist in these countries. Accordingly, the scientific programs in each center will progressively encompass a wide spectrum of factors which directly or indirectly influence disease in the United States and abroad.

These programs include studies of environmental factors which may be related to the development and persistence of acute and chronic diseases. The presence of distinct ethnic and demographic groups in foreign areas permit studies in depth of physical and biomedical factors which may be involved in racial susceptibility to disease.

In addition to the research in progress and being planned, each university is creating an effective training program for U. S. citizens at both the domestic and overseas sites.

The cooperating institutions of the five International Centers now in operation are as follows:

U. S. University	Foreign Cooperating Institutions
John Hopkins University	All India Institute of Hygiene and Calcutta School of Tropical Medicine, Calcutta, India
University of California	Institute of Medical Research, Kuala Lumpur, Federation of Malaysia
Tulane University	Universidad del Valle, Cali, Colombia
Louisiana State University	University of Costa Rica, San Jose
University of Maryland	Institute of Hygiene and Lahore General Hospital, Lahore, West Pakistan

4. Plans for the future

The 1970 President's budget will permit the continuation of the existing five centers.

SCIENTIFIC EVALUATION AND PLANNING GRANTS (CHAIRMAN'S GRANTS)

1. Purpose of the program

To provide funds for the assistance of the national Advisory councils through the technical and scientific review of research grant applications, and through the support of meetings used for the exchange of scientific views.

2. Funds

1962 obligations	$1,244,000
1963 obligations	1,516,000
1964 obligations	1,847,000
1965 obligations	2,030,000
1966 obligations	2,163,000
1967 obligations	2,040,000
1968 obligations	2,134,000
1969 estimates	2,443,000
1970 estimates	2,443,000

3. Present stage of development

Research grant applications are reviewed prior to submission to the advisory councils by the appropriate study section. Each of these more than 50 sections has scientific competency in a particular field or research discipline. Each section is comprised of outstanding leaders in the relevant specialities who are usually not employees of the Federal Government.

In addition to financing these review activities, chairman's grants support an extensive group of ad hoc panels, symposia, converences, and other types of meetings used for the exchange of professional views.

CLINICAL RESEARCH CENTERS

(Includes physical resources portions of program projects)

1. Purpose of program

To provide grants to non-Federal research institutions for the establishment and support of biomedical research resources centers. These centers make possible the performance of meritorious and complex clinical investigation in the preclinical, clinical, and health-related sciences. They provide the opportunity for precise observations and controls which are essential to studies with patients. These centers administratively may be viewed as (a) categorical and (b) general. The categorical centers are supported by the appropriate Institute and are concerned primarily with a specific category or type of disease, such as heart disease, toward which the work of the particular Institute is oriented. In the general clinical research centers program, which is supported by the Division of Research Facilities and Resources, the research activity is not focused primarily on a single Institute-related category of disease, but rather on categories of disease and on numerous areas of preclinical and clinical science. All centers consist of discrete facilities with specialized bed arrangements, core laboratories, and trained personnel. They use a multidisciplinary approach where investigators with varied interests and techniques share the center's facilities. The centers are highly conducive to the advancement of knowledge regarding human health and disease.

2. Funding of clinical research centers program (research center grants and physical resource component of program project grants)

(See the following table.)

3. Present stage of development

The Centers program had its inception in 1960 with an appropriation for general clinical centers. By the close of 1969 awards will have been made to approximately 93 general clinical research centers.

Seventy-eight categorical center grants had been awarded by the close of fiscal year 1968. As with the general clinical research centers program, the categorical programs have yielded important scientific accomplishments.

4. Plans for the future

The 1970 President's budget will be directed toward providing continuing and supplemental support to the centers receiving awards in 1969.

FUNDING OF CLINICAL RESEARCH CENTERS PROGRAM

Research center grants and physical resource component of program project grants

(In thousands)

	Obligations, 1962	Obligations, 1963	Obligations, 1964	Obligations, 1965	Obligations, 1966	Obligations, 1967	Obligations, 1968	Estimates, 1969	Estimates, 1970
Division of research facilities and resources	$22,123	$17,374	$27,057	$26,906	$28,500	$28,463	$30,443	$35,004	$38,964
Child Health	-------	-------	-------	209	198	112	330	500	500
Cancer	805	4,437	4,849	4,898	7,283	1/	1/	1/	1/
Mental	700	781	1,604	1,379	1,292	-------	-------	-------	-------
Heart	1,782	2,048	1,597	1,580	4,500	4,500	4,500	4,500	4,500
Dental	-------	-------	-------	212	344	212	327	400	400
Arthritis	481	1,119	1,202	1,249	1,500	1,500	1,500	1,500	1,500
Allergy	500	237	852	949	881	1,099	869	1,100	1,100
Neurology	577	1,353	1,200	1,200	3,000	3,150	3,005	3,150	2,416 2/
Eye	-------	-------	-------	-------	-------	-------	-------	-------	734
Total	26,968	27,349	38,361	38,582	47,498	39,036	40,974	46,154	50,114

1/ Beginning with 1967 the Cancer Institute funds are included in the table for specialized research centers.

2/ Excludes funds for the "National Eye Institute" established as a separate institute in 1970.

SPECIAL RESEARCH RESOURCES

1. Purpose of program

To provide grants to non-Federal research institutions for support of specialized facilities that provide the basic tools of research and specialized services necessary for the support of institutional research programs. Many areas of such research (such as determination of molecular structure or genetic codes) are enormously dependent upon computer resources, specialized instrumentation and/or commercially unobtainable biological materials. Since facilities to fulfill these needs are usually too costly or to extensive in capability to be assigned or managed by a single investigator, a Special Research Resource is established for use by a community of scientists; the basis for organization can be institutional, regional (city, state, section), or national. The needs of universities, hospitals, and other institutions for computer resources and centralized instrumentation facilities, for laboratories devoted to large-scale preparation of commercially unavailable biological materials, and other Special Research Resources is growing rapidly as the sophistication, capabilities, and costs of modern research increases. Such tools may consist of computers, highly trained technical staff, costly and complex instrumentation, or other aids to a large research operations.

2. Funds

1962 obligations	$4,329,000
1963 obligations	6,117,000
1964 obligations	5,077,000
1965 obligations	8,169,000
1966 obligations	10,618,000
1967 obligations	10,850,000
1968 obligations	10,529,000
1969 estimates	10,494,000
1970 estimates	10,494,000

3. Present stage of development

Program plans for 1969 call for the continuation of support for 45 established resources.

4. Plans for the future

The 1970 President's budget will provide for the continued funding of the existing specialized resources.

ANIMAL RESOURCES

1. Purpose of program

This program is designed to provide grants supportive of facilities which supply laboratory animals for institutional research and do research in laboratory animal medicine. Such grants support renovation and upgrading of animal facilities and research oriented toward improving the stock, health, and well-being of laboratory animals.

2. Funds

1965 obligations	$819,000
1966 obligations	1,527,000
1967 obligations	3,100,000
1968 obligations	5,100,000
1969 estimates	4,568,000
1970 estimates	4,568,000

3. Present stage of development

Plans call for the continuation of support for 45 facilities and the funding of approximately 10 additional resources.

4. Plans for the future

The 1970 President's budget will provide for grants to approximately 7 new resources.

PRIMATE RESEARCH CENTERS PROGRAM

1. Purpose of program

To provide funds for the construction and basic operation of special research facilities or centers devoted to the advancement of all areas of knowledge on the biological characteristics of species structurally and physiologically similar to man throughout the entire lifespan of the subhuman primate. The objective is to acquire basic scientific information which will ultimately be useful in the prevention and treatment of human disease. Research facilities provided by this program are available to visiting scientists from all areas of this country and abroad.

2. Funds

1962 obligations	$9,495,000
1963 obligations	4,444,000
1964 obligations	6,194,000
1965 obligations	7,000,000
1966 obligations	7,000,000
1967 obligations	9,000,000
1968 obligations	10,500,000
1969 estimates	10,500,000
1970 estimates	10,500,000

3. Present stage of development

This program has six regional and one national center, the latter committed to research on the primate itself. The operating award is made each year after a detailed review of the proposed budget by the Division.

4. Plans for the future

The requested funds in the 1970 President's budget will provide for the support, maintenance and some supplementation of the existing seven centers.

LEUKEMIA RESEARCH SUPPORT CENTERS

1. Funds for the program

Leukemia research support centers are utilized to make platelet transfusions and domiciliary care available to children under treatment of leukemia. Platelet transfusions are an essential factor in the modern treatment of childhood leukemia. Marked improvement in the results of anti-leukemic therapy have followed upon the use of this technique. The massive platelet transfusions required have not been widely available and this program provides for the preparation, administration and evaluation of platelet transfusions in institutions across the country responsible for the care of leukemic children.

2. Funds

1966 obligations	$824,000
1967 obligations	1,425,000
1968 obligations	1,257,000
1969 estimates	1,500,000
1970 estimates	1,500,000

3. Present stage of development

In 1969 approximately 30 leukemia centers will be funded. Research on outpatient and inpatient basis, involving new drugs and blood platelet transfusions, will continue.

4. Plans for the future

The President's budget provides continuing support at the same level for 1970. Greater selectivity in funding is anticipated in 1970 with an expected increase in applications. Platelet replacement therapy in connection with the administration of control drugs will continue to be studied.

HEART COOPERATIVE DRUG STUDY

1. Purpose of program

This program is designed and organized as a national cooperative study to determine whether several lipid-lowering drugs will, over prolonged periods of use, reduce the mortality or morbidity of coronary heart disease.

2. Funds

1965 obligations	$447,000
1966 obligations	1,770,000
1967 obligations	3,433,000
1968 obligations	3,820,000
1969 estimates	3,820,000
1970 estimates	4,820,000

(Some additional funds for the study are included in direct operations amounts.)

3. Present stage of development

The feasibility of the study was affirmed over a two year period and the study proper initiated in 1965 with grants for the support of four participating clinics and coordinating center. During 1966 and 1967 the study was expanded to a full complement of 55 clinics.

4. Plans for the future

With the enrollment of clinics completed, more than 6,000 patients have now been enrolled. It is anticipated that in July, 1969, this program will have reached the goal of 8,200 calculated as necessary for statistical validity of the final measured results over a 5 year period of follow-up.

PHARMACOLOGY-TOXICOLOGY RESEARCH CENTERS

1. Purpose of program

The purpose of this program is to extend the program efforts of NIGMS in pharmacology and toxicology and to provide funds for the planning, initiation, and support of centers or large scale projects for research in areas of pharmacology and toxicology related to the use of drugs and chemical toxication. These programs are university based and located in appropriate academic and scientific environments.

2. Funds

1966 obligations	$1,000,000
1967 obligations	3,358,617
1968 obligations	3,500,000
1969 estimates	3,500,000
1970 estimates	3,500,000

3. Present stage of development

The program was initiated in 1966. Nine centers and two large scale projects are presently being supported. Greater emphasis is being placed on clinical pharmacology and implications of new knowledge as it relates to man.

4. Plans for the future

The President's budget will provide continuing support for the program. Particular emphasis will be placed on further development of the clinical aspects of the program.

DENTAL RESEARCH INSTITUTES (CENTERS)

1. Purpose of program

The purpose of this program is to provide funds for the development and operation of dental research institutes as centers of excellence in the sciences related to oral health. Organized on an interdisciplinary basis, these institutes support highly competent researchers as they deal with problems specifically related to oral health as well as perform research in the broader biological sciences and engineering and other physiochemical sciences. In addition, the institutes offer a unique environment for the training of researchers and academicians.

2. Funds

1967 obligations	$2,996,000
1968 obligations	3,000,000
1969 estimates	3,000,000
1970 estimates	3,400,000

3. Present stage of development

Currently, five dental research institutes are in various stages of development at the following universities: Alabama, Michigan, North Carolina, Pennsylvania, and Washington.

4. Plans for the future

The President's budget provides continuing support for the five institutes initially established.

ANESTHESIOLOGY AND DIAGNOSTIC RADIOLOGY CENTERS

1. Purpose of program

The purpose of the anesthesiology and diagnostic radiology centers program is to provide research support for clinical and laboratory investigation related to eaching and patient care in these fields. One aspect of the program will be concerned with research leading to the development and evaluation of new techniques, bringing the fruits of biomedical engineering to the improvement of these specialties which are essential to all branches of health care.

2. Funds

1967 obligations	$500,000
1968 obligations	1,000,000
1969 estimates	1,000,000
1970 estimates	1,000,000

3. Present stage of development

The program was initiated in 1967. Four centers have been established to date.

4. Plans for the future

The amounts in the President's budget provide for the continuing support of the already established centers.

SPECIALIZED RESEARCH CENTERS

1. Purpose of program

The initial design of this program was to provide support for planning and operational grants for specialized centers in the Heart Disease, Cancer and Stroke areas. Each of the three Institutes involved makes awards in its own field for analyses of major problems and for the development of programs and resources, i.e., center establishments, to deal in depth with these disease areas.

2. Funds

	Obligations		
	1968 Actual	1969 Estimate	1970 Estimate
Heart	$584,000	$925,000	$925,000
Cancer	12,582,000	12,950,000	12,950,000
Neurology	747,000	850,000	850,000
Total	13,913,000	14,725,000	14,725,000

3. Present stage of development

Since 1966 the Heart Institute has awarded or approved grants to 14 institutions for planning cardiovascular research and training centers. These awards are for programs of existing or potential excellence and are expected to complete for major operational center funds within the next several years. Cancer Institute now supports 31 specialized research centers which are performing intensive, highly specialized clinical research or laboratory research relating to prevention, diagnosis, and treatment of cancer in man. In addition, the Cancer Institute supports planning grants which are for costs incurred by institutions in the development of longterm plans for cancer research, training, and clinical services. Neurology Institute had 15 centers in 1968; 15 will be in operation during 1969.

4. Plans for the future

Funds in the President's budget will provide for continued planning support to the 1969 awardee institutions as well as a few new developmental awards. The long range plans of the Heart Institute provide for 12 specialized cardiovascular research and training centers during the next five years. Cancer and Neurology Institutes plan to continue the same number of centers in 1970 as in 1969.

ENVIRONMENTAL HEALTH SCIENCE CENTERS

1. Purpose of program

The purpose of the environmental health science centers is to establish university-based resources for both research and training which are embedded in the substance of graduate education. The programs embrace numerous facets of environmental health research--clinical and nonclinical activity, routine work and highly original studies, investigations by individuals and by teams, field studies, etc. They also permit advanced training in environmental health research in a depth that is relatively unavailable elsewhere. University-based center grants may provide for common-use equipment, special laboratories, and salaries for a core group of scientists and administrative personnel. Individual studies are generally supported by funds from other sources.

2. Funds

1967 obligations	$2,529,000
1968 obligations	3,000,000
1969 estimates	3,000,000
1970 estimates	3,500,000

3. Present stage of development

In 1969 the Institute is supporting five university-based centers that have operational status and one that is in the terminal year of a pilot effort.

4. Plans for the future

Funding at the requested level in 1970 would permit further development of the five ongoing centers, transition of the pilot center to operational status, and the establishment of two new centers.

REGULAR RESEARCH FELLOWSHIPS

NOTE: In this, and the following sections on Fellowships and Training grants, data through 1966 include amounts for the National Institute of Mental Health. Beginning with 1967, pursuant to the reorganization of the Public Health Service, the tables omit NIMH but include the Division of Environmental Health Sciences. The principal effects of this change are in Predoctoral Fellowships and in Training grants where there are reductions in 1967 over the amounts shown for 1966. It does not include data for the Bureau of Health Manpower and the National Library of Medicine, although they became components of NIH in 1970.

1. Purpose of program

The purpose of this program is to increase the supply of manpower available for research and teaching by providing qualified individuals with support for training in health related fields. There are three major categories or regular research fellowships; predoctoral, postdoctoral, and special.

Predoctoral fellowships provide assistance to individuals who have a bachelor's degree for further training leading to a doctoral degree. Postdoctoral fellowships support advanced training for an individual who has already earned a Ph.D., M.D., D.D.S., D.V.M., or equivalent degree. Special fellowships are designed to meet training needs not met by other fellowship programs, by supporting qualified investigators who require additional specialized training.

2. Funds

	Predoctoral	Postdoctoral	Special	Total
1959 obligations	$3,180,000	$3,728,000	$901,000	$7,809,000
1960 obligations	4,783,000	5,332,000	1,342,000	11,457,000
1961 obligations	5,200,000	6,857,000	2,188,000	14,245,000
1962 obligations	4,706,000	8,597,000	2,509,000	15,812,000
1963 obligations	7,869,000	8,626,000	3,642,000	20,137,000
1964 obligations	8,522,000	8,460,000	4,233,000	21,215,000
1965 obligations	10,638,000	8,312,000	5,053,000	24,003,000
1966 obligations	12,368,000	8,493,000	5,818,000	26,679,000
1967 obligations	8,234,000	7,999,000	5,920,000	22,153,000
1968 obligations	7,875,000	8,790,000	7,124,000	23,789,000
1969 estimates	8,073,000	9,167,000	7,911,000	25,151,000
1970 estimates	7,061,000	7,666,000	6,984,000	21,711,000

3. Number of awards

	Predoctoral	Postdoctoral	Special	Total
1962 actual	1,469	1,229	273	2,971
1963 actual	1,533	1,210	386	3,129
1964 actual	1,665	1,181	422	3,268
1965 actual	1,964	1,194	501	3,659
1966 actual	2,323	1,287	582	4,192
1967 actual	1,586	1,086	522	3,194
1968 actual	1,556	1,058	579	3,193
1969 estimates	1,428	1,075	623	3,126
1970 estimates	1,221	871	511	2,603

4. Present stage of development

The decrease in the total number of fellowships shown in this program in 1969 is due primarily to increases in the cost of stipends and an increase in the number of special fellowships which have a higher average cost than pre- and post-doctoral fellowships.

5. Plans for the future

The number of fellowships supported in 1970 will decrease by 523 from the number supported in 1969. There is a corresponding decrease in funds available for 1970.

INTERNATIONAL POSTDOCTORAL FELLOWSHIPS

1. Purpose of program

This program provides awards to promising foreign scientists to support their training in the United States. While these awards contribute to the improvement of foreign research capabilities, the primary objectives of this program are domestic. These objectives are achieved by enabling foreign investigators to share their ideas and background with American colleagues, and by encouraging foreign scientists to participate in research bearing on American health problems. As this research is often continued and extended by the fellow upon return to his home, additional opportunities are created for future collaborative efforts in research endeavors of importance to the United States.

2. Funds and number of awards

	Number	Amount
1959 obligations	45	$345,000
1960 obligations	52	400,000
1961 obligations	92	700,000
1962 obligations	91	700,000
1963 obligations	172	1,198,000
1964 obligations	177	1,199,000
1965 obligations	184	1,177,000
1966 obligations	166	1,199,000
1967 obligations	155	1,200,000
1968 obligations	159	1,378,000
1969 estimates	168	1,411,000
1970 estimates	167	1,400,000

3. Present stage of development

This program was established in Western Europe in 1958 with 12 countries participating. Plans were made at that time for an orderly increase in the number of participating countries based on research potential and likelihood that returning fellows would use training in the United States. The increase in the number of countries participating has progressed according to schedule as follows: 1959, 30; 1960, 36; 1961, 40; 1962 and 1963, 41; 1964 and 1965, 42; 1966 through 1968, 43; 1969 and 1970, 44.

4. Plans for the future

In 1970 approximately 167 fellows will be supported. This is a decrease of one over the number supported in 1969.

RESEARCH CAREER PROGRAM

1. Purpose of program

This program is designed to increase the number of stable full-time career opportunities for scientists of superior potential and capability in the sciences related to health. The program consists of two types of awards; career awards and career development awards. Career awards support established investigators of high competence for the duration of their careers. Career development awards support qualified scientists who have three years or more of relevant postdoctor research or professional experience and who require additional training in preparation for careers in independent research. Development awards are normally made for five years and may be extended for not more than a total of ten years.

2. Funds and number of awards

	Number	Amount
1962 obligations	630	$10,012,000
1963 obligations	893	14,224,000
1964 obligations	1,078	19,811,000
1965 obligations	3,659	22,448,000
1966 obligations	4,192	25,937,000
1967 obligations	1,159	25,292,000
1968 obligations	1,157	26,840,000
1969 estimates	1,213	29,421,000
1970 estimates	1,197	30,133,000

3. Present stage of development

Approximately 1,213 fellows will be supported in 1969. This is the sum of 159 Research Career Awards, a decrease of 4 from the 1968 level, and 1,054 Research Career Development Awards, an increase of 60 over 1968.

4. Plans for the future

During 1970, about 1,197 career fellowships will be supported. This represents a decrease of 11 Research Career Development Awards and a decrease of 5 Research Career Awards over the number supported in 1969.

FOGARTY SCHOLARSHIPS

1. Purpose of program

This program is designed to provide an environment conducive to the discussion, expansion and evolution of ideas between distinguished leaders in science, scholars in other disciplines and other creative individuals. The program proposes to select outstanding scientists and scholars from the international biomedical community, bring them to the Center and have them focus their attention on broad aspects of important issues raised by the findings of modern biomedical research.

2. Funds

1969 estimates	$225,000
1970 estimates	170,000

3. Present stage of development

The program is new and most efforts have been devoted to the development of the program. It is expected that by the end of fiscal 1969 plans should be completed and scholarship awards made to a number of outstanding individuals.

4. Plans for the future

Funds in the President's budget will provide continuing support and create a supply of applicants for the opportunity to participate in this program.

TRAINING GRANTS

1. Purpose of program

These grants support training in specified aspects of health, medicine, and allied fields with the major objectives of (a) insuring an adequate supply of competent research and teaching manpower, and (b) facilitating within the student bodies of health-related professional schools the development of knowledge about special areas of disease that have particular significance. The training grant fulfills a dual function. Its funds underwrite certain expenses related to the specific training mission, including the provision of stipends to individuals selected for that training, except in (b) above. It also serves to create and maintain an atmosphere essential to the training by providing a focal point for the specific discipline or disease within the training institutions. It does not include data for the Bureau of Health Manpower and the National Library of Medicine.

2. Funds

1959 obligations	$49,812,000
1960 obligations	74,673,000
1961 obligations	109,928,000
1962 obligations	114,585,000
1963 obligations	135,502,000
1964 obligations	164,895,000
1965 obligations	178,617,000
1966 obligations	208,784,000
1967 obligations	134,403,000
1968 obligations	134,951,000
1969 estimates	141,440,000
1970 estimates	136,418,000

3. Present stage of development

The training programs of most of the NIH Institutes are directed toward the provision of adequate manpower for research in those disease areas for which they have assigned responsibilities. In contrast, the programs of the National Institute of General Medical Sciences are designed to support the fundamental sciences which undergird the disease-oriented interests of the categorical institutes. For this reason, their training programs cover the full range of the basic biomedical sciences.

In 1969 about 2,438 training grants will be supported.

4. Plans for the future

Emphasis will continue in areas where current and projected manpower shortages can be identified. Examples of such program areas to be supported by NIGMS include pharmacology and toxicology, the behavioral sciences, genetics, biophysics, biomedical engineering, and biostatistics. Areas of manpower shortages in programs supported by other Institutes include mental retardation, developmental and clinical pharmacology, aging, congenital malformations, virology, epidemiology, immunology and organ transplantation, artifical organs, orthopedics, urology and kidney disease, and neurology. Approximately 2,275 training grants will be supported in 1970, a decrease of 163 from the number supported in 1969. There is a corresponding decrease in funds available for 1970.

DESCRIPTION OF EACH NIMH GRANT PROGRAM

REGULAR RESEARCH GRANTS

1. Purpose of program

To provide grant support for research on causes, prevention, diagnosis, and treatment of mental diseases including research in the behavioral sciences, clinical, biological, applied and psychopharmacological research. The objective of this support is to add to scientific knowledge of the forces within and around the individual which affect or dictate his emotional and mental health, and the application of this knowledge in effective treatment and prevention services. The grants range from support of smaller, discrete and clearly defined projects, which are defined as project grants, to support of broad programs which integrate the research interests of several investigations, and which are called program project grants.

2. Funds

1960 obligations	$22,690,000
1961 obligations	29,759,000
1962 obligations	39,166,000
1963 obligations	48,456,000
1964 obligations	51,057,000
1965 obligations	55,702,000
1966 obligations	59,874,000
1967 obligations	60,389,000
1968 obligations	66,448,000
1969 estimate	73,029,000
1970 estimate	74,035,000

3. Present stage of development

In 1970 the NIMH will support approximately 1,201 research projects in the following fields: behavioral sciences, clinical research, applied research, psychopharmacological research, narcotics and drug abuse, alcoholism, metropolitan mental health problems, crime and delinquency and other social problems, and research in suicide prevention. As shown in the above table the extent of this support has grown from $22,690,000 in 1960 to $74,035,000 in 1970.

4. Plans for the future

In order to promote the mental health of the Nation, it is necessary to improve our base of knowledge by means of a continuum of scientific investigations from basic, normative studies to community-based evaluations of new approaches to the care of the severely ill.

SCIENTIFIC EVALUATION AND PLANNING GRANTS

1. Purpose of the program

To provide funds for the assistance of the national advisory councils through the technical and scientific review of research grant applications, and through the support of meetings used for the exchange of scientific views.

2. Funds

1965 obligations	$205,000
1966 obligations	215,000
1967 obligations	275,000
1968 obligations	375,000
1969 estimate	375,000
1970 estimate	375,000

3. Present stage of development

Research grant applications are reviewed prior to submission to the advisory councils by the appropriate study section. Each of these sections has scientific competency in a particular field or research discipline. Each section is comprised of outstanding leaders in the relevant specialities who are usually not employees of the Federal Government.

In addition to financing these review activities, chairman's grants support an extensive group of ad hoc panels, symposia, conferences, and other types of meetings used for the exchange of professional views.

HOSPITAL IMPROVEMENT GRANTS

1. Purpose of program

To provide grant support for demonstrations of improved methods of care, treatment, and rehabilitation of mentally ill in state mental hospitals. Its objectives are to strengthen therapeutic services and improve the quality of patient care, and to increase the contributions that these institutions can make as an integral part of the comprehensive community mental health programs of the future.

2. Funds

1964 obligations	$5,991,000
1965 obligations	11,974,000
1966 obligations	17,181,000
1967 obligations	8,990,000
1968 obligations	10,490,000
1969 estimate	10,610,000
1970 estimate	8,000,000

3. Present stage of development

By the end of 1968, a total of 183 Hospital Improvement Program grants had been awarded to 166 of the 302 hospitals eligible to participate in this grant program. In 21 states all eligible institutions had been awarded grants, while only three states had no participating institutions. Approximately 143,363 patients are receiving the benefits of current hospital improvement projects.

4. Plans for the future

The 1970 President's Budget will allow for continuing support of 78 awards made in 1969 and competitive renewal of 14 projects which are receiving current support.

EARLY CHILD CARE DEMONSTRATIONS AND EVALUATIONS

1. Purpose of program

To provide grant support to demonstrate and evaluate various methods of improving early healthy child development to prevent emotional disturbances and mental health problems of young children from poor and culturally deprived families. The program will support grants for the development, demonstration, and evaluation of day-care programs, family day-care programs, home tutoring, and parent training in child care and child education.

2. Funds

1970 estimate	$1,000,000

3. Present stage of development

This is a new program which will be initiated in fiscal year 1970.

4. Plans for the future

In order to plan the most effective methods for fostering intellectual development and social competence of socially handicapped children, the characteristics of their natural environment that influence their development will be determined, and methods to supplement their experience will be explored. In order to determine the critical variables which influence the effectiveness of various preschool intervention programs, a comprehensive systematic and centrally coordinated plan for investigating these factors will be developed.

TRAINING GRANTS

1. Purpose of program

The major objective of this program is to create an adequate supply of competent service, research and teaching manpower. To meet this goal, a wide variety of training opportunities are provided for all levels of personnel engaged in mental health work. Training grants are awarded providing direct support to public and nonprofit institutions to help defray teaching costs and to make financial assistance available to students being trained.

2. Funds

1965 obligations	$72,542,000
1966 obligations	85,102,000
1967 obligations	90,422,000
1968 obligations	96,518,000
1969 estimate	109,046,000
1970 estimate	112,500,000

3. Present stage of development

In 1970 the NIMH will support approximately 2,057 training grants. The awards will be concentrated primarily in training programs in psychiatry, behavioral sciences, psychiatric nursing, social work, and support of general practitioners. Through fiscal year 1968 over 76,000 trained professionals have been added to the mental health manpower pool.

4. Plans for the future

Training efforts are directed at providing by 1970 over 87,000 trained mental health personnel in the four core mental health disciplines of psychiatry, psychology, social work and nursing. The Institute's training program will provide crucial manpower support in behalf of the Nation's community mental health program. Other National programs, e.g., Medicare and Headstart, will increasingly utilize the skills of mental health personnel.

REGULAR RESEARCH FELLOWSHIPS

1. Purpose of program

The purpose of this program is to increase the supply of manpower available for research and teaching by providing qualified individuals with support for training in health related fields. There are three major categories of regular research fellowships; predoctoral, postdoctoral, and special.

Predoctoral fellowships provide assistance to individuals who have a bachelor's degree for further training leading to a doctoral degree. Post-doctoral fellowships support advanced training for an individual who has already earned a Ph.D., M.D., D.D.S., D.V.M., or equivalent degree. Special fellowships are designed to meet training needs not met by other fellowship programs, by supporting qualified investigators who require additional specialized training.

2. Funds

1965 obligations	$5,105,000
1966 obligations	5,203,000
1967 obligations	5,694,000
1968 obligations	5,778,000
1969 estimate	5,688,000
1970 estimate	5,813,000

3. Present stage of development

The Research Fellowship Program has developed a basic cadre of research scientists who contribute both to the understanding of the etiology and incidence of mental illness and to the prevention and correction of such disturbance.

4. Plans for the future

Funds provided in the President's Budget will allow for modest expansion of the program in 1970.

RESEARCH CAREER PROGRAM

1. Purpose of program

This program is designed to increase the number of full-time career opportunities for scientists with superior potential ability in the health sciences. The program consists of two types of awards; career awards and research scientist development awards. Career awards support established investigators of high competence for the duration of their careers. Research Scientist development awards support qualified scientists who have three years or more of relevant postdoctoral research or professional experience and who require additional training in preparation for careers in independent research. Development awards are normally made for five years and may be extended for not more than a total of ten years.

2. Funds

1965 obligations	$2,948,000
1966 obligations	3,159,000
1967 obligations	3,430,000
1968 obligations	4,377,000
1969 estimate	4,953,000
1970 estimate	5,053,000

3. Present stage of development

A portion of this program previously known as the Research Career Development Program has broadened in scope and is now designated as the Research Scientist Development Program. This change reflects a new concept of program development toward promoting and developing research in all aspects of mental health and illness. The objective is to develop research capacity in the psychiatric profession, to engage investigators from a variety of the behavioral and biomedical sciences in mental health research, and to foster interdisciplinary research on mental health problems.

4. Plans for the future

This program will continue to promote the expansion or establishment of mental health research programs by means of individual awards to suitable institutions for the recruitment and development of research scientists.

HIGHLIGHTS OF PROGRESS IN RESEARCH
Conducted and Supported
by the
NATIONAL INSTITUTES OF HEALTH
1968

Atherosclerosis and Coronary Heart Disease

The statistical relationship between hypercholesterolemia and coronary atherosclerosis has long been recognized and, in recent years, confirmed by prospective studies. Hypertriglyceridemia has more recently been found also to bear a similar relationship to coronary disease. It has not yet been established that reduction of serum cholesterol or other lipid levels will retard or prevent the development of new atherosclerotic deposits or lead to the regression of those which have already been formed. Nevertheless, current evidence indicates that some form of lipid-lowering therapy is advisable if hyperlipidemia exists.

Studies by National Heart Institute (NHI) grantees in Wisconsin indicate that nicotinic acid effectively reduces serum cholesterol and triglyceride levels in hypercholesteremic patients without dietary restriction. Dr. William B. Parsons, Jr., of the Jackson Clinic Foundation, studied patients during nicotinic acid administration. During treatment, mean cholesterol levels dropped from a pre-study average level of 334 mg. percent to 234 after 12 weeks. Triglycerides also dropped sharply.

Dr. Lester Morrison of Loma Linda University and the University of California in Los Angeles reports multiple lines of evidence--both experimental and clinical--that chondroitin sulfate A may prevent coronary arteriosclerotic heart disease. Chondroitin sulfate A is present in normal human blood, but is best known as a constituent of cartilage and connective tissue. The concentration of chondroitin sulfate A in the arterial wall declines with the advance of atherosclerosis in various mammalian species, including man.

In recent studies, chondroitin sulfate A reduced the extent and severity of atherosclerosis induced by various atherogenic diets in monkeys, rabbits, and rats. In addition, it appeared to reduce the concentrations of cholesterol and lipoproteins in human coronary-artery segments maintained in culture media. A study was conducted in patients with coronary heart disease. Half received chondroitin sulfate A (1 1/2 to 10 grams a day) for two years. There were 15 heart attacks in the control group, but only one in the group receiving chondroitin sulfate A. Dr. Morrison concludes that larger scale clinical studies are warranted to verify the apparent effectiveness of this compound against coronary heart disease.

SaH-2348 (Sandoz), a chemical structurally akin to clofibrate, seems to have similar--perhaps greater--lipid-lowering potency. These findings prompted Dr. Donald Berkowitz and co-workers to undertake cautious clinical trials in 31 patients with elevated blood lipids at the Sidney Hillman Medical Center in Philadelphia. The scientists report that after four weeks serum cholesterol and triglycerides were significantly reduced. The hypolipemic effects lingered for some weeks after the period of therapy.

Numerous investigators have called for long-term studies of the effect of changes in dietary patterns on the death rate from coronary artery disease. Central to such studies would be a substitution of unsaturated fat for saturated fats in the diet of study subjects.

Dr. Seymour Dayton and co-workers at the Veterans Administration Center and University of California School of Medicine, Los Angeles, studied 846 male

veterans (mean age: 65) for varying periods up to nine years. Half of these subjects received a conventional diet. The experimental group received a lipid-lowering diet relatively high in unsaturated fat. This diet resulted in lower serum cholesterol levels in the experimental group. The experimental group had fewer heart attacks and fewer strokes. These results suggest that lipid-lowering diets confer some protection against atherosclerosis and its complications.

Arterial susceptibility to atherosclerosis may abide within the arterial tissue itself, so that the obstructive lesions may be produced irrespective of hemodynamic and mechanical factors commonly believed necessary to their production, according to Drs. Henry Haimovici and Nelicia Maier, from Montefiore Medical Center in New York.

In their experiments with young adult dogs, a healthy segment of abdominal aorta was spliced, into the jugular vein, where it carried blood under the much lower pressures prevailing in the venous circulation. The treated dogs were then maintained on a diet which had proven highly effective for inducing atherosclerosis in the canine abdominal aorta.

Of the 14 jugular grafts, 10 had developed gross atherosclerosis by the time the animals were killed and autopsied 7 to 13 months later, even though, as expected, intact veins in all animals had remained entirely free of atherosclerosis. Thus, the original susceptibility of the arterial tissue was retained even when transplanted into the low-pressure venous system.

The formation of collateral circulation has been thought to compensate for the dire effects of coronary obstruction mainfested clinically as angina pectoris. However, a study by Drs. Robert Heinle and Richard Gorlin, at Peter Bent Brigham Hospital, indicates that collateral vessel formation does not necessarily protect against angina pectoris (chest pain due to an inadequate oxygen supply to the heart) or heart attacks.

The grantees conclude that collateral circulation develops only in response to severe blood-vessel blockade and seems to offer relatively little protection against the symptoms and consequences of severe coronary stherosclerosis.

The direct surgical removal of atherosclerotic deposits obstructing one or more of the coronary arteries of their major branches, a procedure known as coronary endarterectomy, has usually been reserved for well-localized, segmental deposits. However, initial clinical results obtained with a new endarterectomy method indicate that it may benefit even patients with diffuse coronary atherosclerosis, at least of the right coronary system. The technique, called gas endarterectomy, uses tiny jets of carbon dioxide to separate the diseased inner layers from the healthy outer layers of the artery, after which the diseased core can easily be removed as a single piece through a small blood-vessel incision.

Recently, Dr. Philip N. Sawyer and co-workers at Downstate Medical Center, Brooklyn, employed gas endarterectomy to treat 8 patients with diffuse atherosclerosis affecting all three coronary arteries. The technique took only one-third to one-quarter the time required by conventional endarterectomy procedures, and produced good clinical results in 6 of the 7 survivors.

Investigators at the Medical College of Georgia, Drs. Isam N. Anabtawi, Hubert F. Riegler, and Robert G. Ellison, have reported preliminary animal trials of a revascularization technique which requires no vessel implants. Their technique involved the surgical creation of myocardial tunnels running from the left pumping chamber directly into the surrounding heart muscle.

A preliminary study of another new revascularization technique for angina

pectoris has recently been reported by Drs. George E. Green and David A. Tice at the New York University Medical Center.

Instead of implanting the internal mammary artery directly into the ventricular wall as is done in the Vineberg technique, these scientists splice it end-to side directly into the left anterior descending coronary artery beyond the site of obstruction.

The seven patients undergoing this procedure had severe angina resulting from blockade of the left main coronary and/or the left anterior descending artery. After operation 6 of the patients have been free of angina. One patient subsequently died of non-cardiac causes. The investigators conclude that this method may prove better than older techniques because it provides immediate increases in coronary artery flow.

Radioactive xenon, injected into the coronary arteries, then followed with a scintillation camera, provides a means of visualizing bloodflow to various regions of the heart. It also allows visualization of blood-deprived areas of heart muscle after an acute heart attack, according to Drs. J. I. Haft, P. M. Johnson, and P. J. Cannon, NHI grantees at Columbia. When heart attacks were induced in the animals by selectively blocking a coronary artery or branch, "cold spots" in the scans after xenon-133 injections clearly located and outlined the blood-deprived area of heart muscle. This technique may prove clinically useful in providing additional diagnostic information of value in determining the proper course of treatment.

Hypertension

Up to 15 percent of all hypertension is probably due to disorders of the kidney, most often the obstruction of one or both renal arteries by atherosclerosis, clots, or other impediments to normal kidney blood-flow. Reduced blood-flow to the kideny triggers the relcase to renin, which, in turn, gives rise to angiotensin, a powerful blood vessel contrictor. This renin-angiotensin system is believed to initiate renal hypertension, but it has not been established whether it also sustains the hypertensive state.

A naturally occurring phospholipid isolated from the kidney reduces blood pressure in acute and chronic renal hypertensive rats, according to Drs. Subha Sen, Robert R. Smeby and F. Merlin Bumpus, at the Cleveland Clinic. The phospholipid, called "preinhibitor" by the scientists, reduced plasma renin activity and blood pressure in rats with acute or chronic renal hypertension. When the "preinhibitor" was discontinued, there was a slow rise in plasma renin activity levels and blood pressure. The phospholipid apparently affects blood pressure solely through the reduction of circulating renin rather than through any direct effects on blood pressure.

The antihypertensive agent bretylium tosylate shows unique, often life-saving effectiveness against ventricular fibrillation and related heart rhythm problems, according to Dr. Marvin Bacaner, of the University of Minnesota in Minneapolis. Earlier animal studies had shown that bretylium greatly reduces the heart's vulnerability to arrhythmia. In his most recent work--a pilot study in humans--Dr. Bacaner administered bretylium to a total of 30 patients whose lives were seriously endangered by ventricular arrhythmias following heart attacks, heart operations, or digitalis intoxication.

Bretylium tosylate was of clear value in patients with ventricular tachycardia that had been resistant to other drugs and electrical countershock. Suppression of the arrhythmia occurred within 5 minutes to several hours after initial treatment.

Heart Failure and Shock

NHI investigators report that the activity of the enzyme tyrosine hydroxylase is reduced in experimental congestive heart failure and, from the known role of this enzyme in norepinephrine (NE) synthesis, infer that NE production is impaired in the failing heart.

Tyrosine hydroxylase is an enzyme that catalyzes the first step in NE synthesis, the transformation of tyrosine to DOPA. The NHI scientists placed radioactive tyrosine in extracts of normal and experimentally failing dog hearts, and used the amount of radioactive DOPA produced as an index of NE production. The very small amounts of radioactive DOPA formed by extracts from failing hearts compared to that formed by normal hearts indicated a very slow rate of NE synthesis in the failing heart. These studies were conducted by Drs. Peter E. Pool, James W. Covell, Morton Levitt, James Gibb, and Eugene Braunwald, of the National Heart Institute's Cardiology Branch and Laboratory of Clinical Biochemistry.

NHI grantees Drs. Marcia B. Bull and John H. Laragh, of Columbia University, report that the remarkable potassium-sparing properties of amiloride make this mild diuretic a useful new adjunct to the treatment of even the severest edematous states in man. The new agent was recently introduced by Merck, Sharp and Dohme for clinical investigation. They report that amiloride alone substantially increased sodium excretion but had little effect on potassium excretion while producing mild diuresis. In combination with other diuretics, amiloride facilitates treatment of refractor edema while lessening the attendant danger of potassium depletion. No toxic effects of amiloride were noted in any of the subjects treated.

A deficiency of magnesium may play an important role in digitalis toxicity, with its often dangerous cardiac arrhythmias, according to Dr. Robert H. Seller and associates at Hahnemann Medical College in Philadelphia.

The scientists had previously noted low blood magnesium levels in patients with digitalis intoxication. This prompted them to perform animal experiments in which circulating magnesium levels were deliberately depressed by use of an artificial kidney. They found that a reduction in serum magnesium reduced by the dosage of digitalis necessary to produce arrhythmias. Normal heart rhythm was restored by magnesium infusions. Since serum magnesium levels are reduced by many diuretics widely used in heart patients also receiving digitalis, the authors suggest careful attention to magnesium levels in such patients.

Dr. John H. Siegel and co-workers, of the Albert Einstein College of Medicine, New York, evaluated a relatively inexpensive recording and computer system for the rapid procurement and evaluation of physiological data at bedside and their use of this sytem in over 100 critically ill patients in shock. The system enabled immediate determinations of the type and severity of shock in these patients and their clinical responses to treatment.

The NHI grantees report that their computerized system provided rapid assessment of the type and severity of shock in these patients, as well as of the patients' subsequent responses to therapy, and averted almost certain catastrophe in several patients.

Cardiogenic shock has carried mortality rates of 80-90 percent. By applying balloon pumping techniques in clinical trials, Dr. J. S. Krackauer and co-workers at Maimonides Medical Center, report that they were able to reverse the shock state in 13 of 16 patients.

A polyurethane balloon, surrounding the end of a catheter, was introduced

into the aorta via the femoral artery of the leg. The balloon, inflated as the heart refilled between pumping strokes, helped raise blood pressure in the systemic circulation. Deflated as the heart contracted, it reduced the pressure the heart must work against in expelling blood, thus reducing cardiac work load. Vasopressors were not used during pumping. The study suggests that balloon pumping is effective against shock following acute heart attacks.

Heart Transplantation

Attempts to replace incurably diseased human hearts with healthy hearts obtained from cadavers or animals are an outgrowth of the limited clinical successes attained with other tissue and organ grafts, notably kidneys, and the development of a practical surgical technique of heart transplantation in experimental animals. In turn, this preliminary work was made possible by the development of heart-lung machines, other life support techniques, and advances in other disciplines involved in the performance of successful open-heart surgery.

During the year following Dr. Christiaan Barnard's historic heart homotransplantation in December 1967, 100 people have undergone operations for the implantation of human hearts and 2 additional patients received heterografts (sheep and calf hearts, respectively). Fifty-three of these operations were performed in the U.S. (most of them by NHI grantees).

Qualified physiologic success has been accomplished in more than 90 percent of these operations; that is, for some time after implantation, the transplanted heart fulfilled its normal function of maintaining an adequate circulation. However, only one-third (38) of these patients were alive in mid-December 1968, and only two had survived for six months or longer.

The most frequent causes of death in these patients have been overwhelming infections and acute graft rejection. However, despite an overall mortality rate of about 66 percent during this first full year of experience with heart transplants, both the incidence and duration of survival have increased in operations performed during the last 6 months.

NIH grantees are continuing to attack problems relevant to heart transplantation. Of particular urgency are needs for better methods of preserving donor heart viability and more reliable, sensitive techniques for detecting, following, and managing rejection crises.

One of the most consistently reliable signs of early acute rejection of the homotransplanted heart is a drop in the strength or voltage of the heart's electrical activity as recorded by the electrocardiograph (ECG). Drs. V. Eric Kemp and colleagues, at the Medical College of Virginia, have studied and improved this diagnostic technique through the use of an ECG electrode attached directly to the outer surface of the heart (epicardium) just beneath the pericardium. Voltage from this epicordial lead was unaffected by fluid accumulation that caused a significant drop in voltage recorded by the standard ECG. However, it dropped during acute rejection, then rose, even in the presence of fluid, with successful immunosuppressive therapy of the rejection crisis.

Drs. Claude Chartrand, Norman E. Shumway, and others at Stanford have devised and experimentally tested a method of delivering immunosuppressive drugs, anticoagulants, and other agents directly to the coronary circulation of the transplanted heart.

Such selective perfusion of the heart may enable a reduction in dosage of certain drugs having noxious side effects, while increasing their therapeutic effects by delivering them to the desired site of action. The method also constitutes a new approach for evaluating the selective effects of various drugs

that affect blood flow and vessel diameter or that posses anti-inflammatory or immunosuppressive properties. It has shown considerable promise in limited animal experimentation.

Studies reported by H. A. Kontos, Richard R. Lower and co-workers, at the Medical College of Virginia, indicate that both homotransplanted and autotransplanted hearts become re-innervated within 3 to 5 months, by the parasympathetic and sympathetic divisions of the autonomic nervous system.

The Virginia investigators demonstrated parasympathetic innervation by producing slowing of the heart rate (bradycardia) in response to direct stimulation of vagus nerve trunks in the neck or to an increase in blood pressure. Similarly, sympathetic re-innervation was demonstrated by acceleration of the heart following direct stimulation of sympathetic nerve trunks or by a reduction in blood pressure. Regenerated nerve fibers of both types entering heart grafts were also demonstrated microscopically through the use of special fluorescent staining techniques.

Congenital and Rheumatic Heart Disease

It is not known to what extent congenital heart defects are due to faulty genes passed from parents to their offspring and to what exten such defects stem from adverse effects on the developing fetus resulting from infection, drug reaction, or external environmental influences. Studies by Dr. D. F. Patterson at the School of Veterinary Medicine, University of Pennsylvania, suggest a lesion-specific hereditary basis for a whole series of congenital heart defects in some breeds of dogs.

Their studies in a university veterinary clinic disclosed a prevalence rate for congenital heart disease of 6.8 per 1,000 (240 of 35,280). The most common defects showed prevalence rates significantly greater in purebreds than in mongrels, and the various types of malformations were not randomly distributed among the breeds. The investigator hypothesized that genetic factors are determinants of congenital heart disease in dogs, that these genetic factors have specified effects on cardiac development and produce specific types of anatomic defects. Preliminary genetic studies, including test matings of affected dogs, have tended to confirm this hypothesis.

NHI surgeons have found that heparin and low molecular weight dextran exert appreciable protection against embolism during the postoperative period following surgical removal of left atrial thrombi.

Dr. Lynn M. Peterson and associates in the Clinic of Surgery report that massive clots--often virtually filling the heart chamber--were found in patients undergoing open-heart surgery for mitral stenosis at NHI since 1961. In the course of corrective surgery, the surgeons were able to remove the entire thrombus--however, postoperative emboli occurred in almost 20 percent, and caused more than a third of all deaths.

In a group of patients receiving heparin or low molecular weight dextran within 12 hours after surgery to remove atrial thrombi, not a single embolism occurred.

The NHI study points up the threat still posed by recurrent intra-atrial thrombus formation. Even with complete clot removal and restoration of an apparently smooth surface at the site where the clot was attached, that surface seems to retain a tendency to engender clots. The prophylactic use of anti-thrombotic agents such as heparin and dextran appears to reduce this danger substantially.

A dramatic decrease in blood-clotting (thromboembolic) complications following artificial heart valve implantation in patients has been achieved with a new type of anticoagulant drug that inhibits adhesiveness and aggregation of blood platelets, and thus prevents the formation of "white thrombi". The drug, dipyridamole (Persantine, Geigy), has long been used for its vasodilating properties in the alleviation of coronary insufficiency, but its additional ability (at more than twice the usual dose) to inhibit platelet clumping had never been employed clinically.

A group of Boston scientists, Dr. Jay M. Sullivan and co-workers, report that no thromboembolic episodes occurred in dipyridamole treated patients during period of follow-up, but arterial emboli occurred in 6 of 36 control patients. Furthermore, patients who discontinued dipyridamole experienced cerebral emboli 6 months later.

Hemolytic anemia has been an important complication following implantation of prosthetic valves. Mechanical trauma to red cells, perhaps resulting from contact with foreign surfaces, their being smashed between fixed and moving valve parts, or damage resulting from turbulence, especially in malfunctioning valves, has been implicated as a possible cause.

A study of Drs. Bradley M. Rodgers and David C. Sabiston, Jr., at the Duke University Medical Center, has indicated that reoperation to alleviate hemolysis, which is dramatic in a few cases, is disappointing in the majority.

However the scientists report many patients can be managed satisfactorily with a combination of iron replacement, folic acid, and restricted activity. They recommend that further surgery be undertaken only after these therapeutic measures have failed.

Bioengineering

Artificial pacemakers have been employed with great success to maintain normal heartbeat in patients with heart block. This condition usually results from disease-induced or operative injury to the specialized conduction system that normally originates and conveys to all parts of the heart the electrical impulses that cause the heart to beat. Such injuries may slow heart rate and decrease its output of blood below the level required to sustain normal activity, and they pose an ever present threat of arrhythmias that may progress to heart stoppage and death.

In a study of 150 patients at the Massachusetts General Hospital, transvenous electrical pacing (in which the pacing electrodes are run into the heart through the jugular vein via catheter) has proved to be safer and more reliable than implantation of the electrodes in the heart muscle through a chest incision (transthoracic pacing).

Recent improvements in the radio frequency pacemaker, developed by Dr. William Glenn and co-workers at Yale, have made this device so reliable for long-term pacing that re-operation might never be necessary, even in children.

This radio frequency pacemaker paces the heart from outside the body across a completely intact chest wall. Radio signals from a miniature transmitter worn outside the body are beamed through the chest to a tiny implanted radio receiver, which converts the radio frequency energy to pacing pulses delivered to the heart muscle via a platinum wire electrode.

Although the reliability of artificial pacemakers has continued to increase, episodes of electrode breakage, pacemaker failure, battery failure, electrical

interference with the artifically set rhythm from both within and without the body have continued to occur in significant numbers.

However, the American Optical (AO) Demand Pacemaker, which stimulates the heart only when needed, appears to be immune to outside interference. Moreover, because it does not compete with intrinsic heart rhythm, as is the case in fixed-rate pacemakers, it is not subject to disturbances arising within the heart itself.

A group headed by Dr. Dwight E. Harken, Harvard Medical School, has implanted 60 demand pacemakers in patients aged 54-86 for pacing up to 14 months. No unit has evidenced electrical malfunction and all patients have had salutory responses. In addition to the advantages previously cited, the AO Demand Pacer should have prolonged battery life in patients requiring only intermittent pacing.

The quest for materials compatible with blood has been a major concern of the NHI Artificial Heart Program, because compatibility is a critical problem in the development of artificial hearts and heart assist devices. Most materials used to date have tended to damage red blood cells and other formed elements of the blood, to promote clotting, and to denature plasma proteins.

Although an ideal material has not yet been developed, the Artificial Heart Program is investigating a number of promising approaches. These include the development of permanent heparin surfaces; surfaces with low surface free energy; polymers with "permanent" negative charges on the surface; hydrogels with and without ionically charged surfaces; new and more compatible silicones; and other polymer configurations. Research along these lines has yielded five to six materials that appear promising. One of the best of the new material is a heparin-silicone compound from the Carnegie Tech-Mellon Institute. This material apparently neither damages blood proteins or cells, nor causes blood to clot. This and several other blood-compatible materisl are being evaluated for continued development into materials combining compatibility with other essential characteristics such as flexibility, toughness, and durability.

Two new, potentially important developments in the field of heart assist devices are a new mechnical auxiliary ventricle (MAV) developed by Dr. Tetsuzo Akutsu and co-workers, at the University of Mississippi, and a left ventricular-aortic blood pump recently reported by Dr. C. G. LaFarge and colleagues, of Children's Hospital Medical Center, Harvard Medical School, and the Thermo Electron Engineering Company of Waltham, Massachusetts.

Experiments conducted by NHI contractors--Dr. John C. Norman and co-workers of Boston--indicate that, should an implantable nuclear powered artificial heart become available, the excess heat generated by its radioisotope energy source can be safely transferred to the bloodstream and dissipated into the air from skin and lung surfaces.

The findings, which confirm and extend previous studies with animals subjected to electrically-induced internal heat, involved the implantation of small plutonium-238 fuel capsule astride the aorta in dogs. The capsule generated 16.1 watts of power, more than enough to drive an artificial heart in man.

Because it generated a surface temperature of 360° F the capsule had to be encased in a special 3x4 inch insulated unit. This unit incorporated an anti-coagulant-treated titanium tube that was spliced into the thoracic or abdominal aorta. In operation, heat produced by the radioisotope capsule was transferred to the titanium tube, thence to the blood flowing through it.

The animals tolerated the fuel capsule well during the 6-month period of observation.

Diseases of the mouth and teeth

Research offers the most promising solutions to demands for better health, and in seeking these solutions, the National Institute of Dental Research (NIDR) carries on and supports a broad spectrum of basic, clinical, epidemiological, and applied studies. Problems studied include dental caries (tooth decay), the most common disease of children; periodontal (gum) disorders, which affect to some degree virtually everyone past 50; malocclusion or faulty bite; problems of growth and development, especially cleft lip and palate; oral cancer; and the common and vexing canker sores and fever blisters, as well as more menacing ulcerations of the mouth.

Dental caries

Only within the past 20 years has scientific evidence shown that dental caries cannot occur in the absence of bacteria. Since then, research conducted and supported by NIDR has firmly established that caries results from an interaction of three factors--certain decay-causing bacteria, a diet high in carbohydrates, and individual susceptibility.

Plaque.--Although all microorganisms capable of producing acid may aggravate decay, research has seriously implicated certain strains of streptococci as primary suspects in decay of the smooth surfaces of teeth. These bacteria use sucrose (table sugar) to form a gummy outer coat enabling them to cling to the sides of teeth. This sticky material has been identified as dextran. It forms a glue in which many other bacteria become trapped, eventually forming a film called plaque which tightly covers the teeth. Within the plaque framework, the acids secreted by many bacteria, including the dextran-makers, constantly bathe and eventually dissolve the tooth enamel.

NIDR scientists, R. J. Fitzgerald, P. H. Keyes, and D. M. Spinnell, have tried to dissolve dextran, and with it the plaque, so that saliva can wash away bacterial acids. They collaborated with T. H. Stoudt, of Merck, Sharp and Dohme Research Laboratories, who made available a dextran-splitting enzyme (dextranase) extracted from a penicillin mold. The investigators fed the enzyme to hamsters previously inoculated with plaque-forming streptococci and maintained on a high-sugar diet. These animals developed far less plaque and decay than control animals. If clinical studies show this enzyme is effective in humans, an entirely new way to reduce smooth-surface decay can be developed.

Fluoride studies.--NIDR continues studies of other ways to bring the benefits of fluoride to more people, as well as to raise the level of protection for those drinking fluoridated water. In one recently developed method, a plastic mouthpiece was utilized to hold a gel containing 0.5 percent fluoride close to children's teeth for a few minutes a day. Under subprofessional supervision at school, children are thus able to treat themselves and effect a significant reduction in decay. H. R. Englander of the NIDR, and J. R. Mellburg and C. R. Nicholson of the Kendall Company Research Center, Barrington, Illinois, found that the treated teeth were less soluble in acid than untreated teeth, showing clearly that fluoride increases the resistance of enamel to mouth acids.

Other caries preventives.--Because normal pits and crevices in the grinding surfaces of teeth are especially prone to decay, an effective method for sealing them could prevent much of the commonest type of caries. Recent studies have shown that a number of resins will bind quite well for some months to teeth that have been midly etched with acid. An electron microscopic study by A. J. Gwinnett of the Institute and A. Matsui of Kyoto University, Japan, has shown that while nothing can penetrate the non-porous untreated enamel, etching causes the dense, outer 10-15 microns of enamel to become porous so that liquid resins can penetrate. Because etching works best on young teeth, it is thought that

sealing pits and crevices with resins as a preventive against tooth decay may be most effective in young people. It is in this age group that most caries occur. Work is progressing on the development of resins that are non-toxic, and stable against wear and chemical reactions in the mouth.

Biomaterials

Until decay can be completely prevented, the need for materials to repair and replace damaged teeth will continue. This year NIDR funds have supported K. Asgar and B. Techow of the University of Michigan in the production of a promising cobalt alloy for making clasps to anchor dentures to adjacent teeth. The greater ductility of the new alloy should reduce breakage. The softer metal also should cause less wear on the natural teeth and require less of the dentist's time to grind and adjust dentrues for a proper fit.

Another advance in the alloy field comes from metallurgists who have discovered a new technique for strengthening a gold-nickel alloy with metal fibers. The alloy has potential use in orthodontic wires, denture clasps, and castings for inlays. A. A. Johnson, K. Mukharjee, and J. Ordonez of the Brooklyn Polytechnic Institute report that this new method of fiber reinforcement is less tedious than previous ones, and should be applicable to a wider variety of alloys with potential uses in medical prosthetic devices, and in engineering and space technologies.

Periodontal disease

In periodontal disease, food, bacteria, and calculus (tatar) lodge between the gums and the teeth, forming pockets where more debris collects. Inflammation occurs and spreads until supporting fibers and bone break down. Eventually, the affected teeth loosen and fall out.

Cell studies.--New evidence suggests that a gum-to-tooth attachment forms a barrier to periodontal disease. By using tissue culture techniques, A. C. Taylor at the University of Texas in Houston has shown that epithelial cells which line the gums have special attachment structures at the cell membrane. Further studies with the electron microscope revealed that a cementing substance is discharged through the epithelial cell membrane to form special adhesive structures at the cell surface. The tissue culture techniques employed may help scientists to find ways to promote reattachment of gums to teeth.

Bacterial factors.--Evidence implicating specific microorganisms in periodontal disease is accumulating. Current studies at the Forsyth Dental Center and at Harvard University show that two streptococcal strains cause considerable loss of the alveolar bone that supports teeth in rats and mice. Originally found in human decayed teeth, these organisms can also cause tooth decay in experimental animals. This research by R. J. Gibbons, A. M. Shsrawy, and S. S. Socransky suggests that certain plaque-forming mircrorganisms, already implicated in tooth decay, may also cause bone destruction similar to periodontal disease when they form plaque in gum crevices.

Many microorganisms produce poisonous substances called endotoxins which are released from their cell walls when they die. If endotoxins are absorbed or injected into mammals, they usually cause considerable tissue damage. Because the role of endotoxins in periodontal disease has been questioned, A. A. Rizzo of NIDR tested rabbits to see whether endotoxin could penetrate the membranes which line the gums. His findings suggest that endotoxins do not activate the changes leading to periodontal disease because they do not penetrate normal gum lining, but once this membrane is damaged, endotoxins may enter and aggravate destruction in the underlying tissues.

Hydrogen sulfide is another well-known waste product of bacteria which live in gum crevices. Recently, A. A. Rizzo tested a series of healthy people and found hydrogen sulfide in all the deep periodontal pockets but not in most shallow crevices in the same individual. Proof that this gas is formed deep in periodontal pockets points to its possible role in periodontal disease.

Calculus.--According to present theory, substances in saliva help to mineralize the soft film of dental plaque that originates primarily from bacterial deposits. This mineralized material, called calculus or tartar, increases steadily and, if not removed at regular intervals, eventually pushes the gum away from the teeth. Calculus is a serious factor in periodontal disease.

R. O. Wolf, L. L. Taylor, L. K. Croft, and C. J. MacLean of NIDR analyzed characteristics of parotid gland saliva from small groups of people who form heavy, moderate, or slight deposits of calculus. These factors were then correlated with variations in calculus production.

Malocclusion

Much of the rise in malocclusion, or faulty bite, correlates with increasing disuse of chewing muscles as man has turned from primitive foods to soft diets. The influence of other factors is suggested by studies of the effects of excessive vitamin D in pregnancy. This latter research, undertaken collaboratively in the past year by W. F. Friedman of the National Heart Institute and L. F. Mills of NIDR identified an excessive vitamin D regimen that consistently produces malformations in blood vessels, bones, and teeth in rabbits without an accompanying high fetal death rate.

Malocclusion may not only result in unattractive appearance, speech difficulties, and poorly chewed food, but it may also painfully disturb the hinge (temporomandibular joint, TMJ) between the lower jaw and the skull. The three principal symptoms of TMJ disturbances are unusual motion of the lower jaw, clicking or scraping sounds when the jaw moves, and pain. H. T. Perry of Northwestern University Dental School in Chicago reports that most TMJ distrubances are in fact dental problems that arise from imbalance or disease in muscle, joint, or occlusion which can be satisfactorily handled with conservative therapy once a correct diagnosis has been made.

In some individuals with extreme malocclusion, the chin and lower jaw protrude far enough to cause open bite and overlapping of upper teeth by the lower ones. Until just recently, little was known about the nature and permanance of the resulting adjustments which take place in the hinge, or TMJ region. Now, as a consequence of a new technique of x-ray visualization developed by W. H. Ware and R. C. Taylor of the University of California in San Francisco, it has been found that surgical treatment of malocclusion is anatomically as well as esthetically successful and that, even in middle-aged adults, the jawbone appears capable of remodeling and growth in response to stress.

Soft-tissue studies

In studies by S. Bernick of the University of Southern California, the chief effect of age on dental pulp has been shown to be increased deposits of calcium. Such deposits eventually cut off most of the supply of nerves and blood vessels to the pulp, thereby accounting for the relative insensitivity of the teeth in older people. Age-dependent sclerosis in dental pulp begins with the deposit of a clear, glossy material, neither fat nor calcium, just beneath the inside lining of the vessels. This substance (a mucopolysaccharide) spreads through the vessel wall, then develops fibers which calcify. Found in 90 percent of all those over 40 years of age, it nevertheless appears to be associated

neither with rich diets such as is common in persons with atherosclerosis, nor with high blood pressure so characteristic of arteriolar sclerosis.

Collagen studies.--The principal protein in teeth, bones, skin, the lining of the mouth, and all connective tissues in the body is collagen--a long-chain, fibrous molecule. An enzyme called collagenase splits this molecule into two unequal pieces, one-quarter and three-quarters of its original length. Thus, the appearance of the two pieces is evidence of the presence of the enzyme. Although some collagenase is probably present in healthy tissue to control the day-to-day turnover of collagen, NIDR scientists first demonstrated its presence in humans in culture fluids of diseased gum tissues, and later in culture fluids of human bones and skin. It also occurs in joints of individuals with rheumatoid arthritis. Now, G. S. Lazarus, R. S. Brown, J. R. Daniels, and H. M. Fullmer find that collagenase is also present in the granules of certain white blood cells. Since these cells concentrate in abscesses and inflammations, it it believed that the collagenase, together with other enzymes in the granules, may account for the tissue destruction that occurs in many infections and inflammations.

Oral lesions.--While abscesses and other oral ulcerations constitute a minor proportion of oral diseases and disorders, their discomfort brings them more often to public attention. However, painless white spots on the lining of the mouth should always be medically evaluated because of the hazard of pre-cancerous disposition.

As a result of NIDR studies, a more precise differentiation has been made between two types of white spots known as leukoedema and leukoplakia. H. O. Archard and H. R. Stanley report that leukoedema seems to remain static with no tendency to grow or change into cancer or the leukoplakic type of white spots. No connection with diet or smoking is known. Leukoplakia is a more serious kind of white spot. Although most leukoplakia is chronic and harmless, and may even disappear spontaneously, it sometimes becomes cancerous. However, because there have been few long-term, follow-up studies of leukoplakia, estimates of how often it turns into cancer vary widely.

Because by law all malignancies in Denmark must be recorded, the Danish Cancer Center provides more reliable information for long-term leukoplakia studies than is available in the United Stetes. For this reason, NIDR supported a study in Denmark of malignant transformation of leukoplakia. In this study the majority of the white spots spontaneously disappeared, gradually diminished, or remained unchanged. Only 4.4 percent became malignant. Of these, most transformed in less than a year, but a few required up to as many as four years. From their findings the investigators, J. J. Pindborg, O. Jolst, and B. Roed-Petersen, reported that speckled or nodular leukoplakia is more likely to become cancerous.

Viral study.--A virus may stimulate an animal to make antibodies against viral proteins, and sometimes (particularly those cancer viruses which attack lymph tissues) may suppress these antibodies. This year NIDR virologists have shown that in some instances a virus may also stimulate the body to form antibodies against non-viral proteins which ordinarily are completely tolerated. Research by S. E. Mergenhagen, A. L. Notkins, and S. F. Dougherty indicates the possibility that even mild viral infections could trigger an autoimmune response which would make an individual allergic to one of his own proteins.

Working with the LDV (lactic dehydrogenase virus) and mice, these investigators have shown that infected mice produced antibody to human gamma globulin (HGG), more easily than mice not infected with LDV. Their current research shows that even filtered HGG, which is usually completely tolerated by mice, will stimulate those animals previously infected with LDV to make antibodies against it. Certain bacterial endotoxins, such as those released when oral bacteria die, had the same effect as the LDV in stimulating an immune response to a previously

tolerated protein.

Anesthesiology

For years regional anesthesia has been used to control postoperative pain in specific areas of the body. The drugs used for this purpose by most oral surgeons are narcotics. Yet, because narcotics can depress the cough reflex and may cause vomiting, they can complicate recovery from oral surgery among patients who have difficulty in clearing the upper airway, especially when jaws have been wired together. R. A. Meyer and M. A. Chinn of the University of Washington in Seattle have evaluated the addition of dextran to local anesthetic in nerve blocks for relief from pain after serious jaw surgery. Patients given nerve blocks with dextran were pain-free for longer periods of time, and they had no associated nerve damage. The investigators concluded that use of a dextran-containing nerve block is highly desirable because a pain-free, alert patient with a clear airway and able to cough properly is less likely to develop complications than one who is drowsy and physiologically depressed.

Oral Contraceptives and Thromboembolism

Drs. Daniel G. Seigel of the National Institute of Child Health and Human Development (NICHD) and Robert E. Markush of the National Institute of Neurological Diseases and Stroke have analyzed U.S. mortality trends since 1951 for underlying causes of death that are related to thrombosis or thromboembolism.

This research has confirmed the results of case controlled studies in Great Britain, which indicated that the incidence of thromboembolic disease in women during their reproductive years is increased for those who have used oral contraceptives. In particular, the risk of death from pulmonary embolism or cerebral thrombosis was estimated by the British studies to be seven to eight times higher in such women.

A pattern of significant increases in most age groups for both whites and non-whites was noted in death rates from diseases of veins and other diseases of the circulatory system. These increases were in excess of those seen in the comparison groups. For cerebral embolism and thrombosis, no such consistent increases could be seen, and for arteriosclerotic heart disease, the results were equivocal.

Estimates of the relative risk of mortality from diseases of the veins and other diseases of the circulatory system in oral contraceptive users as compared to persons who do not use such drugs were derived and were found to be of the same order of magnitude as those indicated by the British case-control studies.

Immunologic Infertility

According to a study by Dr. C. Dean Dukes and associate at Baylor University, in Houston, Texas, grantees of NICHD, a number of wives appear to have become sensitized to their husband's sperm. The investigators found that a remarkable percentage of female patients without demonstrable organic cause for infertility possessed circulating antibodies capable of agglutinating human spermatozoa.

Another series of experiments indicated that the antibodies in the female were acting against sperm and not to some other component in the seminal plasma. However, since a variety of different antibodies were found in the human female, a major problem is to determine which one or combination of these is responsible for the immunologic infertility.

A better understanding of the immunologic processes in human reproduction including the site of the antigen-antibody reaction will not only enable us to prevent infertility, but may point the way to new methods of contraception.

Chemical Detection of Ovulation

A positive and simple means of detecting the time of ovulation in women could be an invaluable aid in the understanding of the processes of reproduction, population growth, fertility regulation as coincident with the reproduction and population research program of the NICHD.

Institute supported research being carried on by Edward W. Bermes, Jr., Ph.D., and J. J. Isaacs, M.D., of St. Francis Hospital, Evanston, Illinois approaches the detection of ovulation through an immunochemical detection of LH (luteinizing hormone) in the urine.

The LH peak in most instances occurs on or shortly before the temperature shift traditionally noted in ovulatory cycles. The vaginal smear used to detect the height of the maturation index as an indicator of ovulation correlates with the time of peak LH excretion.

The determinations of LH provided by a relatively simple immunochemical technique will be used to study the abnormality of bleeding, as well as the problem of infertility, and can also be used in the process of child spacing. Its most useful purpose might be in the latter category.

Reproductive Processes in Primates

A vital group of investigators in the Section on Endocrinology of the Institute's Reproduction Research Branch, headed by Dr. Roy Hertz and Dr. William V. Tullner, has been carrying out intensive physiological and pharmacological studies on the reproductive processes in subhuman primates.

Of primary importance in the work of this group last year were their findings concerning alterations in estrogen excretion of subhuman primates.

Precise chemical measurements of estrogen excretion in urine were made throughout the menstrual cycle in a series of adult monkeys for correlating the stage of ovarian follicular development with urinary estrogen levels. Estrone was the principal estrogen found with estradiol and estriol being excreted in smaller, sometime undetectable, amounts.

The peak of estrone excretion closely related to the predicted time of ovulation by timed observation of the ovaries.

Genetic Studies in Mice

Heredity governs and molds our most central characteristics throughout life, yet we are largely ignorant of the ways in which this comes about. Dr. Beatrice Mintz of the Institute for Cancer Research in Philadelphia hes a program which may uncover some of the basic mechanisms by which genes exercise their strategic roles. Valuable information is being revealed through this program, in which the investigators have found a way to produce mice with two sets of parents.

For this purpose, the investigators wash the fertilized ovum (actually an early embryo of 2 to 8 cells) from out of the oviduct, dissolve away the membrane from around it, and place it in an artificial medium along with similar cell masses from other mice. In the medium the mass of cells breaks apart and the

cells recombine with others to form an embryo with genetic material from four parents. The new embryos are then transplanted to the uterus of a foster mother where they continue to develop and are born at the regular time.

Each animal has four parents, plus an "incubator" foster mother. Whereas cells in an ordinary individual have identical genes, the cells within an allophenic mouse are of two different and separate genetic constitutions, each with its expression.

New insights into the basic problem of immunity have been gained by demonstrating that any of these animals will accept a skin graft from either of the two original parental strains. Yet they are capable of immune response, as shown by their rejection of skin grafts from other strains.

Family Planning Success and Viewpoints of American Women

A Princeton University research team has estimated that at least one-third of American couples who have completed their families have had one or more unwanted children. The data on which this conclusion is based are part of a National Fertility Study which compiled the reproductive and contraceptive histories of a national sample of 4,610 wives under age 45. Drs. Norman B. Ryder and Charles F. Westoff this year continued to report the findings of the 1965 survey, conducted under contract with NICHD.

The investigators also asked women about the number of children "intended", "desired", and considered "ideal". Overall averages for these concepts were similar. However, patterns of responses by socioeconomic status revealed important deficiencies in the sbility of some couples to practice family planning successfully.

Observations of Acute Fetal Hypoxia in Sheep

A comprehensive study of the electrical characteristics of the fetal heart and brain during induced and controlled hypoxia in sheep has, in preliminary work, demonstrated the sensitivity of this method for evaluating fetal distress. Dr. Leon Mann and associates of NICHD found the fetal electrocardiogram (EKG) more sensitive than the electroencephalogram (EEG) in monitoring hypoxia and characteristic changes which anticipate irreversible biological changes within the fetus.

In this study, fetal sheep were prepared in utero so that electroencephalographic recordings could be obtained simultaneously with measurements of cardiovascular function, assessment of glucose and lactate levels, and acid base determinations. The study explored the interrelations of heart rate, oxygen, tension, acid-base status, and the EEG during hypoxia and with recovery.

Simultaneous observations of neurophysiological, cardiovascular, and metabolic parameters during and following acute hypoxia with the fetus in utero had not been reported prior to this study. The data obtained from this study provide this information. Hopefully additional research may be directed toward preventing or correcting the alterations observed. Knowledge and understanding of the human development and the etiology of mental retardation, two goals of NICHD are clearly dependent upon a clear concept of normal and abnormal conditions present during gestation in lower animals. This project is intended to provide information of this sort.

The Deleted X Chromosome

Studies at the NICHD Children's Diagnostic and Study Branch have led to the conclusion that the short stature and other physical characteristics of the

Turner's Syndrome are caused by absence of the short arm of the X Chromosome. Turner's Syndrome is characterized by retarded growth and sexual development, webbing of neck, low posterior hair line margin and other abnormailities associated with aberrations in the sex chromosomes.

It was discovered in 1959 that the vast majority of patients with Turner's Syndrome were missing an X chromosome. Now the finding of a patient with a non-mosaic short-arm deletion of her X chromosome and a study of her, her family, and the medical histories of the five other reported cases of this kind, have made it possible to draw some conculsions regarding implications of X chromosome abberrations.

Observations on the six patients with short-arm deletion of the X chromosome were also compared with six reported cases of long-arm deletions of the X chromosome. The findings suggest that the gene or genes which determine the short stature and other phenotypic manifestation in the Turner's Syndrome are located on the short arm of the X chromosome.

Phototherapy Found Effective in Modifying Hyperbilirubinemia

Dr. Jerold Lucey and associates at the Department of Pediatrics, University of Vermont, have reported findings which confirm early clinical observations on the value of light therapy in preventing the development of hyperbilirubinemia.

Dangerous hyperbilirubinemia, manifested clinically as jaundice, is confined almost entirely to newborn infants. Traditional therapy is to conduct an exchange transfusion when the level of bilirubin becomes critical. In premature infants, the risk of this procedure may be greater than--or exceed--the risk of kerniciterus, the condition associated in newborn infants with excessive unconjugated bilirubin in the blood.

In 1958, it was first demonstrated that serum bilirubin concentrations of newborn infants can be reduced by exposure to light. This treatment, however, had not been widely used because of doubts about its effectiveness and concern for the possible toxicity of the photochemical decomposition products of bilirubin. The research findings now reported indicate that these decomposition products of bilirubin after phototherapy are non-toxic.

The simplicity of phototherapy should make it particularly helpful in premature infants who, in addition, may have anoxia, respiratory distress, acidosis, sepsis, or hypoalbuminemia and are receiving drugs. This group of infants is prone to develop high levels of serum bilirubin, and are poor risks for exchange transfusions. Hyperbilirubinemia still developes slowly enough in this group for phototherapy to work.

Birth Defects and Chromosomal Aberrations

A Washington, D. C., geneticist who is studying gestational anomalies has recently found serious brain and skull defects in four fetuses from LSD users who had had therapeutic abortions, and in the spontaneous abortus of a 5th patient.

Dr. Cecil B. Jacobson of George Washington University, working under an NICHD grant, has examined tissue specimens from spontaneous and therapeutic abortions for evidence of chromosome anomalies which may have caused early damage to the fetus. The project was designed to investigate four factors which may cause such damage: seasonal, post-contraceptive, post-infective and post-mutagenic (viral, radiation, or chemical).

In a series of 102 LSD users, aberrations were found in serial blood and fibroblast cultures from both mother and offspring. Of 14 aborted fetuses, four

showed a protrusion of brain through the neurocranium and failure of neural tube closure. Dr. Jacobson also found moderate to severe chromosome breakages in at least 50 percent of 75 female LSD users examined at the hospital since the summer of 1967. The date in this study represent the most conclusive evidence so far that use of LSD may be a teratogenetic agent in man.

In another study, Dr. Maimon M. Cohen and co-workers at State University of New York at Buffalo reported significantly elevated frequencies of chromosomal damage in the cytogenetic investigation of children exposed to LSD in utero, children of other LSD users not exposed in utero, the mothers of these children and six additional adults taking the drug. In spite of obvious chromosomal aberrations, all of the individuals in this study were apparently healthy and showed no obvious birth defects.

Maternal Phenylketonuria

An increasing number of phenylketonuric women with normal intelligence are approching childbearing age. It is therefore important to ascertain the effect of maternal phenylketonuria (PKU) upon the fetus. There have been a number of reports on the relation between maternal PKU and the I.Q. of offspring. Few reports have dealt with the effect of maternal PKU upon fetal growth.

Recently eight non-PKU children born to three women with untreated PKU were evaluated by Dr. William K. Frankenburg, an NICHD grantee, and his co-workers at the University of Colorado Medical Center and the Wyoming Child Development Center. In addition, the investigator evaluated previously unpublished growth data of 13 non-PKU offspring of phenylketonuric mothers, thus summarizing the growth of 21 offspring of phenylketonuric mothers.

All of the eight non-PKU children of phenylketonuric mothers observed by Dr. Frankenburg were mentally subnormal and had developmental and intelligence quotient scores lower than those of their mothers. In addition, all of the offspring were unexpectedly small. The findings of this study suggest the importance of testing for maternal PKU as a public health measure.

Epidemiological Studies of Mental Retardation

Epidemiological studies of normal and aberrant behavior are being carried out on a continuing basis in Aberdeen, Scotland, where the obstetrical and medical history of every child in the community is a matter of record under the British National Health System. In this situation it is possible to determine the prevalence of mental retardation with considerable accuracy.

NICHD-supported research is being conducted by Herbert G. Birch, M.D., Ph.D., Research Professor, Department of Pediatrics at the Albert Einstein College of Medicine of the Yeshiva University, Bronx, New York using statistics and information from the Aberdeen study.

Of the 9,000 children included in the study sample, there was a 2.8 per hundred prevalence of mental retardation. Among the non-institutionalized children with I.Q. of less than 75, prevalence of some degree of subnormality was ten times as great among children from the lowest social class as among those from the upper class.

The size of the family, ordinal position of the child, level of family disorganization, area of residence, chronic unemployment, poverty, and over-crowded housing conditions were cited in the study as providing some relationship to mental subnormality. The prevalence of retardation was found to be higher among fifth, sixth, seventh, and eighth children than among earlier born children. The prevelence of retardation was found to be significantly higher among children

of mothers who moved downward in terms of social class from where they were before marriage.

When children have massive physiological damage, the extent to which development can be modified by improvement of the socio-environmental circumstances is very limited. There is much greater latitude when the child is physiologically intact, and much greater hope of modification even when the retardation is severe.

Malnutrition and Mental Development

If early malnutrition premanently impairs a child's ability to learn and think, the mental capacity of the human race may decline unless remedial action is taken. Currently over half of the 116* million babies born annually in the world are undernourished during their first three years of life. In Guatemala, 85 percent of all children under six are significantly underweight, 85 babies per 1,000 die in the first year of life, and life expectancy is only 37 years.

In 1964 NICHD contracted with the Pan American Health Organization to perform intensive field studies of the benefits of food supplementation of a population in its natural setting. These long-term field studies can be carried out in Guatemala since malnutrition is widespread and many of the people live in isolated villages.

Preliminary studies demonstrated the existence in these villages of marked nutritional deficiencies in pregnant women and young children, reflected in alterations in placentas, poor and distorted physical growth of youngsters, and high mortality rates. Children rehabilitated after severe malnutrition perform less well on some psychological tests than their brothers or sisters who have not experienced malnutrition. This finding suggests that severe malnutrition rather than social environment is associated with deficits in intellectual development.

The results from this carefully controlled, comprehensive long-term study are expected to yield important information about the effects of nutrition on behavior and learning. To date no similar study has been completed.

Overnutrition

Almost one-sixth of all Americans may be classified as obese, a condition which predisposes them to high blood pressure, diabetes, atherosclerosis, and certain kidney diseases. Most important is the fact that childhood overweight patterns tend to persist into adult life, and current therapy for obesity is ineffective. The work of two Institute grantees, Drs. Jules Hirsch and Jerome L. Knittle, may well have laid the foundation for the control and prevention of obesity.

By observing the growth of fat tissue in animals and humans, they found that early nutritional factors such as overfeeding appear to produce some severe obesity by permanently increasing the number of fat cells. Dr. Hirsch reported finding a marked increase in the total number of fat cells, as well as an increase in cell size, in extremely obese adults who had been fat for a long time. When these individuals lost weight, cell size was diminished while cell numbers remained constant. Studying material supplied by others, Dr. Hirsch found that adults who became obese experimentally--prison volunteers eating a high-calorie diet--showed an increase in fat cell size, but not number. Therefore, the number

*Figure supplied by the United Nations Statistical Office, New York, N.Y., Mrs. Nora Powell

of fat cells appears to be established before adulthood.

American Negro Growth Standards

Most American children are growing taller and heavier than their parents or grandparents. However, the growth trend for North American Negro school children had not been calculated until recently, when a staff member of NICHD gathered both published and unpublished data for this group covering a 78-year period. His findings show that on the average, urban 14-year old Negroes are gaining more in height every ten years than their white classmates in Canada and the U.S. Dr. William M. Moore, medical antropologist at NICHD, focused his study of growth trends on North American Negro children, for whom few standards or norms have been established. He found that the average eight-year-old North American Negro boy now is about the same height as the average ten-year-old boy was at the end of the last century, and that eight-year-old Negro girls weigh as much now as ten-year-old Negro girls did in the early 20th century.

Student Attitudes Towards Politics

While student demonstrations have paralyzed operations at various universities during the last few years, the basic question of how representative the militants' views are of the total student population has not been extensively examined until recently. Three grantees of NICHD, Drs. William Simons, Donald Carns, and John Gagnon, while working at the University of Indiana, found the image of a revolutionary generation a myth, creating an impression of more deeply-rooted and massive discontent than actually exists. Basing their observations on a survey of 1200 students from 12 colleges, they found, surprisingly, that student political position did not become more liberal the longer the student attended college. Seniors appeared to be neither more likely nor less likely to be liberal or conservative than freshman.

Stability was the predominant characteristic of the students' politics. Studends had approximately the same political views as their fathers. When students shifted political positions, the predominant direction was from conservative to liberal, reflecting the general values held at most college campuses. In terms of actual participation, over 80 percent of all men and women in the sample took no part in politics during all four years of college and less than five percent indicated extreme interest in politics.

The researchers concluded that the proportion of radical activists is probably extremely small and unlikely to grow.

Early Visual Stimulation and Reading Readiness

Studies of learning in very young infants and their responses to visual stimulation may be important to the understanding of problems of reading disabilities and so-called reading readiness. Dr. Lewis Lipsitt, a grantee at the Walter S. Hunter Laboratory of Psychology at Brown University, has studied specific types of learning processes in the very young infant and the kinds of experiences that control learning behavior. Knowing that good readers tend to be early readers, he believes that early visual stimulation may also serve as visual reinforcement to the child, eventually leading him to seek out visual stimulation in the form of reading.

His studies suggest that the infant, even as a newborn, is extremely responsive to stimulation and that children possess the visual acuity to do many things sooner than is now expected. Pretraining with visual stimulation and, perhaps, coordinated auditory stimulation, could help develop the fascination with reading materials demonstrated by children who read well. Dr. Lipsett capitalizes

on the visual curiosity of the child, rewarding him for it. This curiosity is a precursor of reading behavior.

Dr. Lipsett demonstrates that babies are capable of learning within the first four days of life. The studies utilize the rooting reflex, the tendency of the newborn infant to turn his head in the direction of a touch at the corner of his mouth. He showed that within a one-hour training period, infants learned to discriminate between one touch and one tone and a different touch and tone. When the baby received a reward for turning his head to one side, he learned to turn his head in the direction of the reward. Thus the newborn can be taught to accommodate his behavior to the feeding situation.

Other studies showed that extremely early stimulation increased infants' later ability to learn. Premature babies who had been held, rocked, and talked to while they were in the hospital showed that this stimulation resulted in superior performance in experiments at four months of age compared with infants who had not been so stimulated. Studies such as these illuminate the complex processes underlying learning achievement and should have practical implications for the field of education. Some of the techniques studied may also be useful in refining diagnostic procedures for earlier detection of various sensory and learning deficits.

Age Pigment Studies

One current theory of aging holds that over the years damaging substances accumulate in cells to the point where they interfere with normal cell function. Age pigment (lipofuscin) which accululates in aging cells has been suggested as one substance that might be implicated in the impairment of cellular function in older individuals. This insoluble substance has been observed in a number of human tissues examined at autopsy. It was found in cardiac muscle, brain tissue, and adrenal glands.

For several years, researchers at NICHD Gerontology Research Center in Baltimore, Maryland, have been studying age pigment accumulation in various animal species. This year, one of these investigators, Dr. Melvin H. Epstein, succeeded in developing a technique to maintain central nervous system cells of rats in tissue culture. Dr. Epstein found that age pigment accumulates in these cells while they are in cultures. In fact, it was observed that more age pigment accumulates in cell cultures originating from old rats as compared to those from young animals.

These findings suggest that an age-related morphological change, noted earlier in tissues of various animal species, can be brought about in an *in vitro* system under experimental conditions that can be rigidly controlled.

The Biology of Aging and Tumor Development

Studies of changes in human amnion cells are making important contributions to our knowledge of the biology of aging and the development of those tumors which are commonly associated with older patients.

Dr. R. Chang and associates at Harvard University have established that the human fetal membrane cells may be an ideal system for investigating environmental agents affecting a transformation in shape and growth rate of normal human cells in tissue culture. Such a transformation is characteristic of tumor formation in the body.

In studying the biology of aging in human cells, the investigators had previously used amnion cells to investigate metabolic changes with age. Because division seems to refresh cell functioning, the investigators believed that cells

that could be kept nondividing would show aging most clearly. The only type of human cell that can be kept nondividing in tissue culture long enough to probe for aging is, oddly enough, the amnion cell, harvested from the placenta. Using the tumor causing Simian virus (SV40) in the present study, the investigators found that X irradiation blocks cell transformation, but does not block the synthesis of the virus in the cell.

Some older cultures were more easily transformed by the virus than some younger cultures. The virus caused dormant cells to proliferate, indicating some viral control over cell regeneration.

Transport of Glucose

The discovery of a novel enzymatic pathway in kidney and intestine by Dr. Bertram Sacktor of the NICHD Gerontology Research Center, Baltimore, Maryland, suggest a mechanism for the resorption of glucose from the glomerular filtrate and across the intestinal mucosa. This new system can function in the transfer of glucose across cellular membranes against a concentration gradient.

The key enzyme in the transport mechanism is trehalase, which hydrolytically splits the sugar trehalose into two glucose moieties. This enzyme is present in several mammalian species, including man. In these species, the enzyme's activity is sufficient to account for the total glucose resorbed by the kidney and intestine. Kidney trehalase activity is localized specifically in the proximal tubules of the cortex, the site of glucose resorption.

The discovery of trehalase together with other enzymes that effect the biosynthesis of trehalose from glucose suggests the possibility that the disaccharide functions in resorption of glucose in the kidney.

Age Differences in Problem-Solving and Learning

The elderly individual's performance on tasks of problem-solving and learning is known to be poorer, generally, than that of younger persons. One problems under investigation at the NICHD Gerontology Research Center, Baltimore, Maryland, is the apparent decrement in reasoning ability exhibited by many older persons.

In one series of studies undertaken by Dr. David Arenberg subjects are given certain information and asked to use this information to solve particular problems. Surprisingly, old subjects were able to handle the changing character of information provided on a par with the young subjects.

The addition of redundant information, on the other hand, resulted in more errors by the older men than by the younger ones. In this case the elderly men tended to treat the redundant material as if it were new data and thus were mislead more often. The young men never were thrown off by redundant clues.

In another section of the Gerontology Research Center, Dr. Charles L. Goodrick is trying to analyze the effects of aging on learning in animals.

One study conducted by this investigator involved using a complex maze to determine age differences in rats' abilities to learn. Old rats either failed to learn the maze or did so very slowly while young rats experienced little difficulty.

These results suggest that the age differences in learning and extinction were due to behavioral rigidity or relative lack of variability.

Cancer Survival Rates

Survival of patients, a crucial measure of progress against cancer, shows important gains associated with improved diagnostic and treatment methods. The National Cancer Institute (NCI) reported this evidence at the Sixth National Cancer Conference in September 1968 in its latest evaluation of end results of cancer therapy covering a 25-year period.

From data on nearly 400,000 white patients in more than 100 hospitals in different parts of the country, increased survival was observed among patients with cancer of the colon, rectum, breast, uterine cervix, prostrate gland, and a number of other body sites of a total of about 50 studied.

Additional analysis of the data from the study disclosed that the survival rate for cancer of the colon increased from 31 percent during 1940-49 to 46 percent during 1955-59; for cancer of the rectum the comparable increase was from 28 percent to 40 percent. These cancers together occur more frequently than any other form in the United States. Surgery remains the treatment of choice.

Five-year survival rates for patients with breast cancer, the leading cause of cancer death in women, increased slowly but steadily, particularly among patients whose disease had spread to regional lymph nodes or adjacent tissues. The data suggest that such patients may have been diagnosed in an "earlier" phase of regional disease, but at least 10 years of followup must elapse before it can be determined whether a higher percentage of "cures" will be obtained.

The trend in cancer of the uterine cervix, the third most deadly form of malignancy in women, was toward a marked increase in diagnosis of carcinoma-in-situ, and early stage of the disease, and a decrease in occurrence of invasive cancer. This suggests more effective use of techniques, such as the "Pap" smear, for detecting this form of cancer before it spreads beyond the site of origin.

The outlook for lung cancer, the major cause of cancer death in men, remains grim. Only about one in five lung cancers is discovered in early stages, and only 5 percent of patients ultimately survive.

Drug Treatment

Fast and Slow Growing Tumors. From studies of cell kinetics, the growth characteristics of populations of cells, investigators are attempting to build a theoretical base for cancer chemotherapy. Results of their studies suggest that the sensitivity of cancers to drugs is related to the rate at which they grow. Thus, the types of malignancy in which the major successes in drug control have occurred are rapidly growing tumors, such as acute lymphocytic leukemia; Burkitt's lymphoma, a type of cancer seen most frequently in African children; choriocarcinoma, a highly malignant cancer that arises from the placenta; and Wilms' tumor, a type of kidney cancer in children probably of congenital origin. The types that are poorly responsive to drugs, such as cancers of the lung, breast, and colon, are slowly growing tumors.

Further studies in experimental systems seem to suggest an important difference between the cell populations of tumors that grow rapidly and those that grow slowly. It appears that the fraction of tumor cells dividing at any one time is as high as 90 percent in the fast growing tumors, but may be only 1 percent in the slow growing ones, with 99 percent of the cells of the latter tumors in a nondividing state. Experience has shown that most of the highly active cancer drugs, such as methotrexate and vincristine, affect only cells during the division cycle. Hence, tumors with a large fraction of cells actively dividing would be fast growing and drug sensitive. Tumors with small fractions of dividing cells and large fractions of nondividing cells would be both slow growing and drug sensitive.

Clinical evidence of the increasingly effective use of drugs against the rapidly growing tumors continues to mount. Reports from various clinical studies indicate that 85 to 100 percent of patients with acute lymphocytic leukemia, given combinations of drugs in intensive, intermittent courses, are achieving complete remissions and that the durations of remissions range from 23 to more than 40 months among the various groups. The latest report from the NCI-sponsored Acute Leukemia Cooperative Group B on survival of patients under 20 years of age with acute lymphocytic leukemia shows that about 60 percent of the children are surviving 24 months from diagnosis of their disease. Currently, nine effective drugs, are in use in various combinations: methotrexate, mercaptopurine, prednisone, cyclophosphamide, vincristine, cytosine arabinoside, daunomycin, BCNU, and L-asparaginase. Children with acute lymphocytic leukemia who have begun treatment in the last few years have an estimated median survival of about 3 years (half of the patients will still be alive 3 years from the beginning of treatment).

Studies are in progress in the clinic on cancer of the breast, colon, and lung in attempts to match the administration of drugs to the unique biology of these slowly growing tumors, whose average doubling time is measured in weeks to months. The studies will include trials of both new drugs and new dose schedules.

Mycosis Fungoides. In February 1968 NCI scientists reported to the National Advisory Cancer Council results of a study in which the drug treatment of mycosis fungoides, a cancer of the lymphoma type, was adjusted according to the mitotic rate of cells in the tumor. Dr. Harley Haynes reported that, at the outset of the study, 23 patients with this form of cancer were treated with methotrexate once a week. Eight patients responded completely to this drug schedule; the others showed lesser or no response.

When the mitotic rates of cells from the individual patients were studied, it was discovered that patients with the lowest mitotic count had shown the best response to the drug treatment, while those with the highest mitotic count showed the least response. Accordingly, patients unsuccessfully treated with once-weekly methotrexate were given the drug twice a week. Two patients who had not responded on the original schedule achieved complete remission on the new schedule. The scientists suggested that this method of tailoring drug dosage to cell growth rate might be useful in treating other forms of cancer.

Lymphomas. Encouraging results in treatment of advanced Hodgkin's disease by means of intensive, intermittent combinations of drugs continue in a study first reported in 1967 by Drs. Vincent T. DeVita and Arthur Serpick of NCI. The drugs were vincristine, introgen mustard, ibenzmethyzin, and prednisone. The latest results indicate that 80 percent of the patients achieved complete remissions and 50 percent remained in remission longer than 2 years. Combination drug therapy then makes available a degree of drug control of advanced Hodgkin's disease not previously possible.

At the 1968 meeting of the American Association for Cancer Research, Dr. Raymond E. Lenhard, Jr. of Johns Hopkins Hospital and collaborators in Acute Leukemia Group B and the Eastern Cooperative Oncology Group described results in treatment of other forms of lymphoma with combination chemotherapy. A high-dose combination of cyclophosphamide, vincristine, and prednisone produced higher remission rates than did cyclophosphamide alone. In this study, the high-dose combination produced remissions in 100 percent of patients with lymphosarcoma and 85 percent of those with reticulum cell sarcoma, contrasted with remissions of 40 percent and 50 percent, respectively, achieved with single-drug therapy.

A drug, BCNU, which was established in the last several years as an additional, effective agent in the combination treatment of acute leukemia of childhood was found to be temporarily effective in some drug-resistant lymphomas. In August 1968, NCI grantees cooperating in the Southeastern Cancer Chemotherapy

Study Group reported activity of BCNU, or 1,3-bis-(2-chloroethyl)-1-nitrosourea, in temporarily controlling advanced Hodgkin's disease in 17 of 31 patients resistant to standard drug treatment with alkylating agents. Responses were also noted in patients with lymphosarcoma and reticulum cell sarcoma, although to a lesser degree. The report was prepared by Dr. Howard E. Lessner of the University of Miami School of Medicine for the group of 15 cooperating clinical investigators at eight medical centers.

L-asparaginase. At NCI and a few NCI grantee medical centers such as the Memorial Sloan-Kettering Cancer Center, L-asparaginase is being evaluated in patients. The value of L-asaparaginase, an enzyme, has been found to depend on the presence or absence of another enzyme, asparagine synthetase, in the tumor cells of the patient. According to Dr. Alton Meister, who is investigating L-asparaginase in a NCI-contract-supported study, he and colleagues at the Cornell University Medical College and Sloan-Kettering Institute for Cancer Research found that tumors that are sensitive to L-asparaginase lack the enzyme asparagine synthetase. Tumors that are not sensitive to treatment with L-asparaginase contain asparagine synthetase, often in large amounts.

L-asparaginase exerts its anticancer effect by destroying asparagine, an amino acid essential for all cells, whether normal or cancerous. Tumors sensitive to L-asparaginase cannot synthesize asparagine because they lack asparagine synthetase, which is necessary for its production; they obtain asparagine from the body's extracellular fluids, such as the blood. L-asparaginase breaks down this extracellular asparagine and stops the growth of the tumor.

The NCI is investigating the possibility that the antitumor effect of L-asparaginase can be enhanced in combination therapy with other drugs. The drug is being made available in larger quantities than formerly by a major drug manufacturer for studies by the NCI and several NCI grantee medical centers cooperating in the Institute's chemotherapy program.

PolyI:C, A New Drug. PolyI:C is a new kind of potential cancer drug that results from research on viruses and interferon, a protein produced by cells as a defense against attacking viruses and certain other disease agents, such as the organisms causing psittacosis and trachoma. Certain non-living materials also induce the production of interferon by cells; these include natural and synthetic biologically related substances. PolyI:C is one of these interferon inducers; it is a synthetic double-stranded RNA (ribonucleic acid) formed by mixing two chemical compounds, polyinosinic and polycytidylic acids.

It is believed that interferon acts by inducing an infected cell to produce another intracellular protein, which is thought to combine with ribosomes (the protein manufacturing sites) in the cell. The altered ribosomes then no longer continue to make the proteins essential for continued support of the attacking disease agent but do continue to make the host cell's proteins in a normal manner. Cancer investigators thought that in a similar fashion interferon might inhibit the growth of tumors without affecting normal cell growth.

In a series of experiments carried out by scientists of NCI and the National Institute of Allergy and Infectious Diseases, treatment with the interferon inducer polyI:C resulted in regression of tumors, decreased rates of tumor growth, and increased survival time of laboratory animals bearing several different types of transplanted tumors. These included, in mice, leukemias, reticulum cell sarcomas, tymphatic lymphomas, fibrosarcomas, plasma cell tumors, human adenovirus 12-induced tumors, and Bittner mammary tumors; and a sarcoma in rats. Originally some of the tumors were virus induced and others were spontaneous tumors.

Preliminary studies are under way preparatory to introduction of the drug

into studies of cancer in petients. The mechanism of its antitumor activity is also being studied. The investigators now think that the antitumor effect of polyI:C is more complex than that related solely to the antiviral action of the interferon induced.

Viruses as Possible Cancer Causes

C-Type Particles. To date, virus-like particles of two different types have been detected, and, in some instances, isolated from patients with different forms of cancer. C-type particles, identical with those known to cause leukemia in laboratory animals, have been seen with the electron microscope in pellets obtained by spinning down blood from leukemia patients. It is, however, still difficult to obtain them in sufficient quantity to make definitive progress toward proof of their cancer-causing activity.

Herpes-Type Virus. The second type of virus associated with leukemia and lymphoma is herpes-type virus (HTV). This virus is similar in structure and size to herpes viruses, which cause fever sores and shingles in man, and is similar also to a HTV thought to be involved in Marek's disease, a prevalent type of leukemia in chickens. Large quantities of HTV can be recovered from tissue cultures and it can be further purified and concentrated for identification studies.

One type of HTV, Epstein-Barr virus (EB), has been recovered from cultured lymphocytes derived from patients with Burkitt's lymphoma. Until fairly recently, infectivity or other kinds of biologic activity had not been shown with the EB virus. Der. Werner Henle and colleagues at the University of Pennsylvania presented convincing evidence that the EB virus is closely associated with and may actually cause infectious monomucleosis. Dr. James T. Grace and associates at Roswell Park Memorial Institute obtained clinical proof that EB virus cultivated from Burkitt's lymphoma cells is capable of inducing infectious monomucleosis in human beings. These results suggest that a DNA, herpes-type, virus is capable of inducing rapid and, for a time, uncontrolled proliferation of the human blood cell system.

Of high interest is Dr. Henle's corollary finding that 100 percent of African children with Burkitt's lymphoma have high levels of antibody to this virus, whereas fewer than 50 percent of normal children living in the Burkitt's lymphoma geographical area show these antibodies. Similar sero-epidemiological surveys are being conducted with lymphoma and leukemia patients in the United States to investigate possible causal relationships.

In reports made by two groups of NIH-supported scientists, human cancer of the uterine cervix was reported to be associated with a herpes-type virus. Earlier epidemiological studies had suggested that a venereally transmitted agent, possibly a virus, might be involved in development of this type of cancer, the third most deadly form in women. Drs. William E. Josey, Andre J. Nahmias, and Zuher M. Naib, of Emory University School of Medicine, reported that clinical, laboratory, and epidemiologic evidence supports the suggestion that type 2 herpes virus is a prime suspect as a cause of this disease. The same conclusion was drawn independently by Drs. W. E. Rawls, J. L. Melnick, and co-workers at Baylor University College of Medicine. They found that 83 percent of a group of cervical cancer patients had antibodies to type 2 herpes virus, demonstrating past exposure to the virus. Levels of antibody is matched controls and in women with other forms of cancer ranged from 0 to 20 percent.

Immunology and Osteosarcoma

Drs. Donald L. Morton and Richard A. Malmgren of the National Cancer Institute reported immunological evidence that an infectious agent, possibly a

virus, may be associated with human osteosarcoma (cancer of the bone). Serums from four patients contained antibodies that reacted with a common antigen (or antigens) in the patients' own cancer tissue and in specimens from the other osteosarcoma patients. A high level of antibodies was also demonstrated in serums from members of the patients' families and from close associates of one patient. Tests of serums from normal blood-bank donors revealed a significantly lower level of this antibody than in the serums of patients, relatives, or close associates. The appearance of a low level of reactivity in normal serums against these osteosarcomas suggests that the infectious agent may produce unrecognized infections in normal individuals.

Cancer and Organ Transplantation

An entirely new aspect of research on immunology as related to cancer is suggested by the reports of development of malignant lymphoma in a few patients receiving immunosuppressive therapy to facilitate organ transplants. All patients had received kidneys from live, related donors. All had received azathioprine and predrisone, and several had also received antilymphocytic serum. With one possible exception, there was no evidence that the tumor was present in any of the patients prior to transplantation. There was no evidence that the tumors were transplanted from the donors.

Possible Test for Susceptibility to Cancer

A technique is under study by NCI scientists Drs. Robert W. Miller and George J. Todaro that has the potential for identifying individuals with a high risk of developing leukemia and other types of cancer. The research stems from two recent observations: that persons with certain abnormalities, such as inborn immunological defects, chromosomal disorders, and congenital conditions, have a higher than expected risk of developing leukemia, lymphoma, or other type of malignant disease; and that persons in this high-risk group may be identified by the response of certain of their cells known as fibroblasts in tissue culture to a known cancer-causing (in aminals) virus, with the magnitude of the risk related to the fraction of cells transformed by the virus.

Through use of this technique the NCI investigators have shown that fibroblasts from individuals with two inborn disorders, Down's syndrome or Fanconi's aplastic anemia, which are associated with a high risk of leukemia, are 3 to 50 times more sensitive than are normal fibroblasts to transformation in tissue culture by the virus SV40. Much more work is needed to assess the efficacy of the technique through studies of cells from persons with these various abnormalities, their close relatives, persons exposed to environmental cancer-causing agents, and patients with untreated leukemia or other cancers.

Search for Infectious Cause of Rheumatoid Arthritis

More research has centered on a possible infectious etiology for rheumatoid arthritis during the past five years than during the previous twenty, but as yet no specific agent has been identified positively as a cause of this disease. In research supported by the National Institute of Arthritis and Metabolic Diseases (NIAMD) at the University of California, Drs. E. P. Engleman and K. F. Meyer recently demonstrated that Bedsonia viruses isolated from human patients with Reiter's syndrome, a disease resembling rheumatoid arthritis, cause chronic arthritis when injected into joints of monkeys. This past year, the same scientists extended this finding to rabbits and demonstrated that Bedsoniae infecting the eye may disseminate to joint tissues, liver, kidney, and spleen in a manner suggestive of the occasional involvement of major organ systems accompanying rheumatoid arthritis in humans. Thus, the rabbit may serve as a readily-available animal model for experimental study of Bedsonia arthritis and for evaluation of the mechanisms involved in the initiation of joint damage.

Search for an Immunological Basis

Drs. J. I. Sandson and D. Hamerman of Einstein School of Medicine, New York City, have demonstrated that certain components of human connective tissue and of certain streptococci are so similar that they cross react immunologically. Thus, it is possible that antibodies formed in the body to combat invading streptococci could mistakenly attack similar components of connective tissue, initiating an autoimmune reaction with consequent destruction of joints and/or connective tissues. The finding strengthens the concept that an initial infection and later development of an autoimmune form of rheumatoid arthritis are not mutually exclusive.

Tissue Breakdown Studies

Central to research on rheumatoid arthritis is an understanding of the breakdown of collagen, a chief protein of connective tissue that is vital to the integrity of major body organs and tissues, of joints and of joint linings. An enzyme (collagenase) involved in the destruction of collagen and in the degeneration of connective tissue has been recovered from various sites in the body. This past year collagenase was isolated by Dr. S. M. Krane of Massachusetts General Hospital from synovial membranes sheathing the affected joints of patients with rheumatoid arthritis. The importance widely attributed to this area of investigation is evident in the extent of collaboration in the current work, which is being conducted by researchers representing Massachusetts General Hospital, NIAMD, George Washington University Hospital, Walter Reed Army Medical Center, and the National Institute of Dental Research.

In further research by the investigators, specimens of synovial membrane were taken from the joints of 24 patients with active rheumatoid arthritis, and the enzyme collagenase was found to be more active when the disease process became more active in these patients. Collagen destruction is not unique to rheumatoid arthritis, and the investigators believe that the enzyme activity may be but a non-specific reaction to inflammation. The research now underway in this area may result in more effective therapy for a number of inflammatory diseases.

Diabetes

Recent diabetes research has reflected a trend toward studies of a more fundamental nature which have yielded information leading to a better understanding of the underlying causes of diabetes. This trend is continuing; the most provocative findings pertain to the precise mechanism of insulin secretion and action, findings which could lead directly to the cause of several different forms of diabetes.

Proinsulin. The first of these findings was by Dr. D. F. Steiner of the University of Chicago who has discovered a precursor form of insulin in the human pancreas. The investigator, whose research has long been supported by the Institute, has labeled the substance "proinsulin" and has suggested that a partial or complete failure of conversion of proinsulin to insulin may account for some forms of diabetes.

Big Insulin. Coinciding with the discover of proinsulin was the relevation by Dr. J. Roth, an NIAMD scientist in Bethesda, that the insulin which circulates in the bloodstream may exist in two distinct forms in man: "little insulin", indistinguishable from insulin in the pancreas, and "big insulin", which is a larger molecule and comprises up to 50 percent of the insulin in the circulation. It is believed that the physiology of insulin secretion should be reexamined in light of these new finding, particularly in such conditions as obesity and maturity onset diabetes in obese individuals, which are characterized by glucose intolerance and excessive production of insulin.

Cystic Fibrosis

Dr. A. G. Bearns of Cornell University recently pinpointed a cellular difference between normal persons and those in affected or carrier states of cystic fibrosis. Using a special straining technique, this newly-discovered genetic cell marker can be seen in fibroblasts, the flat elongated cells which form fibrous tissue.

Sodium Levels and Transport. Sodium concentrations in sweat and saliva of patients with cystic fibrosis are known to be elevated. Last year, Dr. J. A. Mangos of the University of Wisconsin demonstrated that perfusion of the rat parotid (salivary) gland with sweat and saliva from patients with cystic fibrosis causes a large increase in sodium output by these glands. The implication of this finding is significant: the same factor in sweat and saliva from patients with cystic fibrosis which causes salty saliva in rats may be responsible for the high salt content of the patient's own sweat and saliva. This factor, once isolated, may help to elucidate the inherited molecular defect which causes cystic fibrosis.

More recently, Dr. L. G. Welt of the University of North Carolina has described a marked decrease in sodium output from the red blood cells of patients with cystic fibrosis, and a similar decrease in the red blood cells of their symptom-free parents. This defect in sodium transport should be of value in detecting cystic fibrosis carriers, and therefore, should be useful in genetic counseling.

Other Metabolic Diseases

Lesch-Nyhan disease, first described by an NIAMD-supported scientist in 1964, is characterized by brain damage, a compulsion to chew away the lips and fingers, excessive production of uric acid, and an early death. In 1967, Dr. J. E. Seegmiller headed a team of NIAMD scientists in Bethesda which showed that such patients, who are all males, are deficient in an enzyme of purine metabolism, hypoxanthine-guanine phosphoribosyltransferase, or PRTase, as a result of a mutant gene on the X-chromosome.

The same scientists now have identified an as yet unborn female child as a carrier of the trait for Lesch-Nyhan disease, by measuring PRTase activity in cells of the fetus grown in cell culture and obtained from amniotic fluid of the mother, a known carrier of the disease trait. Indications are that the same general procedure is capable of detecting a fetus fully afflicted with the disease at an early stage of gestation, as well as victims of other hereditary metabolic disorders. Such early identification of victims of inherited metabolic diserders would be invaluable for genetic counseling of carrier parents.

Gastrin. Several years ago, NIAMD grantees at the University of Liverpool elucidated the chemical nature and structure of gastrin, the hormone which stimulates secretion of gastric juices, and subsequently synthesized the hormone. Dr. J. E. McGuigan, an NIAMD grantee at Washington University, St. Louis, now has located and described the specific cells in human gastric mucosa which contain gastrin.. This finding should shed light on the pathogenesis of gastrointestinal diseases such as peptic ulcer. Current studies are designed to determine whether gastrin is actually synthesized by the gastrin-containing cells identified in this study.

Milk Intolerance. During the past three years, Institute-supported researchers have traced the cause of milk intolerance in certain otherwise normal adults, and in patients with inflammatory bowel disease, to a deficiency of the intestinal enzyme lactase. This enzyme, which converts lactose or "milk sugar" into its simple sugar components, glucose and galactose, is essential to digestion of

of lactose and to subsequent absorption of its products of digestion. Evidence still is accumulating to indicate that intolerance to milk is a realtively common syndrome in adults.

Last year, Dr. T. M. Bayless of Johns Hopkins University demonstrated that milk intolerance associated with lactase deficiency is much more common in Negro adults (70 percent) than in white adults (5-10 percent), suggesting that intestinal lactase activity may be genetically controlled. The same scientist now hes shown that milk intolerance due to a lactase deficiency is also very common among adults of Oriental extraction. Thus, a large part of the world's non-white population may have a genetically determined intolerance to milk, a situation which would require reevaluation of the importance of milk as a source of nutrition and protein among non-white adult populations.

Liver Disease. Previous NIAMD-supported studies have indicated that excessive alcohol ingestion can lead to development of fatty liver, a forerunner of cirrhosis, despite a concurrent well-balanced dietary intake. This finding is contrary to the conventional hypothesis that a poor diet along is the cause of liver damage in alcoholic individuals. Drs. C. S. Lieber and E. Rubin of the Mt. Sinai School of Medicine, New York City, now find that, in persons who drink only occasionally, acute exposure to alcohol may lead rapidly (after only two days) to hepatic fat accumulation and to microscopic structural changes, regardless of nutritional factors. According to the investigators, it is clear that alcohol can rapidly produce liver injury when taken in amounts equivalent to that consumed not only by recognized alcoholic persons, but by many social drinkers as well. Blood alcohol levels measured during the experiments showed that a person need never have been seriously inebriated to sustain alcohol-induced liver injury.

Kidney Disease

Infection and Ureteral Peristalsis. The precise mechanism by which most instances of kidney infection (pyelonephritis) occur is as yet unknown. Dr. Saul Boyarsky of Duke University, Durham, North Carolina, recently has described experiments with animals which suggest that the presence of live or dead bacteria in the ureter, without active infection, may facilitate subsequent development of pyelonephritis by causing cessation of normal ureteral peristalsis. When E. coli bacteria cultured from the urine of patients with pyelonephritis were introduced into the renal pelvis of dogs, ureteral peristaltic activity diminished in most cases to 50 percent and in some cases to zero. Endotoxin, a well-known toxic substance in the cell walls of the bacteria, was also shown to influence ureteral motility in vitro. These findings may open new approaches for research on the precise mechanism of infection of the kidney, perticularly with organisms derived from the intestinal tract.

Kidney Stones. Dr. J. Lemann of Marquette University has shown that both urinary calcium concentration and excretion rise sharply in calcium stone-formers, and in relatives of stone-formers following sugar ingestion, effects which clearly distinguish these subjects from normal individuals. It is suggested that augmentation of urinary calcium excretion and concentration after meals, or after ingestion of carbohydrate-rich foods or berages, may be one factor contributing to calcium stone formation in susceptible individuals. If these findings are substantiated by further study, kidney stone-formers should be advised to avoid high carbohydrate intakes, particularly during climatic or exertional conditions favoring dehydration.

Kidney Preservation. In the relatively fledgling field of organ preservation, a transportable machine has been developed which has preserved excised human kidneys as long as 17 hours and animal kidneys as long as 72 hours prior to transplantation. Human kidneys obtained from cadavers have been transplanted successfully following preservation by the device, which permits transplantation

to be a somewhat more elective procedure rather than an immediate one upon availability of a cadaver kidney.

While the isolated organ is being perfused, time is gained to allow matching of donor and recipient by tissue typing, and to do preparatory surgery. The machine also eliminates the problem of simultaneous surgery, and the need for two surgical teams, one to remove the kideny from its original location, and the other to transplant it into the new host. Because the unit is easily transportable, perfusion of the isolated kidney can be started immediately upon its removal from the expired donor in one hospital, and continued during transfer to another hospital, even in another city, where the recipient is ready for transplant surgery. Although developed specifically for the preservation of kidneys, studies are now underway by the machine's developer, Dr. F. O. Belzer of the University of California, San Francisco, to modify the device for similar preservation of hearts and livers.

Artificial Kidney Program. A new and unique hollow fiber capillary kidney, which is being developed under a contract with the Dow Chemical Company has progressed to full-scale clinical testing at the Northern California Dialysis Center, San Francisco General Hospital.

The hollow fiber artificial kidney consists of 11,000 hollow cellulose threads bundled together into a compact plastic cylinder about the size of a quart milk bottle. Blood is passed through these manmade capillaries and they, in turn, are constantly washed on the outside by a blood pruifying dialyzing solution. The unique construction of the kidney provides an enormous surface at the cellulosic blood-dialysate solution interphase at which toxic waste products migrate from the blood into the dialysate fluid. This new dialyzer is designed so well that no external blood pump is needed to drive the blood through it. Moreover, its internal blood compartment volume is so small that only about 70 milliliters of the patient's own blood are needed to prime the unit, thus eliminating the need for compensatory blood transfusions (and their attendant hazard of hepatitis) associated with the use of most conventional artificial kidneys. The new compact capillary kidney is easy to use in a hospital or home dialysis setting since it comes pre-sterilized, filled with saline and ready for operation. Its cost projections make it more than competitive with conventional disposable coil dialyzers.

The new device has now proven its clinical effectiveness during more than 1000 dialyses. It is routinely re-used three times before it is discarded. It has been established experimentally, however, that it can be re-used up to nine times and further studies are planned on this economically important facet.

Diet Therapy. During the past year, the Artificial Kidney Program has striven to encourage clinical studies in the United States of a special diet, and modifications thereof, which has shown in trials in Italy and England that it permits moderate-term survival, cessation of symptoms, and rehabilitation in certain types of patients with chronic renal failure who are otherwise faced with the need for chronic dialysis or kidney transplantation. During a 21-month study period, Dr. Charles Kleeman and associates at Cedars-Sinai Hospital in Los Angeles have demonstrated that a 20 gram, balanced, low-protein diet limited largely to essential amino acids, but unlimited in carbohydrates and fats can ameliorate uremic symptoms in patients with minimal, residual kidney function.

Similar encouraging results were obtained by Dr. Kurt Lange at New York Medical College who has already progressed to maintenance of patients with a combination of this diet and infrequently applied hemodialysis (once every two weeks rather than the conventional three times per week).

Hematology

The NIAMD, largely through grant-supported studies, has made several significant findings related to such blood diseases as hemophilia, aplastic anemia, and gamma globulin disorders.

Aplastic Anemia. Aplastic anemia is a severe blood disorder in which the bone marrow fails to produce adequate amounts of essential cellular blood elements. Periodic whole blood transfusions are the mainstay of therapy. Although the prognosis for affected children has improved substantially with the discovery in the late 1950's that the hormone testosterone stimulates bone marrow regeneration, mortality has remained at greater than 50 percent.

A scientist at Mount Sinai Hospital, New York City, Dr. W. Dameshek, has shown that oxymetholone, a synthetic derivative of testosterone, is a potent bone marrow stimulant and, thus, of possible value in the therapy of aplastic anemia. Five children with aplastic anemia, including two who were refractory to testosterone therapy, had a satisfactory bone marrow and clinical response to oxymetholone therapy, and 3 of the patients remained free of all medication and remained well throughout the follow-up period (18 to 24 months). Thus, the use of oxymetholone in the treatment of aplastic anemia, particularly in refractory cases, seems to warrant further study.

During the past decade, 16 cases of aplastic anemia following hepatitis have been reported. In 1968, other investigators at Mount Sinai Hospital, Drs. E. Rubin and C. Gottlieb, described 10 additional cases of this syndrome, all of which were observed within a two-year period. The increased frequency of the syndrome would appear to exclude a coincidental relationship between these two entities.

Hemophilia. Classical hemophilia A is marked by an inborn, permanent tendency to bleed, due to a deficiency of antihemophilic factor, or AHF, one of several substances essential for normal clotting of blood. There are more than 10,000 such patients in the United States, and a temporary or permanent source of AHF could be valuable in their treatment.

Perfusion of normal pig spleens with blood obtained from hemophilia patients has been found to stimulate production by the pig spleen of AHF, apparently by a hiterto unknown substance in the hemophilia patient's blood. The finding suggests that transplantation of a normal human spleen might provide a permanent source of AHF for patients with hemophilia and that it may alleviate their bleeding symptoms.

Several months after he reported this finding, Dr. J. C. Norman of Harvard University reported that classic hemophilia A in dogs, which is pathologically, genetically, and hematologically indistinguishable from that occurring in man, may indeed be cured by splenic homotransplantation. Such surgery was performed successfully in six hemophilic dogs, one of which was alive and well almost one year later. Dr. Norman's findings may have implications for clinical hemophilia in man.

Endocrinology

Drs. A. G. Frantz of Columbia University and B. Kliman of Massachusetts General Hospital have shown that excessive plasma growth hormone (HGH) in acromegalic patients can be effectively reduced by means of irradiation of the hyperactive pituitary gland with heavy-particle proton-beam therapy. Reduction in circulating HGH levels was accompanied by return of the patient's blood chemistry and clinical status toward normal, with only a few relatively minor and transient complications. It is believed that proton-beam therapy compares

favorably with other procedures in its ability to suppress plasma HGH levels and in the infrequency of serious complications.

It is well-known that thyroid cancer can be induced in animals by prolonged overstimulation with thyroid stimulating hormone (TSH). Measurements of TSH levels in human serum and thyroid tissue now have shown that such levels are consistently higher in thyroid cancer patients than in patients with other thyroid diseases, suggesting that chronic overstimulation of TSH may play a causal role in human thyroid cancer.

Such measurements were made possible by the recent development of an extremely sensitive immunofluorescent assay for TSH by Dr. F. S. Greenspan of the University of California, San Francisco. This assay has also been used to establish TSH blood ranges in normal males and females.

Recent research has shown that the mammalian pineal gland synthesizes the hormone melatonin at a rate that aries with a 24-hourly rhythm in response to the 24-hour light-dark cycle. It has been suggested that the pineal gland may function as a "biologic clock" which regulates certain endocrine and neural functions in cyclical or "tidal" fashion according to the time of day. Little has been known, however, of melatonin's mechanism of action, which is essential to understanding the function of the pineal gland.

It has now been shown by Dr. R. J. Wurtman of the Massachusetts Institute of Technology that administration of melatonin to rats results in a rapid rise in serotonin concentrations in the brain, especially in the midbrain region. Here, serotonin uniquely regulates the activity of certain nerves which partially control hypo halamic activity and, thus, pituitary activity. This may be the mechansim by which the pineal gland is sble to superimpose a 24-hour rhythm on the body's endocrine system.

Studies of parathyroid hormone by Institute scientists in Bethesda, Drs. L. R. Chase and G. D. Aurbach, have shown that parathyroid hormone and vasopressin have identical modes of action within the kidney, although they act at anatomically separate sites, the former in the cortex and the latter in the medulla. This finding supports the theory that hormones may exert their effect on widely different target cells by a common mechanism.

Dr. Aurbach has also demonstrated that infection of human parathyroid tumor tissue with simian virus 40 permits long-term growth of monolayer cell cultures that produced parathyroid hormone through 13 subcultures for more than nine months. Such studies should permit detailed evaluation of factors which influence the synthesis and secretion of parathyroid hormone in normal and abnormal parathyroid tissues.

Nutrition

Nutrition is another important field in which the Institute has a vital interest. Several research findings in this particular area during the past year merit special recognition. The first of these concerns vitamin D, which, by regulating the absorption of calcium and phosphorus from the intestinal tract, acts to maintain normal bone metabolism.

A University of Wisconsin scientist, Dr. H. F. DeLuca, has isolated the major biologically active component of vitamin D and has termed it 25-hydroxycholecalciferol, or 25 HCC. Tests of its ability to prevent or cure rickets in animals have shown it to be 40 percent more effective than vitamin D, suggesting that it may be superior to the vitamin in the treatment of rickets and other vitamin D-deficiency diseases.

Basic Research

The importance of stimulating and supporting basic research is best illustrated by some exciting advances made possible by new fundamental knowledge. For example, NIAMD scientist Dr. Maxine Singer's arduous experimentation utilizing a specific enzyme led to the easy, and previously impossible, preparation of synthetic, double-stranded ribonucleic acids (RNA) of pre-determined composition. Subsequently, it was found by other investigators that a combination of two of these, called PI:C in biochemical shorthand, can induce interferon production in animal cells. Interferon, the body's natural virus-fighting substance, has long been known for its ability to prevent viral diseases. A scientist from a sister Institute, the National Institute of Allergy and Infectious Diseases, now has provided solid evidence that interferon stimulation with PI:C can cure an acute and often fatal viral infection, herpes simplex keratoconjunctivitis, in rabbits. The use of these RNAs which stimulate the body's interferon system, now has opened possible new therapeutic approaches to a host of other viral infections. Thus, a research effort best characterized as "basic research" again has made available new materials of great potential usefulness in clinical medicine.

Another example of basic research resulting in handsome dividends came when National Cancer Institute scientists reported that a drug called cytosine arabinoside, or Ara-C, had produced complete remissions in 19 of 40 patients with acute myelocytic leukemia, a form of cancer against which little progress has been made to date. This clinical accomplishment stemmed directly from earlier basic laboratory research conducted by an NIAMD scientist in Bethesda, Dr. C. Glaudemans, who devised a wholly new method for synthesizing several precursor forms of Ara-C. Other investigators subsequently extended his methods to permit the synthesis of a variety of related agents, including Ara-C. Were it not for the basic research by Dr. Glaudemans, such drugs as Ara-C would not be available for clinical studies and commercial production at the present time.

Organ Transplants

In 1968, "The Year of the Heart Transplant", interest in immunology was most urgently directed toward the problem of graft survival. Antisera against lymphoid (immune) cells, have proved potent graft rejection suppressors. Their effective use has, however, required relatively prolonged and painful administration, pointing up the need for further research. The National Institute of Allergy and Infectious Diseases (NIAID) investigators M. A. Mandel and R. Asofsky have used an accurate quantitative assay to measure the degree and duration of immunosuppression produced by antithymocyte serum (ATS) and to identify its active components. It was found that the effects of ATS lasted several weeks, but that immune reactivity had to be lowered about tenfold in order to prevent graft rejection. The bulk of activity was found in one serum component known at the IgG fraction. Studies are continuing on this fraction and its remarkably enhanced effect in germfree mice.

One NIAID grantee, A. P. Monaco of Harvard Medical School, has succeeded in reducing the necessary dose of ALS by using it in a novel fashion. After treating mice with ALS for one week only, he immediately applied temporary skin grafts to the animals. This method induced lasting specific immunologic tolerance to tissue of the grafted type, without the need for further ALS administration.

In another development in this area, F. P. Stuart and F. W. Fitch at the University of Chicago have reported success in preventing kidney graft rejection in rats indefinitely by treating grafted animals with donor cells plus antibody against these cells. Unlike the usual method of inducing specific tolerance, this approach dose not require large amounts (as yet unavailable) of purified

transplantation antigen.

The immune reactivity of the grafted cells was much less than might have otherwise been expected. The scientists are continuing their investigations of this method for preventing graft rejection and are testing its use in combination with ALS to determine if a synergistic effect can be obtained.

In a major step toward application of current transplant research findings to man, NIAID researchers, working in collaboration with Italian scientists, have succeeded in isolating a water-soluable transplantation antigen from human spleen cells. Meanwhile, a grantee at the Roswell Park Memorial Institute has established reliably-growing mass cultures of human white blood cells--an excellent source of antigens.

Recent findings by contractors and grantees of NIAID indicate that sensitized cells are not the sole agent of graft rejection, as had been widely believed. The NIAID-supported scientists demonstrated a significant association between graft rejection and the presence of certain circulating antibodies. In particular, "hyperacute" graft rejection--the type of dramatic rejection occurring within one hour of transplantation--was convincingly related to the pretransplant finding of cytotoxic (cell-killing) antibodies in the patient's blood.

An NIAID-supported scientist, P. A. Terasalci at U.C.L.A., whose earlier work had shown the usefulness of tissue typing with related donors, has now demonstrated its effectiveness with unrelated (cadaver) donors as well. By several measures, this investigator, found significantly better acceptance of well-matched than of mismatched kidney grafts in a large series of cases.

In 1968, improvements in tissue matching resulted in an important clinical finding--the first successful bone marrow transplants reported by F. H. Bach of the University of Wisconsin and R. A. Good of the University of Minnesota. These were especially difficult since bone marrow cells themselves have immunologic capabilities and, when transplanted, may react seriously against the host. The two surviving marrow recipients had suffered from immunologic definciencies which were corrected by the grafts. This technique may also be envisioned as offering an approach to treatment of leukemia, as well as some autoimmune disease states.

Autoimmune Disease

In rare instances, the general rule of immune non-reactivity to self is violated, and so-called "autoimmune" disease results. For many years it was assumed that tissues receiving injury in such diseases were always those against which immune reactivity had been directed. Recently, however, F. J. Dixon and his asssociates at the Scripps Clinic and Research Foundation have established that kidney damage occurring in mice with an experimentally induced autoimmune disease results from deposition in part of the kidneys of antigen-antibody complexes formed elsewhere in the body. In a related study, also at Scripps, researchers found that a kidney disease developing spontaneously in mice was similarly caused by deposition of immune complexes. Both the experimental and spontaneous mouse diseases resemble human ailments, giving rise to the hope that the findings of these studies may ultimately be applied to the treatment of certain autoimmune conditions in man.

Allergy

More common, although usually less serious than problems of graft rejection and autoimmune disease, are the distressing symptoms of allergy. Recent discoveries by K. F. Austen and his colleagues at the Robert Breck Brigham Hospital may some day enable physicians to control these symptoms, which are produced by

irritating chemicals released by body cells following exposure to allergens such as pollen. The scientists found that certain drugs selectively block the release from cells of particular irritants, despite reaction between allergen and antibody. Histamine release, for example, is blocked by chromoglycate, while diethyl carbamazine prevents so-called "slow-reacting substance" (SRS) from leaving cells. As long as they remain within cells, histamine and SRS produce no symptoms.

Further progress has been made in the study of such common allergy-inducers as timothy. A component of timothy pollen known as "antigen D" has been found by A. M. Malley at the Oregon Regional Primate Research Center to possess properties suggesting that it may constitute a superior desensitizing agent for timothy-sensitive patients.

Asthma is one of the more serious forms allergy may take, and it sometimes proves fatal. Physicians regard these deaths as potentially preventable. Several studies published in 1968 detailed methods of dealing effectively with life-threatening asthma by employing mechanical respirators along with steroid drugs, antibiotics, and ancillary measures.

New information about aspirin, reported by R. S. Farr and associates at the Scripps Clinic and Research Foundation, may lead to prevention of some cases of allergy and other disease states. The Scripps researchers found that one portion of the aspirin molecule--the acetyl group--attaches itself in vitro to a variety of body constituents, including human plasma proteins, several enzymes, and DNA (genetic material). Many untoward reactions ascribed to aspirin, including kidney damage and gastric hemorrhage, may prove related to the acetylating properties of this drug. Allergic and autoimmune manifestations in particular might be expected to result from acetylation of body chemicals.

Basic Research

Using relatively simple synthetic antigens, H.O. McDevitt at Stanford University Medical School has investigated genetic control of the antibody response in mice. Certain inbred strains respond well to particular antigens (i.e., they form high levels of corresponding antibody), which others respond poorly. Studying one class of "nonresponders", McDevitt found they lacked a gene whose action is evidently required for the specific antibody response to take place. Elucidation of this gene's mode of action--the goal of present research--should significantly increase our understanding of the immune response.

Employing another approach to the problem of antibody formation, C. J. Nossal of the Hall Institute in Australia, has shown that production of an immune response requires cooperation between at least two distinct cell types--one reacting to antigen and another forming the antibody.

Of special interest to NIAID clinical immunologists A. S. Blume, R. K. Root and S. M. Wolff has been a rare inherited disease known as the Chediak-Higashi syndrome. Children with this syndrome lack pigment in the eyes, skin, and hair and are subject to recurring severe infections, due, in part, to a deficiency of white cells in their blood. In addition, giant lysosomes--cellular structures containing enzymes--are seen in the cells of such patients. In collaboration with other NIH scientists, NIAID physicians have shown that the decreased numbers of white blood cells in Chediak-Higashi patients results from destruction of these cells in the bone marrow before they can reach the circulating blood. These studies are not only helping to provide some answers to the enigma of the Chediak-Higashi syndrome but are providing basic information on why human beings become infected.

Leprosy

In the Phillippines, a new, long-acting form of DDS--a recently discovered anti-leprosy drug--has been found as effective as the standard drug in limiting multiplication in patients of leprosy bacteria. These clinical trails, supported by NIAID and the National Communicable Disease Center, were carried out at the Eversley-Childs Sanitarium, Cebu. The new compound, known as "DADDS" is injected intramuscularly and released slowly by tissue enzymes in the form of DDS.

The potential value of DADDS in treating leprosy lies in the infrequent administration required by this drug, especially under the medically difficult conditions characteristic of many endemic leprosy areas. DADDS may also prove useful in prevention of the disease.

Tuberculosis

Tuberculosis, another ancient scourge, is today treated successfully with such drugs as streptomycin, isoniazid, ethionamide, or the thiosemicarbazones, but in some cases tubercle bacilli develop resistance to the drug being used. A combination of drugs may then be substituted for the primary agent in retreatment. A grantee has attempted to expose tuberculosis bacteria to simultaneous peak concentrations of all drugs employed in such combined therapy, by careful individual timing of daily doses. In a series of 139 patients so treated for at least six months, tubercle bacilli disappeared from the sputum of 125, or almost 90%, P. Johnston of Hahnemann Medical College reported.

Staphylococcal Disease

A novel approach to treatment of recurrent staphylococcal infection in families, known as "bacterial interference" has been employed by M. Boris at North Shore Hospital, New York. Following antibiotic therapy, he nasally inoculated members of affected families with a benign strain of Staphylococcus. Compared with controls, these families subsequently showed a greatly lessened incidence of staphylococcal disease.

Streptococcal Infection

Rheumatic fever and glomerulonephritis (kidney inflammation) as sequelae of streptococcal infection continue to exact a toll. While streptococci are, fortunately, highly sensitive to antibiotics, inapparent or undiagnosed infections may go untreated, leaving patients vulnerable to late consequences of the illness.

Recently, B. F. Anthony of the University of Minnesota has shown that streptococci causing the skin disease impetigo may have the same potential virulence as those isolated from more serious infections. Prevention of outbreaks has proven difficult.

A basic research finding has recently been reported in the study of Group A (virulent) streptococci. Utilizing bacteriophages (viruses which infect bacteria) as carriers of genetic material from one strain of the bacteria to another--a phenomemon known as "trans-duction"--NIAID scientists C. G. Leonard, A. E. Colon and R. M. Cole, have been able to render normally sensitive Group A streptococci streptomycin-resistent. This marks the first time that these organisms have been transduced, and the genetic conversion was successful in only one of six different strains tested. The availability of this technique now makes feasible genetic studies on virulence and other properties of Group A streptococci--studies which are likely to enhance our understanding of and ability to control microorganisms in general and disease-producing streptococci in particular.

Fungal Diseases

Treatment of fungal diseases remains unsatisfactory. Available drugs, such as Amphotericin B, tend to be highly toxic. While this agent is the preferred drug for treatment of life-threatening histoplasmosis, cryptococcosis, coccidioidomycosis and candidiasis, its side effects--minor and serious--are legion and frequent in occurrence. An NIAID grantee M. G. Koenig of Vanderbilt University has now developed a regimen of Amphotericin B. administration which reduces toxic side effects while successfully controlling infection. Therapeutic results were excellent, while acute toxic reactions were minimized. This treatment regimen may also produce less permanent kidney damage than the usual dosage schedules.

Antibiotics

Dr. Hans Muxfeldt and a co-worker of Cornell University have synthesized the remarkably complex molecule of oxytetracycline, a versatile broad-spectrum antibiotic known commonly as Terramycin. The synthesis was performed in sixteen complicated steps from which emerged a molecule identical in content, form, and biological action to the naturally made oxytetracycline. This highly sophisticated achievement increases the probability of manufacture of closely related molecules not available in nature, which may prove to be better antibiotics than oxytetracycline itself.

Vaccine Development

In 1968, success was reported in NIAID contractor trials of a live attenuated (weakened) rubella vaccine on the island of Taiwan. Once viewed as just another "childhood illness", rubella (German measles) has aroused much concern since the observation some years ago that infection of pregnant women often results in serious birth defects. The Taiwan trials, which involved some 10,000 children, were carried out during a rubella epidemic. Fewer than 10% of vaccinated children contracted the natural infection, in contrast to 50% of the unvaccinated, J. T. Grayston of the University of Washington reported.

Suspected exposure to rabies occurs all too frequently in humans, and once symptoms of the disease appear, it is almost invariably fatal. While anti-rabies prophylaxis currently administered to persons bitten by suspect animals seems effective, it has deficiencies and even frank dangers. Dr. H. Koprowski and his associates at the Wistar Institute have now been awarded a patent for a safer rabies vaccine. By growing virus for the new vaccine on human cells in tissue culture, the scientists have eliminated a major problem--sensitization and resultant allergic brain damage caused by introduction of the non-human brain tissue used in previous mediums. Negotiations are now underway for commercial production of the vaccine. The Wistar researchers are, in addition, studying a drug which was unexpectedly found to inhibit growth of the rabies virus in tissue culture.

J. L. Melnick at Baylor University has reported on a novel technique for virus vaccine production which may have broad application. In this process, the virus is first made sensitive to light by cultivation with certain dyes, following which it is exposed to light and thereby rendered non infectious. In this form it is suitable for use as vaccine. Since light inactivates only the infectious central core of the virus, and not the surface components which induce immunity, the vaccine is more potent, though no less safe, than the conventionally killed preparation. Vaccine produced in this fashion might be particularly useful for initial smallpox immunization, to preclude the untoward reactions that sometimes occur with the first dose of a live smallpox vaccine.

Investigators at NIAID, J. A. Kasel and R. V. Fulk have participated in a

study which showed that nasal spray immunization with killed influenza virus produces higher and longer lasting levels of respiratory tract antibody than does subcutaneous inoculation of the same virus.

A live attenuated influenza virus vaccine has also been administered intranasally on an experimental basis. The strain was obtained by an NIAID scientist, J. Mills, and investigators at the University of Maryland, who gradually adapted the virus to growth at low temperatures, a method used by other investigators to attenuate polio and measles viruses. For unknown reasons, cold-adapted viruses lose much of their potential to cause disease. The nasally administered flu virus was found to stimulate, safely, the production of respiratory tract antibodies in adults.

Development of an intranasal live vaccine is also being carried out by NIAID scientists and a grantee against respiratory synctial (RS) virus, known throughout the world as the most important respiratory tract disease germ of very young children. Serum antibody does not protect against RS virus, but local respiratory tract antibody is believed to furnish protection. Cold-adapted RS virus administered intranasally to adults and to children 7 to 13 years of age produced infection without manifest disease. The vaccine will be carefully tested in progressively lower age groups until it is ready to be tried in infants under six months of age, 5,000 of who die each year of pneumonia caused by RS virus.

Interferon

Virus vaccines are, of course, directed toward prevention of disease. Another approach to control of viral infections involves the study and exploitation of the interferons. Produced by living cells in response to viral infections, these proteins short circuit the normal course of events in which virus particles multiply within cells, are liberated, and go on to infect other cells. Studies by H. B. Levy and W. A. Carter of NIAID have demonstrated that mouse interferon prevents synthesis of viral components by blocking formation of an essential complex between viral genetic material and the protein-synthesizing machinery of the cell.

Interferons are species-specific; the effectiveness of mouse-produced interferon, for example, is restricted to mice, that of human interferon to man. This is one of the problems which has hampered development of what might otherwise be an ideal antiviral agent. Another difficulty has been the relative ineffectiveness of interferon once infection is established. Results of experiments performed recently by S. Baron of NIAID suggest that both of these obstacles may have been overcome. A synthetic inducer of interferon, polyinosinic-polycytidilic acid (polyI:C), cured rabbits of eye infections caused by experimentally administered herpes simplex virus. Recovery was promoted even when treatment was begun as late as three days after virus inoculation, by which time the infection was well-established. Poly I:C is also highly active in inducing viral resistance in human cells, which underlines the possibility of its use in human herpetic eye disease and other virus infections.

Tested against a variety of experimental cancers in mice and rats, poly I:C has also been shown effective as an antitumor agent. The chemical caused disappearance of the tumors in some cases and produced temporary remissions in others. The investigators do not believe these effects are primarily attributable to antiviral action of induced interferon, although this remains a possibility. Rather, the scientists feel antitumor activity of poly I:C may be related to general enhancement of the body's immune response, direct effects on genetic material and metabolism of tumor cells, or changes in blood supply to the tumor, leading to tissue death. Examination of these alternatives is now in progress.

Viruses and Cancer

The possible role of viruses in human cancer has received increasing attention. W. E. Rawls and J. L. Melnick at Baylor University now have evidence suggestive of a link between herpes virus and cervical carcinoma. The scientists have isolated four different strains of the virus from genitalia of male partners of women with this cancer. These four strains were found to resemble each other structurally while differing from two non-genital strains. Statistical evidence further supports the possibility that cervical carcinoma may be an infectious disease.

Infectious mononucleosis may furnish a sought-after link between viruses and human cancer. While, in contrast, to cancer, infectious monomucleosis is self-limited, (that is, patients recover spontaneously) its rapidly accumulating evidence suggests that this disease may be caused by the so-called "EB virus", a herpes-like virus also found associated with a cancer of children known as Burkitt's lymphoma. At the same time, scientists have demonstrated that lymphocytes (one type of white blood cell) from mouonucleosis patients will proliferate in long-term suspension cultures, an ability which had been believed to characterize malignant cells only. The cells in culture appear immature, and bizarre forms are frequently seen. These findings appear to support the belief of some researchers that infectious monomucleosis represents an atypical form of leukemia that runs a self-limited course. With an in vitro cell culture system now available, further exploration of the relationship between infectious mononucleosis, viruses, and cancer may be anticipated.

Influenza

Epidemiologic studies of influenza have led to the suggestion that the new strains of virus which emerge periodically to cause worldwide outbreaks may originate from "matings" between human and animal influenza strains. E. D. Kilbourne of Cornell University Medical College has now succeeded in producing such a hybrid strain by combining equine and human influenza viruses. This achievement supports the possibility that such "matings" may occur in nature, accounting for the sudden appearance of a new strain in association with an influenza pandemic.

Potential Health Hazards in Pesticidal Synergists

Insecticide synergists are chemicals that, at the level employed, are relatively non-toxic per se and are able to enhance to a marked degree the effectiveness of insecticides with which they are combined. They, therefore, insure more economic and efficient control of insect pests.

National Institute of Environmental Health Sciences (NIEHS) scientists, however, have found that administration of pesticide synergists results in interference with detoxification mechanisms in the rat. Such interference over a prolonged period of time occurs by inhibition of the liver microsomal enzyme systems. A hazard to the health of man exists because these chemicals (pesticidal synergists) are eliminated relatively slowly from the organisms and their continued presence over a prolonged period of time prevents the normal detoxification of other hazardous chemicals.

These studies suggest potential hazards to the health of man resulting from repeated contact with certain pesticide synergists owing to the interference with detoxification mechanisms so essential to man in his struggle to cope with toxic chemicals in his environment.

Home Usage Responsible for Higher Levels. A group of NIEHS grantees under the direction of Dr. William B. Deichmann of the Department of Pharmacology in the University of Miami School of Medicine at Coral Gables, Florida, have developed a rapid, reliable procedure capable of detecting pesticides in concentrations of a fraction of a part per billion. This highly sensitive procedure has subsequently been utilized by the scientists in attempts to discern current levels of exposure to pesticides in the general population as well as in the occupationally exposed.

A striking correlation was observed between the concentration of the insecticide DDT and the degree of exposure in the home. The average DDT concentration in the group with high household usage of the insecticide was over four times the average concentration among individuals who rarely used pesticides in the home. There was no correlation with pesticides that are not used in household preparations.

The results suggest that while an average base-line concentration may be produced by pesticide-containing food, the household use of pesticides is responsible for increased pesticide levels in the body.

Role of Metals in Development of Chronic Disease

There is a growing recognition and concern that certain environmental agents, in addition to pesticides, are stored and accumulated in body tissues. This is particularly true of certain metals; for example, lead. Cadmium tends to localize in such organs as the liver and kidney. It also tends to displace zinc, a trace element essential for certain cellular functions. Both the fact that the body burden of cadmium increases with age and the fact that cadmium is increasingly used in industry suggest a potential health hazard and support further emphasis on the role of long-term exposures to cadmium to human disease.

Effect of Lead Oxide on Lung Function. Long-term exposures to lead sesquioxide may also have important implications for the health of man. Drs. Eula Bingham, Emil A. Pfitzer, William Barkley, and Edward P. Radford, scientists at the University of Cincinnati's Center for Study of the Human Environment, report significant decreases in the number of alveolar macrophages washed from the lungs of rats after prolonged inhalation of low-level concentrations of lead sesquioxide obtained by combusion of tetraethyl lead. Alveolar macrophages are important in removing dust particles and bacteria from the respiratory tract.

The concentration of lead particles in these experimental atmospheres (10 and 150 micrograms per cubic meter) are similar to concentrations encountered in human environments. The upper range is often duplicated near certain industrial operations throughout working hours, and the lower range is occasionally reached in urban air. The threshold limit established by the American Conference of Governmental Industrial Hygienists is 200 micrograms per cubic meter for daily exposure during a 40-hour week; i.e., higher than the levels studies in these experiments.

Health Hazards in Uranium Mining Industry. Other potential hazards, such as that of long-term exposure to radiation, have been studied by NIEHS scientists. Data and analyses relating lung-cancer mortality to uranium miners to radiation exposure, prior hard-rock mining, and cigarette co sumption were reported by Dr. Frank E. Lundrin, Jr., (NIEHS), Dr. Victor E. Archer (CEPHS), Duncan A. Holaday (CEPHS), Dr. J. W. Lloyd (NIEHS), and Elizabeth M. Smith (NIEHS).

To delineate health hazards in the uranium mining industry, these scientists conducted periodic medical surveys of uranium miners from the Colorado Plateau States during the period 1950 through 1967. During this period, a total of 398 deaths occurred among white underground uranium miners, whereas only 251 deaths

would be expected if rates for the white male population of the area had prevailed. This excess mortality was largely accounted for by violent deaths (120 vs. 50.5 expected) and malignant neoplasms of the respiratory system (62 vs. 10 expected).

Because cigarette smoking is associated with an increased risk of lung cancer, it might be expected that smoking-habit differences between uranium miners and the general population could explain part of the excess of lung cancer. Smoking histories of uranium miners were collected in the medical surveys and in each annual census starting in 1963. It was concluded that even though smoking alone cannot explain the marked excess of lung cancer in uranium miners and smoking difference cannot account for the progressively increasing cancer risks as radiation exposures increase, the great increase of lung-cancer deaths in cigarette smokers makes it advisable that uranium miners should not smoke cigarettes.

Parkinson's Disease

L-DOPA. A major breakthrough in drug therapy for Parkinson's disease appears to have been confirmed this year by National Institute of Neurological Diseases and Stroke (NINDS) grantees and other government scientists. Trials of amino acid levodihydrophenylalanine (L-DOPA) have been conducted with approximately 350 patients at Brookhaven National Laboratory, Columbia University, Cornell University Medical Center, and Northwestern University. Preliminary reports have indicated that 75 percent of the patients treated have benefitted substantially, and efforts are in progress to speed analysis of the data produced, so that the compound can be manufactured in quantity and marketed.

Stroke

Epidemiology. Of interest this year have been reports from an NINDS-supported collaborative study being conducted by scientists at Kyushu University in Japan, and at the University of Minnesota. For years the Japanese have been reporting a higher incidence of brain hemorrhage in relation to infarction, or clotting, than seemed to be the case in the United States. The study has shown the reports to be incorrect--that the ratio in Japan is quite close to that in the U.S. It has also brought out an unexpected finding: that in Japan, cerebral infarctions occur more often because of obstruction in the smaller vessels of the brain; in the U.S. they occur more often in the middle-sized and larger vessels.

Diagnosis. A painless diagnostic method was furthered this year by NINDS grantees who have utilized the familiar "Doppler effect" to obtain profiles of the velocity of carotid artery blood flow in thirty patients. In the project, a sonic beam is directed transcutaneously along the carotid (neck) artery. The researchers noted that atherosclerotic disease at the carotid bifurcation causes easily recognizable changes in the velocity profile, and that the method may prove to be a useful adjunct to auscultation, angiography, thermography, and other methods of detecting lesions in this area.

Muscular Dystrophy

Researchers may soon be able to identify women who carry the gene for the X-linked disorder, Duchenne dystrophy, by chemical tests and muscle biopsy. The Medical Neurology Branch of NINDS has shown that clinically normal carriers of the disease have atrophy and architectural derangement of scattered or slightly grouped muscle fibers. Identification of carriers is essential for genetic counselling.

Better understanding of the progressive degenerative process in muscular dystrophy may result from observations made by NINDS grantees at the University of Connecticut. A decrease in the enzyme alkaline phosphatase in the capillaries and small arterioles precedes degeneration of muscle fibers in chickens with

hereditary MD. High oxygen therapy (70 percent oxygen) has been shown to retard progress of the steps in muscle breakdown in the chickens.

Enzymatic and immunochemical studies by NINDS grantees at Columbia University showed that several enzymes are missing or abnormally low in the serum of Duchenne dystrophy patients. This finding is important to elucidating the fundamental defect in this disorder.

Inborn Errors of Metabolism

Metachromatic leucodystrophy (MLD), a progressive degenerative neurological disease characterized by a defective enzyme, can now be specifically diagnosed by a blood test developed by the NINDS Laboratory of Neurochemistry. This new clinical technique is significantly more practical than the current screening method of urinalysis which is confused by several variables or other earlier methods which depended upon brain or peripheral nerve biopsy.

The metabolism of the ganglioside which accumulates in the neurons of patients with Tay-Sachs disease has been successfully demonstrated for the first time by intramural scientists in the NINDS Laboratory of Neurochemistry. The investigators have synthesized this ganglioside, whose accumulation produces the symptoms of the disorder, and have labelled it radioactively for use in experiments to study the specific abnormal enzymatic reactions which produce the metabolic defect.

Epilepsy

Scientists have discovered a baboon (Papio papio) in Senegal, Africa, that sustains an epileptic seizure in response to a flickering light stimulus. This animal model should provide the basis for research into the physiology of this pathological response to light as well as a model for testing drugs with a potential efficacy in this condition.

Small doses of thiopental, a rapidly acting barbiturate commonly used to induce surgical anesthesia, has been found helpful in pinpointing areas of diseased brain tissue responsible for epileptic seizures. NINDS grantees at the Brain Research Institute of the University of California at Los Angeles, have shown that gradual administration of thiopental evokes specific brain wave patterns that can be used as markers. By exact localization of the diseases area, surgeons are able sometimes to remove it, relieving seizures.

Multiple Sclerosis

The first strong evidence that viruses may be implicated in the etiology of certain neurological disorders, including MS, was gained by NINDS scientists about three years ago by the transmission of kuru to an animal host, the chimpanzee. Kuru, a degenerative neurological disease found only in a small population of New Guinea natives, resembles MS in some respects. Further proof was gained this past year that kuru is of infectious origin when it was transmitted to the spider monkey in the NINDS "slow virus" laboratory. Spider monkeys are considerably less expensive and easier to obtain in large numbers than are chimpanzees. Use of this new experimental animal should facilitate characterization of the virus and study of the pathogenesis of the disease.

The disease which in America and elsewhere throughout the world bears the closest resemblance to kuru is Jakob-Creutzfeldt disease, also called spongiform encephalopathy of gray matter. It is a nervous system disease usually fatal within several months, which occurs sporadically throughout this country. At the special NINDS virus laboratory, a brain biopsy from a case with the disease has

been used for successful transmission of the same neurological disease to the chimpanzee after 13 month's incubation.

NINDS scientists last year isolated a virus from lung and brain explants of sheep dying of Montana sheep disease, which is an enzootic disease of long-standing in the United States. It has now been shown that this virus is similar to a neurological form of sheep infection in which this slow virus infection causes widespread demyelination, somewhat similar to that seen in multiple sclerosis.

Subacute Sclerosing Panencephalitis (SSPE). SSPE, a fatal disease of children, has been shown to be caused by a measels virue residing in the body for many years after acute measles infection. Research at NINDS and elsewhere has since further incriminated measles as the cause of SSPE, which claims the lives of several hundred American children each year. Recently, experimental work at the Wistar Institute, supported by a grant from NINDS, resulted in passage of an agent infectious for ferrets from brains of human cases of SSPE.

Brain and Spinal Cord Injury

Whiplash. Whiplash injury has been shown to cause brain concussion and hemorrhage inside the covering of the brain and neck portion of the spinal cord (subdural), in a study with monkeys conducted by NINDS scientists.

Diagnosis. A radioactive tracer was successfully used to localize the leak of cerebrospinal fluid, due to accident or spontaneous occurrence. The technique developed by the researchers at NINDS proved to be simple and safe. No complication nor untoward effects were observed. A radioactive agent was introduced and its course followed by a scanner and a camera as detecting devices.

Mental Retardation

Mental retardation has been found to be three times as frequent in children of mothers who had acetonuria (an excess of acetone bodies in the urine) in the last third of their pregnancies as compared with children of acetone-free pregnancies.

Cerebral Palsy

Animal Model. Scientists at the NINDS Laboratory of Perinantal Physiology in Puerto Rico reported the discovery this past year that it is long-term partial oxygen deprivation rather than sudden total deprivation, which produces the types of cerebral palsy seen in humans. Partial deprivation in the rhesus monkey produces a variety of nervous system injuries similar to recognized patterns seen in the brains of humans damaged during gestation or at the time of birth.

Barbiturate Protection against Asphyxia. The barbiturate nembutal has been shown to have a strikingly protective effect against brain damage from asphyxia during delivery by Caesarian section. Using the rhesus monkey, whose gestational physiology closely resembles that of the human, NINDS scientists attempt to replicate various kinds of nervous system damage based on human data in the monkey. This effort is helping doctors to understand the causes and results of different types of human cerebral palsy. There are now more than 1000 rhesus monkeys in caged and free-ranging colonies in which pregnancy and infant development can be studied.

Spastic Diplegia. Spastic diplegia is a type of cerebral palsy in which both arms and both legs of the body have tense, stiff muscles. NINDS Collaborative Project scientists reported earlier that spastic diplegia appears to be almost invariable a disease of the small (under 4 and one-half pounds) and early

born (less than 36 weeks) child and that such infants suffered a post-natal weight loss of more than 10 percent. New studies this past year suggest that the cause of this type of CP may be internal hemorrhaging.

In-utero Test for a Type of Cerebral Palsy. An in-utero test procedure to detect the presence of genetic determinants for Lesch-Nyhan disease in the developing fetus was discovered by NIH scientists this year. This disease, characterized by spasticity, choreoathetosis, and psychomotor retardation, was shown earlier to be caused by a defect in an enzyme of protein metabolism. The test involves withdrawing a little of the amniotic fluid surrounding the fetus and culturing the cells. This procedure increases the possibility of satisfactory counseling of families in which this and other hereditary diseases have been detected.

Hearing, Language, and Speech

Hearing. The value of X-ray methods for diagnosing inner-ear hearing loss caused by otosclerosis was confirmed by histologic study. Temporal bones of deceased persons who had been diagnosed while alive by radiologists as victims of cochlear otosclerosis revealed that the X-ray techniques were indeed accurate. This advance supports further the value of Temporal Bone Banks, supported by NINDS, important sources of our current knowledge of the causes of hearing loss.

Various surveys indicate that thousands of children who have congenital damage caused by the rubella (German measles) epidemic of 1964-65 are probably still undetected. One of the surveys was on an NINDS pilot study in Montgomery County, Maryland. In a four-day, pre-school communications screening program conducted in August 1967, a significant number of children were detected with hearing defects caused by rubella infection in the mother during pregnancy. Since then, many similar programs conducted throughout the country have drawn the same conculsions and emphasized that much more needs to be done to find the rubella-affected children so that they may be helped to overcome impairments which can become serious handicaps if neglected.

Speech. NINDS grantees at the University of Tokyo have devised a thin, flexible, fiber-optics cable which can be inserted through the nasal passage to provide clear observation of laryngeal conditions in the course of normal speech. A significant recent accomplishment in speech research, this technique will hasten the acquisition of knowledge about the ways that our speech is produced in the different registers and the fundamental frequencies.

Blindness

Cataracts. The first real breakthrough toward the goal of prevention of cataracts resulted from the recent discovery that certain chemicals are capable of inhibiting the galactose type of cataract. Grantees at Harvard Medical School found that the formation of aldose reductase within the lens system could be held in check by the use of chemicals. The discovery offers potential in other body systems, too, particularly in diabetes with respect to the kidneys.

Use of the cryoprobe has advanced far in the past year and research has confirmed the usefulness of cyrosurgery. The cryoprobe has facilitated the extraction of lenses in cataract surgery as well as the production of pigment in retinal detachment work. Cryo-extraction proved to be the preferred technique for cataract surgery in a series of 1,000 cataract extractions, as compared to a control series of 1,000 extractions by other techniques, as reported by NINDS grantees at Harvard Medical School.

Corneal Grafting. The surgical technique and postoperative management of

corneal grafting with artificial materials have been improved. It is now possible to use nonviable donor tissue for this procedure. The silicone membrane can be sutured to the graft in the laboratory and the whole specimen can be conveniently stored in glycerin at room temperature. The research was conducted by NINDS grantees at the Retina Foundation, Boston, and the University of Florida, Gainesville.

Herpes Simplex. Chronic infection of the conjunctiva and lacrimal gland with herpes simplex virus is believed to be a probable source of virus for recurrent corneal infection. This conclusion followed a study in which sections of lacrimal gland and conjunctiva with fluorescein labeled antibody to herpes simplex virus showed virus antigens in both patients with active and inactive disease. The NINDS grantees at the University of Florida College of Medicine pointed out that the rate of recurrence of herpes simplex keratitis in man is 25 percent within two years. Patients with more than one attack have a 43 percent chance of having an additional episode within two years.

Macular Edema. Successful results were obtained by NINDS grantees at Stanford University School of Medicine using laser photocoagulation for the treatment of several types of macular edema. Since diseases involving the macula of the human retina usually reduce central vision, and sine currently used methods of treatment are far from satisfactory, the outcome of this experimental use of a new therapeutic procedure is of considerable significance, warranting further study and evaluation.

Myopia. Scientific data on how the eye focuses, provided through the ultrasonographic technique, have collapsed a century-old theory by demonstrating that it is not the lens alone, as had previously been supposed, but also the globe that changes shape as the eye shifts focus. This finding, reported by NINDS grantees at the Columbia University College of Physicians and Surgeons, also indicated that ultrasonography may be able, in a matter of minutes, to determine the child slated to become a high myope. The investigators have proposed a revised theory of accommodation that modified current concepts of why myopia (nearsightedness) progresses during the growth period and how presbyopia (physiological changes in the lens developing with age) develops.

Oxygen Therapy. Frequent ophthalmoscopic examinations to prevent blindness from retrolental fibroplasia heve been recommended for premature infants receiving high oxygen therapy when they are suffering from respiratory distress. An NINDS-supported research scientist at Johns Hopkins University Hospital, Baltimore, has indicated that the establishment of guidelines to safe levels of arterial oxygen through monitoring may save not only many lives but many eyes.

The investigator and his team have urged that all ophthalmologists in hospitals, which are properly equipped to do so, examine for retinal vasoconstriction the eyes of infants receiving significant amounts of oxygen so that the arterial oxygen levels that are safe and do not cause retinal damage can be scientifically established. The close cooperation of ophthalmologist and pediatrician in every phase of the treatment is recommended.

Retinal Degeneration. Advances in the early detection and localization of various forms of progressive retinal degeneration, and conclusive evidence of the genetic character of such degeneration, have been described in reports by researcheres in the NINDS Ophthalmology Branch. Means of diagnosing rod responses in retinitis pigmentosa (night blindness), progressive cone-rod degeneration, and progressive cone degeneration were described.

Retinal Detachment. One of the most promising innovations of the past year in retinal surgery was the use of inflatable balloons, air, and other products in

vitreous surgery in an attempt to free adhesions so that vitreous and the retina may be restored to their usual prositions and the giant tears occurring in retinal detachment treated. Studies to improve retinal surgery have been conducted by NINDS grantees at the Retina Foundation, Boston.

A technique for treating cases of retinal detachment that cannot be corrected by standard procedures was reported by an NINDS grantee at Washington University, St. Louis. In most cases, detached retinas can be reattached to the wall of the eye by heat, cold or laser applications. But in about 10 percent of cases, the retina becomes "glued" in the detached position by a fibrous membrane that forms in the eye. Within-the-eye surgery then is needed to loosen the retina and return it to its normal position. This is accomplished by inserting a blunt needle and injecting liquid silicone between the membrane and the retina until the retina breaks loose, at the same time draining the fluid from behind the retina. The investigating team found that approximately 75 percent of patients treated in this way had vision restored on what appeared to be a lasting basis.

Toxoplasmosis. Recurrence of toxoplasmosis, which accounts for from 30 to 50 percent of all posterior uveitis, was prevented by NINDS grantees at Columbia Presbyterian Medical Center, New York, through the employment of laser energy to create scar tissue around the lesions in the retina surrounding the initial focus of infection. Patients so treated had few recurrences of the disease, as contrasted to many recurrences previous to such treatment. Prolonged observations will be necessary to prove the efficacy of this treatment.

Tumors. Ultrasonography of the orbit has been used successfully to diagnose intra-orbital tumors and found to be easily performed and harmless when done properly. NINDS grantees recommend this useful diagnostic method in the routine investigation of unilateral exophthalmos when the conventional tests have failed to reveal the cause.

Visual Physiology. Scientists have found that the ability to see things in three dimensions is possible because objects at different distances from the eye excite different neurons in the brain. This conclusion was reached by NINDS grantees at the University of California, Berkeley, and others who examined the way 87 separate neuron units in the primary visual cortex of the cat brain were triggered by various visual stimuli.

Biomedical Engineering

Automation of Clinical Laboratories. In the field of biomedical engineering, the National Institute of General Medical Sciences (NIGMS) supports a major program of basic and applied research leading to the automation of clinical laboratories.

Performing blood tests, urinalysis, assays for infectious agents and many other chemical-biological determinations, clinical laboratories occupy a crucial position in modern medicine. However, depending largely upon time-consuming manual methods, these laboratories find it difficult to cope with vast new demands for services brought on by rapidly rising hospital admissions and the tendency of physicians to request complete lab work-ups for nearly all patients admitted.

The NIGMS expects eventually to achieve a single on-line analytical system capable of performing rapidly and accurately a broad spectrum of laboratory analyses. The overall concept is a series of computer-controlled modular units with built-in quality control and standardized processes, easily adapted to benefit all sizes of hospital.

One such module is being developed with NIGMS support by Dr. George Brecher

at the University of California medical center in San Francisco. A totally on-line computer information system, it collects and rapidly reports laboratory test results to inquiring physicians.

Housed entirely in an 8 x 10-foot room, the system has been used operationally in the University's 550-bed hsopital for a number of months, reducing to 40 percent the time spent by hospital staff handling lab data. It has, in effect, demonstrated the feasibility of a minimum computer installation for laboratories in busy, medium-sized community hospitals.

In the Body Fluids Analysis program supported by NIGMS as a part of the Molecular Anatomy (MAN) Program at Oak Ridge National Laboratory, prototypes of two automated high resolution analytical systems were built and placed recently for clinical evaluation and field testing purposes in selected hospital-medical research complexes. Culminating several years of concerted effort in both basic and applied research, these prototype systems are now being evaluated.

Essentially, each of the systems employs highly advanced continuous flow chromatographic methods at high pressures for separating bio-organic compounds in solution. One reliably detects up to 140 different constituents in urine, more than four times the number detected by conventional urinalysis methods. A number of these have been identified chemically and may well serve as "fingerprint" substances for detecting early onset of disease. Inasmuch as some 500 pathological or physiological states are now associated with urinary components in man, the importance to medicine of new ultra-sensitive methods for their rapid and accurate detection cannot be overestimated.

Lung Function Monitor. Highly significant is a new instrument to monitor lung function in critically ill patients, developed last year by Dr. Richard Johns, Dr. Richard Shepard and engineering associate Wardell Lindsay at Johns Hopkins University. This device has now been greatly refined and will soon be made comercially available on a widespread basis. As such, it will be useful in patient intensive care and could be employed also in diagnosing early or incipient lung disease. It consists of a miniaturized diffusion-electrode sensor device which can be fitted wrist watch-like around a patient's arm or leg to measure continuously, through the intact skin, the amount of carbon dioxide present in tissues and the arterial blood. High CO_2 readings would, of course, be a direct indication of improper lung function. Measurements from the sensor are converted to numerical values displayed constantly by a digital recording instrument, located either at the patient's bedside or as part of a central ward or hospital console monitoring station.

Because skin puncture is not required, the device causes no pain or discomfort to the patient and is particularly suited to the care of infants and children. By contrast, the most commonly used current method of monitoring CO_2 blood levels requires repetitive blood sampling which increases the patient's risk of infection, and time-consuming laboratory analyses, often at times when the slightest delay in getting needed information poses a crucial hazard.

Pharmacology-Toxicology

NIGMS-supported studies by Dr. Herschel I. Jick of Tufts University recently produced highly convincing evidence that women who have type "A" blood are at much greater risk than others of developing thrombophlebitis as a consequence of using birth control polls. Although thrombophlebitis ordinarily is not a serious problem, it can on occasion produce pulmonary embolism, which is extremely dangerous. As a result of Dr. Jick's findings, physicians are better able to point out to susceptible women the higher risk they face, and thus help them make wiser decisions concerning the use of oral contraceptives.

Other findings by Dr. Jick's group suggest that several widely used tranquilizers cause excessive sedation more often in older patients than in younger persons receiving comparable doses, and that certain barbiturates produce a higher incidence of side effects in patients of lighter body weight compared to patients who weigh more.

Dr. Jick has in effect pioneered the development of a comprehensive drug surveillance system covering initially three, and now operating in six, Boston hospitals. It also is being adopted in several other clinical drug studies supported by NIGMS and conceivably may serve as a model for application in hospitals throughout the country.

Attacking the problem of drug interaction, Drs. L. K. Garrettson, J. M. Perel, and P. G. Dayton at Emory University, demonstrated that methylphenidate, a mild stimulant which normally brightens a patient's mood and improves his ability to think and work, may produce dangerous side effects when given in combination with other drugs.

Scientists headed by Dr. Chozo Mitoma at the Stanford Research Institute have demonstrated in basic studies that caffeine increases the drug metabolizing activity of the liver, a process known as enzyme induction. Their data was obtained by administering caffeine orally to animals in regulated doses. Extrapolating these findings to man, the SRI scientists suggest that caffeine taken in moderate-to-heavy amounts may similarly effect drug-metabolizing systems in the liver, perhaps neutralizing or reducing the therapeutic effectiveness of some drugs.

Applying combined gas chromatography-mass spectrometry to drug studies, Dr. Bo Holmstedt at Karolinska Institute in Stockholm and Dr. Donald Jenden of the University of California at Los Angeles have for the first time isolated and identified the nerve chemical acethylcholine in animal brain tissue. Acetylcholine plays a key biochemical role in transmitting impulses from one nerve cell to another. Determination of this chemical in the brain may be an important fundamental step toward the developmentoof more effective central nervous system drugs and lead to better understanding and more effective treatment of some mental disorders.

Dr. Leon I. Goldberg and other scientists working in the Institute-supported pharmacology research center at Emory University have shown that dopamine, a naturally occuring adrenalin-like body substance, amy be extremely effective as a new drug for treating shock patients. Dr. Goldberg and his associates found that dopamine, administered intravenously, improved blood circulation to the extremities and urinary output in 16 patients in various stages of shock. The investigators also found dopamine to be generally more effective than isoproterenol, another adrenalin-like compound, in the management of patients in shock.

Scientists at the University of Southern California have devised a central, computerized resource that permits physicians to tailor dosage of digitalis to meet specifically the needs of individual heart patients. Under this experimental system, developed by a grantee of NIGMS, Dr. Richard Bellman, and Dr. Roger W. Jelliffe, a grantee of the National Heart Institute, area physicians phone the Unviersity medical center to indicate which digitalis drug their patient is taking, the dose prescribed, and results of kidney function tests. The computer responds with a suggested dosage program tailored to the patient's kidney function and overall state of health, enabling the physician to achieve and maintain maximum therapeutic effect for his patient.

Trauma

A basic discovery that cells consume oxygen more rapidly in early stages of tissue repair led a group of NIGMS-supported scientists at the University of California Medical Center, San Francisco, to develop new methods which appear to speed greatly the healing of wounds. This was achieved recently in two injured patients by surrounding the wounds with a humidified oxygen filled bag, and by the administration of oxygen. According to the principal investigators, Drs. J. Englebert Dunphy and Thomas K. Hunt, the rate of wound healing increased substantially in each case.

This significant observation was first made in animals, where it was discovered that the amount of oxygen in the dead space of wounds remains low, and that carbon dioxide is high, during the cellular synthesis of collagen, a major substance of tissue repair. This suggested that the addition of small amounts of oxygen might increase the rate of wound healing in trauma patients.

Another team of scientists headed by Dr. John M. Kinney at Columbia University is studying a variety of problems related to the effects of acute injury on energy exchange and other component factors of body metabolism. Part of the work in this NIGMS-supported trauma research center concerns careful studies of changes in the content of body fluid in patients throughout the critical periods of injury treatment.

In another trauma center supported by NIGMS at the University of Cincinnati, investigators working under Dr. William A. Altemeier are focusing on complications posed by bacteria and other infectious agents in wound healing. They are interested also in the resistance and susceptibility of severely injured persons to such infections. Burns and penetrating wounds which admit large amounts of infectious agents into the body are eepecially hazardous. During the past year, Dr. Altemeier and his associates demonstrated that intensive and changing antibiotic therapy for persons suffering penetrating wounds may be associated with significant changes in the flora or bacteria content of wounds and that antibiotics may in some instances accelerate some types of bacterial infections.

Burn injuries, complicated by infection and fluid loss, present a particularly challenging problem to scientists and physicinas. Ten thousand people die of burns each year in this country while another two million are hospitalized for burns, often requiring many months for their recovery.

Promising work on burn therapy is being conducted by an NIGMS grantee, also at Columbia, Dr. Charles L. Fox, Jr. A new topical antibacterial agent synthesized by Dr. Fox was shown to be highly effective in controlling burn wounds among Vietnamese civilian war casualties and among burn patients at Columbia Presbyterian Hospital and Bellevue Hospital in New York. Known as silver sulfadiazine, it particularly has been useful in stemming infections from the bacterium Pseudomonas aeruginosa--a common microorganism that becomes severly infectious when protective body mechanisms are weakened by burn wounds. Recent tests also demonstrated that some burns treated with the new ointment healed well without the need for concurrent administration of supplementary fluids. In several cases, areas of partly destroyed skin were completely saved without skin grafts.

Genetics

A major area of investigation in the fundamental sciences program of NIGMS is that of basic and human genetics. Here the objective is two-fold. One is to elucidate developmental processes from the standpoint of basic genetics, to understand how organisms reproduce their kind, how abnormalities occur in the process, and how they can be prevented or corrected. Another is to apply this knowledge to the solution of genetic diseases in man.

At the most fundamental level of investigation, scientists are focusing on deoxyribonucleic acid (DNA), the principal substance of genes whose role in heredity and protein synthesis has been recognized within this decade. This recognition has come from the outstanding work of many individuals, anong them Institute grantee and Nobelist James D. Watson who with Francis Crick demonstrated the helical configuration and nucleic acid structure of DNA; and Dr. Arthur Kornberg, a Nobel winner and grantee of NIGMS for more than a decade, whose synthesis of truly viable DNA just last year won international acclaim.

Certainly no less important is decipherment of the genetic code, a feat for which NIGMS grantees Robert W. Holley and H. Govind Khorana shared the 1968 Nobel Prize in medicine with Dr. Marshall W. Nirenberg of the National Heart Institute. Although these scientists worked independently, their investigations converged on a common interpretation of the code and its indispensable function in directing the cellular synthesis of proteins.

Other NIGMS grantees, Drs. Masayasu Nomura and Peter Traub of the University of Wisconsin, assembled in the test tube ribosomal parts from several different kinds of bacteria, producing in effect a hybrid but wholly functional ribosome. Of themselves, ribosomes are minute subcellular particles known as "protein factories" which receive amino acids from tRNA and assemble them in chain-like molecules called polypetides, the principal substance of proteins. Besides shedding new light on how ribosomes are constructed, this achievement relates importantly to knowledge concerning the basic compatibility of genetic materials among different organisms.

In the area of human genetics, NIGMS grantees have reported new findings concerning a sex chromosome abnormality found exclusively among males. This condition is known as the XYY or "supermale" syndrome. Its terminology is derived from the fact that men normally have but two sex chromosomes, one X and one Y.

Although little studied in the United States, investigations in other countries, notably England, have revealed an incidence of XYY as high as 1 in 20 among male prisoners, many of them convicted of crimes of severe violence.

Among the few American investigators who thus far have undertaken to study the XYY phenomena are NIGMS grantees Drs. Herbert A. Lubs and F. H. Ruddle of Yale University School of Medicine. For more than a year these scientists have analyzed the chromosomes of fetal cells obtained from cord blood for every infant born at Yale New Haven Hospital. Of 4,000 infants studied thus far, 18 had some identifiable chromosome abnormality, a frequency of about 1 in 200 births. Approximately half the infants studies were males. Of these, two proved to be XYY, a ratio of 1 in 1,000 births.

In related studies, Dr. Lubs is working to determine the practicality of analyzing the chromosome complement of an unborn child by focusing on cells taken from the amniotic fluid which surrounds the fetus, a procedure known as amniocentesis. He has developed safe and relatively simple methods to obtain such samples after the 18th week, or during the mid-period of pregnancy. Close examination of these cells for genetic characteristics indicates whether the chromosomal make-up of the fetus is normal or abnormal. Thus, for parents where the hereditary risk is high of having a mongoloid child, for example, a determination can be made before the baby is born as to whether or not the pregnancy in question might produce a defective offspring. This permits the opportunity of genetic counseling of parents affected, and the opportunity for them to consider possibilities of therapeutic abortion.

MORTALITY, MORBIDITY, AND COST BY DISEASE CATEGORIES

MORTALITY AND MORBIDITY FROM CANCER

Department of Health, Education, and Welfare
National Cancer Institute

Statistics on the annual number of deaths and total current number of disabilities caused by the major diseases dealt with in the National Cancer Institute.

I. Cancer deaths in 1967 (Estimated data in Provisional Report of the National Center for Health Statistics, Division of Vital Statistics):

Mouth and Pharynx	6,770
Digestive system	95,170
Respiratory system	59,160
Breast	28,960
Genital organs	40,130
Urinary organs	14,760
Leukemias	14,510
Lymphomas	16,740
All Other Sites	38,430
Total, all forms of cancer	314,630

II. Cancer disability in 1967 (estimated on the basis of data supplied by the National Cancer Institute and the National Center for Health Statistics):

(a) Estimated cases under treatment	940,000
(b) Estimated person-days of disability (these estimates have a large margin of error):	
Restricted activity	63,000,000
Sick in bed	36,000,000

III. Cancer's cost to the Nation in 1963 (Source--Estimating Cost of Illness - Health Economics Series - No. 6. These figures refer to all neoplasms - benign, malignant and unspecified. No more recent analyses are available and current costs are undoubtedly higher. The 3rd National Cancer Survey to be conducted in 1970 is designed to include some information of this kind).

(a) $1.3 billion were spent for direct costs, hospital care, nursing home care, physicians' services and nursing services for neoplasms.

(b) A total of 153,000 man-years of productivity, amounting to $850.7 million, were lost in 1963 as a result of illness and disability for members of the labor force, housewives, and others who were alive but unable to attend to their usual activities because they had cancer. The loss was far greater for persons who had died of cancer, but might otherwise have still been alive and productive.

(c) Total economic costs which include estimated direct expenditure, indirect cost of morbidity and present value of life time earnings amounted to approximately $9 billion.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
National Institutes of Health
National Heart Institute

CARDIOVASCULAR DISEASES

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases dealt with in the National Heart Institute, and the estimated cost to the Nation:

I. Deaths from cardiovascular diseases during 1967--preliminary report (Division of Vital Statistics, National Center for Health Statistics):

Category:	Number
Arteriosclerotic heart disease (includes coronary disease or "heart attacks")	575,540
Cerebrovascular lesions (include strokes and other blood vessel diseases in the brain)	202,940
Hypertension	61,950
Non-rheumatic chronic endocarditis and other heart muscle degeneration	52,500
General arterioslcerosis	37,670
Rheumatic fever and rheumatic heart disease	14,120
Other cardiovascular diseases	62,740
Total	1,007,460

II. Disabilities from cardiovascular diseases (unpublished figures from Division of Health Interview Statistics, National Center for Health Statistics, based on data collected during the period July 1966 to June 1967).

	Disability Category	
	Restricted activity	Bed disability
Average annual number of disability-days (in millions):		
Cardiovascular conditions	452	160
Heart conditions	206	73
High blood pressure a/	66	17
Other cardiovascular conditions	180	70
Average number of persons (in thousands):	b/	b/
Cardiovascular conditions	1,238	437
Heart conditions	565	199
High blood pressure a/	180	46
Other cardiovascular conditions	493	192

a/ without heart involvement
b/ disability days/365

III. Estimated annual cost to the Nation:

A. Estimated economic impact (Based on Health Economic Series Number 6, Estimating the Cost of Illness, USPHS, DHEW, May 1966).

The total economic impact of cardiovascular (including cerebrovascular) diseases on the Nation was estimated at $29.7 billion for the year 1966. This figure includes:

Direct costs (hospital and medical services).....	$4.6 billion
Indirect costs (non-productivity):	
From illness during 1966.....	3.8 billion
Discounted future earnings of persons who died in 1966.....	21.3 billion

B. Veterans compensation and pension payments (Unpublished data from Veterans Administration)
Payments to veterans (primarily World War I) disabled by diseases of the circulatory system are estimated to total $568 million for fiscal year 1968.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health

National Institute of Dental Research

Statistics of the annual number of deaths and total current number of disabilities caused by each of the major diseases dealt with in the Dental Institute, and the estimated annual cost to the Nation.

1. Deaths related to oral disease

Oral cancer causes the death of more than 7,000 Americans each year.

2. Disabilities related to oral disease

The oral diseases, ranging from tooth decay and gum infections to malignancies, are the most universal afflictions of mankind. Their total impact on the physical, mental, and social well-being of millions of Americans is immeasurable. Very few people escape one or another of these disorders at some time during their lives.

Dental caries is the most prevalent disease, affecting about 98% of the population. It is responsible for most of the loss of teeth in children and young adults. This loss accounts for impaired speech, faulty chewing, and malocclusion which may lead to later damage to the supporting tissues of the teeth. The physical trauma associated with extracting decayed teeth poses still other problems. Moreover, persons with certain heart conditions may be endangered by the introduction of harmful bacteria into the blood stream as the result of tooth extractions. Fear arising from extractions in childhood discourages many adults from seeking necessary periodic preventive dental care for themselves and their children.

Periodontal disease causes the greatest loss of teeth in persons over age 35. This disorder has robbed approximately 20 million Americans of all their teeth, compelling them to wear dentures. While early signs of this disease may appear between 20 and 30 years of age, its prevalence and severity increase with age. Half of those over sixty have destruction of gum and bone tissue. Once it starts, the disease becomes progressively more destructive. Its ramifications extend beyond nutritional and esthetic problems associated with loss of teeth. Bacteria from periodontal pockets and abscesses may also invade the blood stream and undermine the general health.

Unlike most oral diseases, cancer of the mouth can be fatal. Readily visible oral cancers are often ignored because of the absence of early warning pain. About nine-tenths of those treated for lip cancer can expect at best a five-year survival after treatment, as compared with only three-tenths of those treated for tongue cancer. While tumors can occur anywhere in the mouth, including the tonsils and salivary glands, they are found most often on lips, tongue and cheeks.

Each year approximately one of every 800 babies born in the United States has cleft lip or palate or both. Over 6,000 victims and their families will need help this year to bear the heavy medical, psychological, and financial burdens occasioned by these birth defects. Formerly, congenital defects were generally considered hereditary accidents. Today it is known that unfavorable events occurring during pregnancy as well as faulty heredity play a part. If they are to lead normal productive lives, clefted children require coordinated assistance from many clinical specialists. For this reason, centers in which orthodontists, plastic surgeons, psychologists, otolaryngologists, speech therapists, and social

workers can work together to solve the problems of the individual and his family are especially helpful.

The contributions of dental research frequently extend to other branches of medicine and science. For example, the addition of dextran to a non-narcotic local anesthetic doubles the effective time of a regional nerve block given to control pain following repair of broken jaws. Similar pain relief could be applied in other types of surgery. Also, studies of immune responses of animals to endotoxins from oral bacteria suspected of aggravating periodontal disease show that antibodies are formed in regional lymph nodes when minute amounts of endotoxin enter through the lining of the mouth, and in the spleen when entrance is through a vein. Probably other immune reactions are also localized. Other dental studies of immune responses to viruses show that a viral infection can stimulate an animal to make antibodies against a foreign, non-viral protein which is ordinarily tolerated. This finding suggests that viral infections could trigger an allergy to one of the body's own proteins.

3. Estimated annual cost to the nation

The annual expenditure for private dental care in this country emphasizes the seriousness of the dental disease problem. Approximately $3 billion was spent in 1967 for private dental care. This represents about 10 percent of the $32.1 billion spent for all private health care during that year. More significantly, only about 40 percent of the American population visits a dentist each year, and in any given year, three-fifths of the population receive no dental care at all.

The cost of dental neglect is dramatically demonstrated in the dental needs presented by inductees into the military service. On the average, every 100 inductees requires 505 fillings, 80 extractions, 25 bridges and 20 dentures. It is currently estimated that approximately 100 million man-hours are lost from productive work annually due to oral problems.

ARTHRITIS AND METABOLIC DISEASES

Statistics concerning the number of deaths and disabilities caused by some of the major diseases under study in the National Institute of Arthritis and Metabolic Diseases, and the estimated annual cost of arthritis to the Nation.

I. Estimates of the number of deaths during 1967 (Source: National Center for Health Statistics, PHS)

Category:	
Diabetes mellitus	34,430
Gastrointestinal diseases (ulcer of stomach and duodenum, cirrhosis of the liver, gastritis, duodenitis, enteritis, and colitis)	45,390
Total	79,820

II. Disabilities
(Source: Diabetes and Arthritis Control Program, National Center for Chronic Disease Control, PHS, 1968.)

Number of persons in U.S. reporting chronic activity limitation due to arthritis (excluding gout and bursitis) during 1965-67: 3,248,000.

III. Estimated annual economic cost to the Nation
(Source: Diabetes and Arthritis Control Program, National Center for Chronic Disease Control, PHS, 1968.)

Arthritis and rheumatism, $4 billion.

Neurological and Sensory Disabilities: Estimated Numbers and Cost

Introduction

The mission of the National Institute of Neurological Diseases and Stroke (NINDS) is to conduct and support research and professional training on the problems of neurological and sensory disabilities. These are a leading cause of chronic human suffering and economic burden in the United States.

As much as 10 percent of the total population of the Nation may be suffering from one of the approximately 200 disabling neurological or sensory disorders. An estimated 20 percent of hospital admissions are related to these neurological and sensory ailments.

Impairments range from speech defects and hearing problems to blindness and nervous-system disorders which cause crippling and death. Multiple handicaps are common.

Such conditions include cerebral palsy, mental retardation, strokes, epilepsy, multiple sclerosis, muscular dystrophy, and spinal injury, also loss of vision, hearing, and language. The vast majority of these problems are still incurable.

Mortality Statistics

Neurological ailments have been causing about 12 percent of the total U.S. deaths. A Pennsylvania study has shown that 2 of every 1,000 live newborns die of neurological conditions before thay are one year old. Although certain chronic neurological conditions contribute to death, they often are not listed as cause of death. Mortality statistics, therefore, do not portray the full magnitude of the neurological and sensory disease problem.

Prevalence

Exact figures on prevalence are not available for various reasons:
Case finding is difficult because neurological and sensory diseases are not reportable. Many conditions become evident to the individual only after they have progressed to a point of disability. Or, persons affected by some neurological disorders conceal their handicap, as in epilepsy, because of job discrimination and other forms of social non-acceptance. Moreover, medical diagnosis of neurological problems is still difficult in certain disorders; many cases are incorrectly diagnosed or missed for long periods.

NINDS's Estimate of the Problem

NINDS can only estimate the range of neurological and sensory disability. In doing this, it has drawn on figures from various voluntary health organizations, the Department of Health, Education, and Welfare's National Center for Health Statistics, and other sources.

Voluntary and Government agencies recognize the need for more reliable data on chronic impairments among our population. Such information has decided importance in promoting a solution to the vast problems raised by chronic illness.

Range and Cost of Major Chronic Neurological and Sensory Disorders

Disability Category	Mortality [1]	Estimated Total Cases [2]	Estimated Annual Cost of Care [3]	Remarks
NEUROLOGICAL				
Amyotrophic lateral sclerosis (ALS)	1,349	5,000 to 10,000	$ 10,000,000	As is true of many neurological ailments, ALS reported deaths do not reflect the estimated number of patients. (ALS Fact Sheet, NINDS)
Cerebral palsy (CP)	1,161	600,000	$500,000,000	National Health Education Committee (NHEC) estimates one-third of the patients are under 21 years old. United Cerebral Palsy estimates 25,000 born each year with CP.
Epilepsy	2,043	1,000,000 to 2,000,000	$750,000,000	About 80 percent of seizures start in childhood or adolescence. (NHEC)
Head injuries	50,000(est.)	700,000		Over 700,000 persons are bed-disabled for 1 day or more as a result of injury to the head. (National Center for Health Statistics)
Multiple sclerosis (MS)	1,533	250,000	$250,000,000	MS is a long-term progressive disease affecting mainly persons between 20 and 40 years old.
Muscular dystrophy (MD)	921	200,000	$125,000,000	Nearly two-thirds of known MD patients are children between ages 3 and 13. (Muscular Dystrophy Associations of America, Inc.)
Myasthenia gravis (MG)	250	30,000	$ 40,000,000	Again reported deaths do not reflect estimated total cases. (MG Fact Sheet, NINDS)
Parkinson's disease (paralysis agitans)	3,108	200,000 to 1,000,000	$400,000,000	Parkinson deaths may be 5 times higher than cited, as an indirect cause. (Parkinson's Disease Foundation) Estimates of the amount of Parkinson's disease range widely, depending upon the definition used for the disease and on the estimation of the number of persons with mild symptoms of undiagnosed parkinsonism.
Reading disability		2,500,000 to 5,000,000		An estimated 5 to 10 percent of all school children have some type of reading disability.

Range and Cost of Major Chronic Neurological and Sensory Disorders

Disability Category	Mortality 1/	Estimated Total Cases 2/	Estimated Annual Cost of Care 3/	Remarks
NEUROLOGICAL (con't)				
Spina bifida including meningocele	1,151			An estimated 11,000 babies are born annually with spina bifida or related birth defects (often incurable). (Spina Bifida, HIR, NINDS)
Spinal cord injury	1,800 to 3,000 (est.)	60,000 to 100,000	$2.4 billion	Economic loss to patient and society of 10,000 traumatic paraplegia and quadriplegia patients is estimated by an insurance company.
Strokes (cerebrovascular accidents--CVA)	204,841	2,000,000	$440,000,000	One-third of patients with strokes are wage earners under age 65 made unemployable by the residuals of a stroke. (NHEC and President's Commission on Heart Disease, Cancer, and Stroke)
Tumors of the brain and other parts of the nervous system	8,328	140,000	$272,000,000	Brain tumors cause about 40 percent of the deaths from diseases of the central nervous system exclusive of strokes.
SENSORY				
Eye disorders			$1 billion (est.)	An estimated 77 percent of legally blind population in the U.S. is 40 years old or over. (National Society for the Prevention of Blindness) 1966. Estimate of the partially seeing: National Center for Health Statistics.
legally blind		426,000		
partially seeing		5,693,000		
Hearing disorders				In 1967, 38,391 pupils were enrolled in 736 American schools and classes for the deaf. Deafness and combined deafness-blindness from the recent German measles epidemic has reached the pre-school-agers, and will create a serious national problem of their education. (American Annals of the Deaf.)
totally deaf		71,000		
other hearing impairments		8,578,000		
Speech impairments		1,298,000 (5% of school children)		Hearing and speech impairments frequently occur together, making it difficult, statistically, to separate them.

REFERENCES

1/ Deaths during 1966 from Division of Vital Statistics, National Center for Health Statistics, Department of Health, Education, and Welfare.

2/ Morbidity estimates obtained from the respective voluntary associations.

3/ Costs calculated on these assumptions per year for maintenance:

a. Partially disabled individual: $500 drugs, physicians' fees, and special management.

b. Totally disabled individual cared for at home: $1,000.

c. Totally disabled individual cared for in public and private institutions: $2,000 to $4,000.

January, 1969

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Statistics covering the annual number of deaths and reported illnesses caused by selected diseases dealt with in the National Institute of Allergy and Infectious Diseases are presented in Table I. Only those deaths and new cases reported by professional health personnel are included.

Table II reports annual disability and estimated cost to the nation's populace of infectious, parasitic, and respiratory diseases.

Table I

Category	Morbidity 1967	Mortality 1966
I. Parasitic Infections		
Amebiasis	3,157	54
Malaria	2,022	5
Schistosomiasis	264 (NYC only)	3
Trichinosis	66	3
Aschariasis	594 (7 states)	19
Toxoplasmosis	32 (8 states)	4
II. Bacterial Diseases		
Brucellosis	265	3
Diphtheria	219	20
Leptospirosis	67	9
Meningococcal infections	2,161	876
Pertussis (whooping cough)	9,718	49
Salmonellosis (excluding typhoid, including paratyphoid)	18,120	73
Tularemia and Leprosy	265	8
Septicemia and Pyemia	2,515 (1 state)	2,532
Tetanus	263	158
Tuberculosis	45,441 (new active cases)	7,625
Typhoid fever	396	15
Strep sore throat and Scarlet fever	453,351	65
Rheumatic fever, acute	3,985 (38 states)	456
Chronic rheumatic hearth disease	*	14,556
Shigellosis (bacillary dysentery)	13,474	86
Venereal diseases (new cases)		
Syphilis	102,581	2,193
Gonorrhea	404,836	18
Other	1,309	9
III. Rickettsial diseases		
Typhus (inc. Rocky Mountain spotted fever)	357	23

IV. Viral Diseases			
Chicken pox	116,478	(42 states)	137
Encephalitis (acute infectious)	1,478		579
Hepatitis (infectious and serum)	41,367		757
Herpes zoster	1	(1 state)	69
Influenza	*		2,830
Measles (rubeola)	62,705		261
Mumps	185,691	(43 states)	43
Mononucleosis	8,272	(30 states)	18
Poliomyelitis	41		9
Rubella	46,888		12
V. Fungal Diseases			
Actinomycosis	10	(5 states)	21
Coccidioidomycosis	860	(8 states)	45
Blastomycosis	40	(9 states)	12
Cryptococcosis	18	(7 states)	90
Moniliasis	*		87
Histoplasmosis	206	(18 states)	60
VI. Allergic Disorders			
Asthma	*		4,324
All other	*		107
VII. Multiple or unspecified classifications			
Bronchitis	*		6,151
Emphysema	*		20,252
Meningitis (except meningococcal and tuberculous)	2,290	(32 states)	2,324
Pneumonia	*		60,785
Respiratory Infections, acute upper	*		670
Gastroenteritis and colitis (age 4 weeks and over)	*		3,086

* Not Reported

Morbidity statistics taken from MORBIDITY AND MORTALITY WEEKLY REPORT, Annual Supplement, 1967, Vol. 16, Number 53, November 1968, National Communicable Diseases Center, Atlanta, Georgia.

Mortality statistics taken from VITAL STATISTICS OF THE UNITED STATES, 1966, Volume II - Mortality - Part A. National Center for Health Statistics, Public Health Service, U. S. Department of Health, Education, and Welfare.

TABLE II

Cost to the Nation's Populace
July 66-June 67

Item	Acute Condition Group	
	Infectious and Parasitic	Respiratory
Number of cases	45,526,000	201,016,000
Restricted activity (days)	182,699,000	590,783,000
Bed disability (days)	85,526,000	283,324,000
Work loss (days)	19,290,000	94,400,000
School loss (days)	41,954,000	96,560,000
Work loss (cost)	$468,554,100.00	$2,292,976,000.00
	TOTAL WORK LOST	$2,761,530,100.00

From VITAL AND HEALTH STATISTICS - CURRENT ESTIMATES UNITED STATES, July 1966-67, Series 10, No. 13, January 1968, and ACUTE CONDITIONS, Series 10, No. 34, March 1968 (DHEW, National Center for Health Statistics, Washington, D.C.)

Department of Commerce, National Income Division, Personal Income Section, Average Income of Full-time worker, all industries, 1967 ($6,209 annually. Days lost from work cost based on average of 256 working days a year - thus $24.29 per day).

WEDNESDAY, MARCH 26, 1969.

DIVISION OF BIOLOGICS STANDARDS

WITNESSES

DR. RODERICK MURRAY, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GEORGE A. BRUST, EXECUTIVE OFFICER, DIVISION OF BIOLOGICS STANDARDS
MRS. ELIZABETH GRUBBS, BUDGET OFFICER, DIIVISION OF BIOLOGICS STANDARDS
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	2,371	2,493	2,574
Positions other than permanent	40	30	30
Other personnel compensation	60	49	49
Total personnel compensation	2,471	2,572	2,653
Personnel benefits: Civilian employees	235	250	255
Travel and transportation of persons	84	108	112
Transportation of things	15	10	15
Rent, communications, and utilities	45	51	51
Printing and reproduction	14	10	10
Other services	3,422	4,153	4,050
Supplies and materials	1,019	983	1,015
Equipment	209	171	180
Subtotal	7,514	8,308	8,341
Quarters and subsistence charges	−3	−3	−3
Total obligations	7,511	8,305	8,338

PERSONNEL SUMMARY

Total number of permanent positions	310	280	285
Full-time equivalent of other positions	8	5	5
Average number of all employees	285	281	280
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,995
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
Biologics standards (program costs, funded) [1]	7,373	8,305	8,338
Change in selected resources [2]	138		
Total obligations	7,511	8,305	8,338
Financing:			
Comparative transfers to other accounts	188	194	
Unobligated balance lapsing	950		
Budget authority (appropriation)	8,649	8,499	8,338
Relation of obligations to outlays:			
Obligations incurred, net	7,699	8,499	8,338
Obligated balance, start of year	2,639	2,725	3,044
Obligated balance, end of year	−2,725	−3,044	−3,975
Adjustments in expired accounts	−33		
Outlays	7,580	8,180	7,407

[1] Includes capital outlay as follows: 1968, $184,000; 1969, $171,000; 1970, $180,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $2,162,000; 1968, $2,300,000; 1969 $2,300,000; 1970, $2,300,000.

Mr. NATCHER. The committee will come to order.

We have before the committee at this time Dr. Roderick Murray, the Director of the Division of Biologics Standards of the National Institutes of Health.

Dr. Murray, it is a pleasure to have you appear before our committee, I believe you have a statement.

Dr. MURRAY. I would like to introduce Mr. Brust, my executive officer, and Mrs. Grubbs, the budget officer.

Mr. NATCHER. We are delighted to have you folks before the committee.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

We will place your biographical sketch in the record and then you may proceed, Dr. Murray.

(Biographical sketch follows:)

BIOGRAPHICAL SKETCH

Name: Roderick Murray, M.D.; Position: Director, Division of Biologics Standards, National Institutes of Health; Birthplace and date: Christchurch, New Zealand, August 12, 1909; Education: B.S., University of Witwatersrand, South Africa; M. Sc., University of South Africa, 1931; M.D., Harvard Medical School, 1941.

Experience: 1956–Present, Director, Division of Biologics Standards; 1949–56, Assistant Chief, Laboratory of Biologics Control, NIH; 1947–49, Laboratory of Biologics Control, NIH; 1947, commissioned officer, USPHS; 1946–47, Research fellow, Thorndike Memorial Laboratory, Boston City Hospital; 1942–46, U.S. Army Medical Corps (major); 1942, assistant residency, Second Medical Service, Boston City Hospital (interrupted by military service); 1941–42, medical internship, Second Medical Service, Boston City Hospital, Boston, Mass; 1931–37, biochemist, South African Institute for Medical Research, Johannesburg.

Association memberships: American Medical Association; American Public Health Association (fellow); American Association of Immunologists; American Academy of Microbiology (fellow).

Special awards, citations, or publications: Cullen Medal, faculty of science, University of Witwatersrand, 1930; Alpha Omega Alpha; Distinguished Service Medal USPHS, 1965, 39 publications.

General Statement

Dr. Murray. Mr. Chairman and members of the committee, it is once again my privilege to appear before you on behalf of the Division of Biologics Standards.

The mission of the Division is the exercise of controls on the safety, purity, and potency of biological products. This is accomplished through a system of licensing of manufacturing establishments and of products, as well as research related to these objectives, so that decisions made and actions taken can be based on sound information.

It is the responsibility of the Division to recommend standards for all biological products, such as vaccines, serums, human blood and its derivatives. These include written standards, eventually promulgated as regulations, some of which apply to individual products and some to products in general and physical standards, that is, preparations with extensively characterized properties and qualities. The latter are issued to manufacturers and other research laboratories for evaluation of their products.

The acquisition of information needed to develop written standards and laboratory investigations leading to the development and selection of suitable physical standards are extensive in character and often time-consuming. This is particularly true of standards for the tissue-culture-prepared virus vaccines.

When a vaccine against a disease appears achievable, it devolves on the Division to develop standards before the product is in the final stages of manufacture. This requires research involving most of the Division's laboratories as well as the testing of samples of both experimental and final product. During this period, close contact with the manufacturer is maintained so that problems relating to standards can be resolved during the developmental phases. In addition, clinical investigations conducted by the manufacturer come under review by the Division.

It is very difficult to describe the activities of the division in detail and so to illustrate the activities and responsibilities of the division, attention will be devoted to two products:

The first, a vaccine in course of development and on the threshold of general use—rubella vaccine.

The second, a product which has been in use for many years but which requires great attention because of changing conditions—influenza vaccine.

I apologize because you will probably hear during the course of these hearings about rubella vaccine and influenza vaccine from more than one witness. I assure you they are responsible for different tasks involved with these vaccines.

Rubella Vaccine

The virus responsible for rubella was first isolated and identified in 1962 simultaneously by scientists working at the Walter Reed Army Institute of Research and at the Harvard School of Public Health. This accomplishment was immediately recognized as the key to the development of a vaccine which might prevent rubella. Many scientists in Government, industry, and in the universities addressed themselves to the study of rubella virus. The resultant studies, which have de-

veloped much information on rubella as a disease, have shown that an inactivated vaccine analogous to Salk polio vaccine is not feasible with present technology, but that live virus vaccines made from attenuated strains, analogous to the Sabin polio virus strains, are possible. Anticipating the great public interest in a rubella vaccine, Division of Biologics Standards' scientists embarked at an early stage on a program of research designed to develop the information needed to establish standards for safety, purity, and potency, were any such vaccine developed.

In the course of this work an attenuated strain of rubella virus (designated HPV–77) was developed. The initial studies in a closed group of children of an experimental vaccine prepared from this strain showed that it was antigenic, protective, and noncommunicable from person to person. The strain was immediately made available to scientists for possible vaccine production. Additional strains have since been developed by a number of groups using similar processes of attenuation.

Early work with rubella virus had been hampered because of the cumbersome methods needed to detect the presence of antibodies in the blood of persons under study. Development of a rapid, easy, and sensitive hemagglutination-inhibition test in the laboratories of the DBS has foreshortened the period of development and speeded the evaluation of the antigenic properties of rubella vaccine. One of the problems in rubella vaccine development has been a suitable tissue culture system for the production of the vaccine virus. Chick embryo tissue culture, so successfully used for measles vaccine, would have been ideal but this was not possible because of poor virus growth and the low immunizing capacity of experimental vaccines produced in this way. Other systems had to be used. At present, vaccines produced in duck embryo, dog kidney, and rabbit kidney tissue cultures are under commercial development.

With a variety of strains and production systems, the task of the Division in developing control systems is much more extensive than when we were dealing with one strain and one system, for example, when measles (rubeola) vaccine was introduced. A great deal of clinical data is necessary to validate such vaccines. In this regard, the programs of the Vaccine Development Branch of the National Institute of Allergy and Infectious Diseases accumulated essential information, and many commercially sponsored studies have also been conducted.

The necessary regulations concerning safety, purity, and potency of rubella vaccine are being drafted and will presently be published as a "Notice of Proposed Rule Making."

I should amend that because of the passage of time since this was written. They have been drafted and have been forwarded.

Adoption of final regulations will lead the way to licensing. It is anticipated that at least one manufacturer will be licensed for commercial distribution this spring. The International Conference on Rubella Immunization, held in February of this year at NIH, greatly accelerated this process by providing a means of presenting much published and unpublished information, and bringing it to the attention of the scientists involved. It is anticipated that only limited amounts of vaccine will be available immediately after licensing, but as the pharmaceutical firms get into their stride, substantial amounts should reach the market by fall and early winter.

Simultaneously with licensing the rubella vaccine, it will be necessary to develop requirements for use. I enter this at this point because such questions are frequently asked.

Paradoxically, this vaccine will be strongly contraindicated for pregnant women. Since it is a live vaccine it may cause damage to an unborn child, but this aspect of vaccine safety is virtually unprovable. Vaccination of adult women who are not pregnant, although apparently feasible, is complicated in some by the occurrence of arthalgia and transient arthritis (also a complication of natural rubella). The latter is bound to be a matter of partisan dispute since the amount of arthritis encountered in the studies conducted thus far has varied with different vaccines and in the different studies, and in different locations; however, it seems to be related to attenuation. Highly attenuated strains produce less arthritic manifestations, but also lower levels of immunity. Adult women may be vaccinated on an individual basis by their physician when it is definitely known they are not pregnant. Every effort will be made to eliminate the disease by vaccinating the most susceptible group—children of school-entering age, thereby eliminating the reservoir of the disease and removing the threat of rubella epidemics. Actual recommendations for use can be expected to vary from time to time according to priority, to experience, and to jurisdiction, whether it is in this country or some foreign country.

Once a product has come into use, its safety and potency must be continuously monitored. The knowledge and skill required to do this also provides a sound basis for consideration of problems associated with other products as they are developed.

INFLUENZA VACCINE

We had an example during the past year of an old product which presents new problems.

Influenza vaccine, because of the changing character of the virus, presents problems in biologics control almost every year. During the fall of 1968, it became a matter of unusual concern because of the emergence in the Far East of a highly divergent A_2 strain. In late June, an increase in respiratory illness was noted in Hong Kong. Isolation of viruses were made in Hong Kong and cultures were transmitted to laboratories in different parts of the world for study. By August 13, there was general agreement among the virologists concerned that these cultures differed markedly in character from A_2 strains which have been prevalent in recent years. The change was so marked that the ultimate development of an epidemic was clearly predictable since available vaccines could be expected to provide no more than limited protection, if any.

This epidemic did materialize in the United States, but curiously enough, it has not materialized in other parts of the world such as some countries in Europe or even in Canada.

Knowing that the normal leadtime for production of influenza vaccine is 4 to 5 months, the DBS immediately provided cultures of this Hong Kong variant to the vaccine manufacturers so that they could study its properties and determine whether a vaccine could be produced from it by their production methods.

Manipulation of influenza virus preparatory to vaccine production is sometimes a lengthy and troublesome process since a new strain must be adapted to growth in fertile hens eggs through an unpredictable number of generations or "passages." While this work was in progress, a new isolate of the virus was received from the Far East which clearly had a superior vaccine production potential. This strain was provided to the manufacturers on September 9 by the DBS. Testing methods and procedures were worked out by DBS and correlated in numerous conferences and laboratory demonstrations with the manufacturers. To expedite the processing and release of vaccine, concurrent testing of vaccine lots was carried out by the DBS and the manufacturers. This required an intensive commitment of DBS resources to testing and review procedures prior to release of vaccine lots.

When the first experimental lots became available, the DBS was able to embark on a program of clinical evaluation of the vaccine. In addition, the Division diverted a portion of its early Hong Kong vaccine which was reserved for control purposes to special volunteer studies which can best be performed during an epidemic situation. The vaccine was made available by DBS to collaborating scientists through the NIAID Vaccine Development Branch, and to other investigators. Because of the nature of these studies, however, it will be several months before the results are available.

The first lot of Hong Kong influenza vaccine, containing 110,000 doses, was released on November 15, 1968. By January 31, 1969, nearly 21 million doses had been cleared by the Division.

The last time a comparable influenza vaccine emergency situation arose was 1957 when the Asian or A_2 strain of influenza virus appeared. A comparison of the rate of availability of vaccine in these two situations shows that in 1957, requirements were established 55 days after the strain was available, whereas in 1968, they were established in 15 days. In 1957, the first 5 million doses were released in 120 days, whereas in 1968, the same amount was released in 87 days. This comparison is even more illustrative of the effort involved this year when it is realized that the 1957 vaccine was only half the strength of the 1968 vaccine.

I mention these two items to illustrate the kind of fine structure or the tapestry of the activities of the division.

Attention must also be given to new products. The enzyme asparaginase is undergoing clinical investigation at present and this will come under control of the division. There is also a need to develop standards for reagents related to tissue transplantation such as typing serums and also products such as antilymphocytic serum. These will require additional effort by the Division during the forthcoming years.

In conclusion, the request of the Division of Biologics Standards for 1970 of $8,338,000 is $33,000 over the $8,305,000 available for obligation in 1969. This includes a program increase of $138,000 in order to accelerate viral and tissue immunology research and a $5,000 mandatory increase offset by a decrease of $110,000 in the NIH management fund.

I will be pleased to answer any questions.

ADDITIONAL POSITIONS REQUESTED

Mr. NATCHER. Thank you, Dr. Murray.

First, why is the $138,000, and I believe five additional people, necessary, Dr. Murray?

Dr. MURRAY. In reveiwing our program, we find that during the next year and looking forward beyond that, we must devote much more attention in the fields of virology, immunology, and serology. This will also be concerned with the development of standards for tissue typing reagents and the work that has to be done in connection with antilymphocytic serum. We believe that the number of positions which we have requested here would be required to start that work.

LEUKEMIA AND HEPATITIS

Mr. NATCHER. On page 12, you mention the potential future importance to biologic control of research on leukemia and hepatitis. What do you have in mind, Dr. Murray?

Dr. MURRAY. We have had a continuing interest in hepatitis, going back over almost 20 years now. Very little progress has been made in this area, although it is believed that infectious hepatitis is due to a virus as yet unidentified. Many efforts have produced potential culprits, but none of them have proved to be the agent. Recent work does indicate there seems to be some possibility of applying new techniques to the identification of potential agents of hepatitis. Some work is going on in our laboratories, and some work is going on in many other laboratories. We are doing this work within our existing funds. The effort is on a limited scale in order to be current and up to date with advances in the field of hepatitis.

As far as leukemia is concerned, this at the present time in our division, is something which is only being done on a small scale, looking at some potential agents which may have a relationship to leukemia. In this we cooperate with the scientists in the National Cancer Institute. I mention this here merely to indicate the scope of things we will be facing in the future.

NEED FOR INCREASED FUNDS

Mr. NATCHER. Dr. Murray, you have had some nonrecurring workload this year, I believe, such as on Hong Kong flu vaccine and rubella vaccine. Why could you not make some internal adjustments to take some of this new work you anticipate without an increase in your budget?

Dr. MURRAY. The answer to that is, nothing is impossible. This would mean that some things would have to be delayed or pushed aside. If it were necessary to do this, I would have to answer yes, we could do it, but it is going to slow down some of the work that is needed in the rapidly opening field like tissue transplantation reagents and other areas. We would have to reprogram and cut out other parts of the total program. I must also say at this point that we are pressed because of the enforced inability to fill all the vacancies that do exist.

RUBELLA VACCINE

Mr. NATCHER. Mr. Shriver?

Mr. SHRIVER. On page 5 of your statement, Dr. Murray, you say that actual recommendations for the use of rubella vaccine can be expected to vary from time to time, according to priority, experience, and jurisdiction.

Dr. MURRAY. Yes.

Mr. SHRIVER. What do you mean by that?

Dr. MURRAY. At the beginning, the attempt will be to abate the disease in its epidemic form, using the vaccine supplies that are available. The best recommendation to accomplish this, being made at present, is to vaccinate children of school-entering age since they are the ones who spread the agents most frequently.

After these children become vaccinated, it may be possible to extend the age groups that would be recommended for vaccination in order to do a better job of immunizing the population.

Then, I am cognizant of the fact that at the conference we had visitors from other countries who indicated that if the vaccine was available to them, they would use it differently, they would try first of all to vaccinate young women before being married.

The statement was put in to indicate that these recommendations are not necessarily the only ones that will be made. They will vary according to place and jurisdiction.

Mr. SHRIVER. I notice in your statement you said it is anticipated that only limited amounts of vaccine will be available immediately after licensing, but as the pharmaceutical firms get into their stride, substantial amounts should reach the market by fall and early winter.

There is going to be considerable demand for this, I assume, because of all of this publicity we have had. Is it going to be embarrassing if you are not going to be able to right away supply it, especially in view of the requests for supplemental appropriation?

Dr. MURRAY. The manufacturing of vaccines is a batch process.

For instance, each batch may consist of say 100,000 doses, and the manufacturer may make two of those a week. That is the limit of his capacity not only for manufacturing, but for testing, which is also very onerous. With this kind of a batch process, it is not like opening the floodgates and letting the vaccine out. Manufacturers are licensed when they can qualify, even if they have only manufactured a small amount. The vaccine subsequently reaching the market would be in successive batches.

NEED FOR SUPPLEMENTAL APPROPRIATION FOR RUBELLA VACCINE

Mr. SHRIVER. In view of this statement, I am wondering why we do not just appropriate the amount for 1970 instead of also appropriating a supplemental for the balance of this fiscal year.

Dr. MURRAY. I really cannot answer that question because this involves programs of other parts of the department but I could say this: If the vaccine were licensed this spring, that is before the end of the fiscal year, and money were available, this money could be used for two things: One is to make contracts with the manufacturers for later delivery of vaccine as it becomes available. Large volumes can be expected toward the end of the year.

Another important matter is to provide funds for mounting programs—for getting the mechanism ready to initiate vaccination programs.

Mr. SHRIVER. The 1970 fiscal year starts the 1st of July, so why wouldn't a 1970 appropriation be soon enough?

Mr. CARDWELL. Mr. Shriver, I think Dr. Murray's answer is really the right answer, but I would like to underscore a couple points.

The whole issue is just a matter of about 3 or maybe 4 months. You have to answer the question, do you want to delay mounting this vaccination program, even for 3 or 4 months, when you will have a licensed vaccine in your hand.

Mr. SHRIVER. Nor do we want to hold out too great hopes and expectations.

Mr. CARDWELL. I do not think you will.

Mr. SHRIVER. Because of the vaccine not being available.

Mr. CARDWELL. I really do not think that would happen. The program cannot start from point zero and immediately operate at 100-percent effectiveness or full volume no matter when you start it. This program necessarily involves a gradual buildup, especially regarding the volume of vaccine available. But we can start the buildup of the program as soon as we are sure we have the authorization to make procurement and lay the plans.

The proposed supplemental for the rubella vaccination program would give us that opportunity, we think, 3 to 4 months in advance of a regular appropriation, and that is the issue. It really rests in the hands of Congress. We are recommending that we jump out ahead; it might be a wise choice not to. But they are the values.

Mr. SHRIVER. Undoubtedly you thought about people being disappointed in not being able to get the vaccine until fall or winter when the appropriation has already been made.

Mr. CARDWELL. I certainly am not expert in this field, but I think you will always find there will be some people disappointed. I can remember when the red measles vaccine first came upon the market several years ago. I happened to have at that time some small children and my wife felt she should have her children vaccinated then and there. One pediatrician said, "I do not have the vaccine now, I will have it later."

So you do have those kinds of disappointments, I think, even in the best developed program. But I do not think there would be any mass national disappointment.

TETANUS STANDARDS

Mr. SHRIVER. On page 14 of the justifications, it is stated that the supply of dried master standards used in the preparation of the U.S. tetanus antitoxin is nearly depleted. What does this mean in terms of tetanus control?

Dr. MURRAY. This has really no bearing on treatment of tetanus. It only indicates that the standard which was adopted in 1907 and which has been the international standard since that time is now about exhausted and we have to go through the laborious laboratory procedures of establishing a new standard of identical strength to be used for the same purpose.

Mr. SHRIVER. Thank you.
Mr. FLOOD. Mr. Hull?
Mr. HULL. No questions.
Mr. FLOOD. Mrs. Reid?

PROTECTION OF PREGNANT WOMEN FROM RUBELLA

Mrs. REID. Doctor, you said, and we have discussed this on other occasions too, that the rubella vaccine should not be used by pregnant women. Is there any present treatment available to this group which will in part reduce the danger from rubella?

Dr. MURRAY. I think first of all, no live vaccine should be given to any pregnant woman whether it is rubella vaccine or any other live vaccine. Gamma globulin prepared from blood obtained from convalescents from rubella is being used experimentally but the results are unclear. Presumably this would contain sufficient antibodies to protect the women if given immediately at the time of infection or shortly before exposure.

Mrs. REID. Is this being used now?

Dr. MURRAY. It is being used experimentally.

Mrs. REID. You mentioned commercially sponsored studies in connection with rubella immunization. How are the efforts of the Federal Government and private industries coordinated, do they overlap in any way?

Dr. MURRAY. I do not think so.

The efforts of the Government are in three areas really. One is control, which is our problem; another is research; the third relates to programs against infectious diseases. The manufacturers are in the business of making vaccines for sale, but they also are interested in having their products subjected to evaluation in the field and these are done in clinical trials which are conducted alike by the manufacturers and by the Government supported investigators.

The information on this is all available and published and pooled except for the proprietary information that the manufacturers might develop for themselves which would involve strictly manufacturing know-how.

One of the mechanisms whereby we try to coordinate this is by holding conferences, small ones sometimes, and sometimes rather large conferences like the Rubella Conference which was held at the NIH recently under sponsorship of the Division of Biologics Standards and the National Institute of Allergy and Infectious Diseases, in collaboration with New York University Medical School.

This was attended by approximately 400 people. All the manufacturers were represented as well as potential manufacturers and scientists from foreign countries.

Mrs. REID. Does the increasing number of heart and other organ transplants affect your budget?

Dr. MURRAY. Not yet. This is what I was alluding to a little earlier. We foresee that when these tissue reagents which are used to type the tissues of the individuals who are involved in the transplantation become commercially available, there will be a need for standards. The budget of the division will be affected by this need.

Mrs. REID. Does this add to your research load?

Dr. MURRAY. Yes, it would add to the research load, and it would also add to the control load.

WHOOPING COUGH

Mrs. REID. What about whooping cough? Is it gradually being eliminated as a health threat?

Dr. MURRAY. The graph of the cases of whooping cough reported over the last 20 years, and also whooping cough-related deaths over the same period of time shows a really dramatic fall in a disease which was quite prevalent and caused a lot of permanent damage to children.

Mrs. REID. Thank you, Doctor, that is all.

Mr. FLOOD. Thank you, Doctor.

JUSTIFICATION MATERIAL

NATIONAL INSTITUTES OF HEALTH

Biologics Standards

Amounts Available for Obligation

	1969	1970
Appropriation	$8,499,000	$8,338,000
Comparative transfer to "Salaries and expenses, Office of Director"	-194,000	---
Cutback required by P.L. 90-364	-114,000	---
Total currently authorized for obligation	8,191,000	8,338,000
Plus: Proposed release of reserves for increased pay costs	114,000	
Total obligations	8,305,000	8,338,000
Disposition of cutback: To be used for pay costs in this account	$114,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
9	Biologics standards (Total obligations).	280	$8,305,000	285	$8,338,000	+5	+$33,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions....	280	285	+5
Full-time equivalent of all other positions.....	5	5	--
Average number of all employees.....	281	280	-1
Personnel compensation:			
Permanent positions.....	$2,493,000	$2,574,000	+$81,000
Positions other than permanent.....	30,000	30,000	---
Other personnel compensation.....	49,000	49,000	---
Total personnel compensation....	2,572,000	2,653,000	+81,000
Personnel benefits.....	250,000	255,000	+5,000
Travel and transportation of persons...	108,000	112,000	+4,000
Transportation of things.....	10,000	15,000	+5,000
Rent, communications, and utilities....	51,000	51,000	---
Printing and reproduction.....	10,000	10,000	---
Other services.....	4,153,000	4,050,000	-103,000
Supplies and materials.....	983,000	1,015,000	+32,000
Equipment.....	171,000	180,000	+9,000
Subtotal.....	8,308,000	8,341,000	+33,000
Quarters and subsistence charges.....	-3,000	-3,000	---
Total obligations by object.....	8,305,000	8,338,000	+33,000

Summary of Changes

1969 estimated obligations	$8,305,000
1970 estimated obligations	8,338,000
Net change	+33,000

Increases	Base Positions	Base Amount	Changes from Base Positions	Changes from Base Amount
A. Built-in				
1. Annualization of 1969 pay raise costs	---	---	---	$5,000
B. Program				
1. Immunology	31	$417,000	5	138,000
Decreases				
Payment to "National Institutes of Health management fund" for centrally furnished services	---	1,686,000	---	-110,000
Total net changes requested	---	---	5	+33,000

Explanation of Changes

Direct operations--The program increase of $138,000 and 5 positions will be used for research in the areas of viral and tissue immunology.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to: "Salaries and expenses, Office of Director".....	-$194,000	---	To provide funds covering expenses for the Office of the Director which were previously funded thru the NIH Management Fund

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Biologics Standards

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	$4,817,000	$4,787,000	$4,787,000	$4,787,000
1965	4,969,000	4,969,000	4,969,000	4,969,000
1966	6,406,000	6,406,000	7,206,000	6,806,000
1967	7,905,000	7,904,000	7,904,000	7,904,000
1968	8,649,000	8,649,000	8,649,000	8,649,000
1969	8,499,000	8,499,000	8,499,000	8,499,000
1970	8,338,000			

Biologics Standards

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	280	$2,819,000	285	$2,905,000	+5	+$86,000
Other expenses.....	--	5,486,000	--	5,433,000	--	-53,000
Total.....	280	8,305,000	285	8,338,000	+5	+33,000

1969 Program Plans

The Division of Biologics Standards is responsible for assuring the public that biological products, introduced into interstate commerce, such as vaccines, serums and human blood are potent, safe and pure for use in human beings. In previous justifications it has been stated in very general terms how the Division carries out its responsibilities and duties concerning its prime function of control as well as its related product-oriented research. At this time we would like to present more fully specific areas and the methods being utilized in attaining the Division's goals to illustrate the complexity of the operation and to indicate how present and future program plans are related.

At the present time Rubella Vaccine is a matter of major interest and concern. In future years attention will undoubtedly shift to other areas according to the development of new information.

Rubella Vaccine

As stated last year, "An experimental live rubella virus vaccine produced by the Division has been subject to additional clinical trials by the Division's scientists as well as other groups here and abroad..."

The Division has maintained a position at the center of the international program to develop a vaccine to control and perhaps eradicate rubella, a cause of crippling birth defects. The strain of rubella virus designated as HPV-77, developed by scientists in the Division of Biologics Standards has been used by pharmaceutical companies in preparing a substantial amount of experimental vaccine. At present these preparations have been field tested, with approximately 20,000 persons being inoculated. Rubella vaccine, if current progress continues, will become commercially available during calendar year 1969. These clinical trials, while crucial, are only one part of this total program. Others include studies of the biological characteristics of rubella virus; studies directed toward the standardization of serologic tests for rubella; studies of the tissue culture systems used in manufacture and studies of possible oncogenic effects. In addition, conferences with scientists and manufacturers are being held for the joint purpose of pooling together knowledge gained from the numerous field trials and laboratory investigations, and drafting proposed standards for the manufacturing and licensing of rubella vaccine. In the mean time other strains have been developed by independent scientists so that there may be the possibility of a choice of several vaccines.

Influenza Vaccine

Influenza Vaccine, because of the continuously changing character of the virus which causes the illness, presents problems in biologics control almost every year. During the fall of 1968, however, it became a matter of unusual concern to the Division because of the emergence of a highly divergent A2 strain in the Far East. Starting in late June an increase in respiratory illness was noted in Hong Kong. Isolation of influenza virus strains were made by a laboratory in Hong Kong and cultures were transmitted to laboratories in different parts of the world for study. By August 13th, there was general agreement among the virologists who studied the characteristics of these cultures that they differed markedly in character from A2 strains which have been prevalent in recent years including those responsible for the epidemic in the winter of 1967-68. The change was so marked in fact, that the data indicated clearly that the ultimate development of an epidemic was predictable because neither the immunity produced by previous influenza attacks nor that produced by currently available vaccines could be expected to provide more than limited protection, if any.

To be effective against this new strain influenza vaccine would have to be manufactured from this strain right from the beginning. Knowing that the normal lead-time for production is 4 to 5 months, the Division of Biologics Standards immediately provided cultures of this Hong Kong variant influenza virus to the manufacturers of influenza vaccine so that they could study its properties and determine whether influenza vaccine could be produced from it. This study and manipulation of the influenza virus is sometimes a lengthy and troublesome process since a new strain must be adapted to growth in fertile hens' eggs through an unpredictable number of generations or "passages". While this work was in progress a new isolate was received from the Far East which was quickly shown to have a superior vaccine production potential. This strain was provided to the manufacturers on September 6th by the Division of Biologics Standards. Testing methods and procedures were worked out and correlated in numerous conferences and laboratory demonstrations with the manufacturers. Everything was done to expedite the processing and release of vaccine including concurrent testing of samples by the Division of Biologics Standards. Samples for testing were even "hand-carried" to the Division's laboratories. All this required an intensive commitment of the DBS's resources to the testing and review procedures preliminary to the release of vaccine batches. In addition, when the first experimental lots of the new vaccine became available, the Division was able to embark on a program of clinical evaluation of the vaccine. By the very nature of such studies however it will take several months before the results are in. The first lot of vaccine was released on November 15, 1968.

The last time a comparable Influenza Vaccine emergency situation arose was in 1957 when the Asian or A2 strain of influenza virus appeared. The following is a comparision of the rate of availability of influenza vaccine in these two situations, on a time scale of days.

	Days	
	1957	1968
Production strain available.....	0	0
Requirements established.....	55	15
First batch released.....	94	66
First 5 million doses released.....	120	87

This comparison is even more illustrative of the effort involved when it is realized that the 1957 vaccine was only half the strength of the 1968 vaccine during the time period covered by this table.

In all this effort, the Division worked closely with the National Communicable Disease Center which was concerned with the epidemiological and virological aspects of the epidemic and with the National Institute of Allergy and Infectious Diseases which is concerned with research on influenza and other respiratory diseases.

Mycoplasma Research

The importance of Mycoplasma research was emphasized last year. Currently, studies of Mycoplasma in human disease and biologics production are being pursued to examine the biology, metabolism, and pathogenicity of these microorganisms; to develop new methods and to improve existing methods for their isolation as this relates to the testing needed to exclude Mycoplasma from biologic products such as those produced in tissue culture systems.

Pertussis Vaccine

Studies of Pertussis Vaccine are being continued to ensure that the pertussis vaccine component of products issued by U.S. licensed establishments has optimum properties, adequate and stable potency through the dating period and relative freedom from untoward reactivity. Objectives of current studies are to relate reactivity of vaccines and fractions of the constituent bacteria, as determined by laboratory tests, to clinical reactivity, and to investigate the cause of the neurological reactions that sometimes follow pertussis vaccination.

Yellow Fever Vaccine

Yellow fever vaccine research continues in an attempt to purify the current vaccine by removing the contaminating avian leukosis virus; to study the immunogenicity of purified vaccine in monkeys and man; and to select a purified strain capable of producing a vaccine with properties at least equal to that which has been used for the last quarter of a century.

Human Blood and Blood Products

The blood research program includes studies of the stability of products derived from human blood. Such studies yield information needed to determine acceptable storage conditions and for prescribing dating periods for materials derived from blood. Proteins of the clotting and fibrinolytic systems are targets of active investigation which is designed to provide a basis for improved control tests for these blood products. Increasing attention is being devoted to the characteristics and assay of globulin preparations in view of the increasing interest in immunologically specific products derived from human blood.

In view of the need for precise control of the recently licensed Rh_o (D) Immune Globulin, much effort is being devoted to developing potency assay methods. A suitable preparation has been obtained which can be used as a reference in anti-Rh_o (anti-D) assays. Since this material is in short supply, several

other preparations have been examined by a variety of methods to determine their suitability to serve as further reference preparations. A radioimmunoassay with its required ancillary procedures (radio-labeling, chromatography, ultracentrifugation, counting, computerization of data, etc.) is being carried out with some success.

* * *

In addition to work on specific products the basic methods and "state of the art" involved in research and control are constantly being reevaluated in terms of known information as illustrated by the following projects.

Selective breeding to establish a "standard" mouse

A mouse strain that has superior and consistent characteristics suitable for the potency and toxicity assays of biologics, particularly bacterial vaccines is urgently needed and is being sought. Starting with the NIH strain of mouse, which experience has shown is the superior to a number of strains available for biological assays, a group of mice were selected for further development. The progeny of each is tested for ability to be sensitized to histamine by pertussis vaccine, a reaction which correlates with the suitability of such animals for use in testing the potency of pertussis vaccine. Mice with optimal ability are selected for further breeding. This process of selection is continuing and it is anticipated that in the course of two or three years it will be possible to establish the desired "standard" colony.

Detection and characterization of viruses

This is a study which is designed to correlate the physical and biological properties of viruses, and to develop specific and more sensitive methods for detecting, identifying and classifying viruses using a variety of modern methods. The systems being studied are precipitin reactions, a method for concentrating small quantities of virus for thin sectioning-electron microscopy and the use of immunofluorescence. Another study which utilizes electron microscopy concerns the structure and immunologic reactions of viruses at the molecular level; such as the properties of adeno-associated viruses (AAV) and their interactions with adenoviruses.

Developmental studies for control testing of attenuated live virus vaccines

Information is being gained concerning the pathogenesis of rubella virus, mumps virus, and adenovirus infections in monkeys so that safety test for attenuated live virus vaccines can be developed or improved.

In this study, rhesus monkeys are inoculated with both "wild" and attenuated virus preparations, using various routes of inoculation depending on the mode of action of the particular virus. Animals are observed for evidence of virus multiplication. Uninoculated animals may be placed in cages with inoculated animals or in the same room in order to study transmissibility of the "wild" or attenuated infection.

Leukemia and Hepatitis

Scientists of the Division are continuing exploratory research in two areas of potential future importance to biologics control: leukemia and hepatitis.

Recently a previously unknown virus has been recognized as the possible cause of infectious mononucleosis. This virus has also been detected in malignant cells of some leukemic children as well as in white blood cells of many seemingly healthy individuals. The role of viruses in general and this agent in particular in triggering the malignant process is uncertain and is the subject of basic research in a great many laboratories. However the need for ongoing research in this area as it relates to present and future biological products can be appreciated.

Another area of continuing concern involves hepatitis. Viral hepatitis has for many years been of particular interest to the Division because of the need for a detection system that will identify those individual donations of blood for transfusion as well as blood products which are contaminated with hepatitis viruses, and the need of a means of preventing hepatitis. As new research becomes available, each in turn is being brought to bear on the hepatitis problem.

Studies of marmosets and their suitability for the testing of biological products

Marmosets have been proposed as suitable animals for use in studies of hepatitis and other diseases. The Division has therefore been developing a small colony of these primates. The initial goals of this program were to maintain such a colony under laboratory conditions, and to study its microbiology. From such work, personnel have become familiar with maintenance methods unique to these animals. Also means of recognizing and controlling marmoset diseases and microflora have become available.

Studies to be initiated in the coming year are: (1) ability of marmosets to develop antibodies to commonly used antigens; (2) ability to develop a delayed hypersensitivity state; (3) types of immunoglobulins that can be produced; (4) pathogenesis in marmosets of agents associated with cases of human hepatitis and (5) possible usefulness of marmosets in the study of the safety and freedom from oncogenicity of viral vaccines.

* * *

The Division's responsibility for making recommendations for standards (both written and physical) for all biological products has been discussed in previous justifications. Physical standards are issued to pharmaceutical manufacturers and other research laboratories concerned with biological standardization to provide uniform evaluation of their products, particularly with respect to potency, or strength.

A few examples of studies related to standardization are cited.

Development of an improved opacity standard

The objective of this project is to prepare a stable solid opacity standard by suspending finely divided particles in a resin, to standardize this preparation in terms of the current opacity standard which is an aqueous suspension of glass particles, and to determine the practicability of distributing a solid standard for use by manufacturers.

Standardization of reference diphtheria antitoxin for flocculation test

Very little diphtheria antitoxin is produced today, a situation which is explained by the drop in the number of cases of diphtheria from 200/100,000 of population in the mid-twenties to 0.1/100,000 in the present decade. Nevertheless diphtheria antitoxin is still needed to treat the cases of diphtheria which do occur and standards must be maintained. The Division is attempting to select a suitable diphtheria antitoxin to replace the present reference Diphtheria Antitoxin for the Flocculation Test and to establish certain values equivalent to the existing reference. If found to be satisfactory, it will be adopted as the new reference.

Replacement of the U.S. Standard Tetanus Antitoxin

The supply of the dried master standard used in the preparation of the U.S. Standard Tetanus Antitoxin is nearly depleted. This dried preparation was adopted in 1907 and has been in use since that date. Five lots of equine tetanus antitoxin and one lot of tetanus immune globulin of human origin are being studied in order to select one having suitable properties for use as a replacement for the master preparation.

In order to maintain an adequate supply of references and standards, it was necessary during a recent twelve-month period to prepare and calibrate 15 antitoxins, 3 serums, 11 vaccines, 2 toxins and 4 skin test antigens. In addition, 1 antitoxin, 9 serums, 6 vaccines, 4 toxins, and 4 virus preparations were purchased from commercial sources and prepared for distribution by the Division. The technique of freeze-drying is a key procedure applied in the preparation of standards and reference materials whenever possible in order to achieve stability over long periods of storage. In this connection the following number of ampules of various preparations were freeze-dried: 1,106 cultures, 3,515 serums, 6,035 vaccines and 200 viruses for a total of 10,856. Shipments totaling 879 in number were distributed to manufacturers, state health laboratories, and other institutions concerned with biological standardization, consisting of 9,429 individual items.

During the same 12 month time period, 3,996 lots of biological products were submitted to the Division. Of these, 3,899 lots were released, 38 lots were rejected, and 59 lots were withdrawn by the manufacturer.

1970 Program Plans

The Division's efforts will be directed along the lines set forth for 1969 with emphasis on the licensing of rubella vaccine and continued research in such changing areas of interest as influenza virus vaccines, oncogenesis, hepatitis, mononucleosis, etc.

It is incumbent upon the Division, in view of recent developments in organ and tissue transplants, to keep abreast of the "state of the art" as it may apply to any new biological product forthcoming in the field of tissue immunity. Accordingly, $138,000 is being requested to support three medical officers and two supporting staff who will help to accelerate the viral and tissue immunology programs. The research and control work involved will be somewhat comparable to that already being performed in the case of blood and blood products.

Included in this budget request is $5,000 for the annualization of the 1969 pay raise as well as a decrease of $110,000 in the NIH management fund. Together with the program increase of $138,000, this results in a net increase of $33,000.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Biologics Standards			
Medical Officer	GS-15		$21,098
Medical Officer	GS-14		19,771
Medical Officer	GS-13		18,249
Scientist	GS-12		12,174
Scientist	GS-11		10,203
Total new positions, all activities		(5)	81,495

WEDNESDAY, MARCH 26, 1969.

NATIONAL CANCER INSTITUTE

WITNESSES

DR. KENNETH M. ENDICOTT, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
ROBERT E. LEARMOUTH, EXECUTIVE OFFICER, NATIONAL CANCER INSTITUTE
JESSE L. STEINFELD, ASSOCIATE DIRECTOR FOR PROGRAM, NATIONAL CANCER INSTITUTE
EARLE L. BROWNING, FINANCIAL MANAGER, NATIONAL CANCER INSTITUTE
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
NATIONAL INSTITUTES OF HEALTH			
Personnel compensation:			
Permanent positions	13,351	14,511	14,650
Positions other than permanent	288	278	278
Other personnel compensation	137	149	149
Total personnel compensation	13,776	14,938	15,077
Personnel benefits: Civilian employees	1,523	1,651	1,667
Travel and transportation of persons	586	661	690
Transportation of things	123	128	128
Rent, communications, and utilities	488	501	501
Printing and reproduction	457	467	467
Other services	57,836	60,085	63,071
Supplies and materials	3,350	3,481	3,486
Equipment	2,570	2,550	2,550
Grants, subsidies, and contributions	94,232	96,067	95,875
Subtotal	174,941	180,529	183,512
Quarters and subsistence charges	−10	−10	−10
Total obligations, National Institutes of Health	174,931	180,519	183,502
ALLOCATION TO VETERANS' ADMINISTRATION			
Personnel compensation:			
Permanent positions	614	563	574
Positions other than permanent	133	137	137
Other personnel compensation	1	1	1
Total personnel compensation	748	701	712
Personnel benefits: Civilian employees	55	52	52
Travel and transportation of persons	58	65	60
Transportation of things	1	1	1
Rent, communications, and utilities	2	2	2
Printing and reproduction	1	1	1
Other services	5		
Supplies and materials	39	30	30
Equipment	69	48	42
Total costs, funded	978	900	900
Change in selected resources	−2		
Total obligations, Veterans' Administration	976	900	900
Total obligations	175,907	181,419	184,402

PERSONNEL SUMMARY

	1968 actual	1969 estimate	1970 estimate
NATIONAL INSTITUTES OF HEALTH			
Total number of permanent positions	1,419	1,390	1,427
Full-time equivalent of other positions	41	35	35
Average number of all employees	1,430	1,417	1,409
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466
ALLOCATION TO VETERANS' ADMINISTRATION			
Total number of permanent positions	82	74	74
Full-time equivalent of other positions	10	10	10
Average number of all employees	91	82	82
Average GS grade	5.4	5.5	5.5
Average GS salary	$6,591	$6.809	$6,883
Average salary of ungraded positions	$16,216	$15,236	$15,527

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	79,163	80,052	80,488
(b) Fellowships	4,019	4,374	4,201
(c) Training	11,050	11,641	11,186
Total grants	94,232	96,067	95,875
2. Direct operations:			
(a) Laboratory and clinical research	15,082	16,114	17,178
(b) Collaborative research and development	66,719	64,380	66,102
(c) Biometry, epidemiology and field studies	1,265	1,380	1,565
(d) Review and approval	2,427	2,459	2,598
(e) Program direction	1,079	1,019	1,084
Total direct operations	86,572	85,352	88,527
Total program costs, funded [1]	180,804	181,419	184,402
Change in selected resources [2]	−4,897		
Total obligations	175,907	181,419	184,402
Financing:			
Comparative transfers to other accounts	1,442	1,467	
Unobligated balance lapsing	6,007	2,067	
Budget authority	183,356	184,953	184,402
Budget authority:			
Appropriation	183,356	185,150	184,402
Transferred to other accounts		−197	
Appropriation (adjusted)	183,356	184,953	184,402
Relation of obligations to outlays:			
Obligations incurred, net	177,349	182,886	184,402
Obligated balance, start of year	122,467	111,398	132,859
Obligated balance, end of year	−111,398	−132,859	−138,666
Adjustments in expired accounts	−2,385		
Outlays	186,033	161,425	178,595

[1] Includes capital outlay as follows: 1968, $2,036,000; 1969, $2,550,000; 1970, $2,550,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $48,761,000; 1968, $43,864,000; 1969, $43,864,000; 1970, $43,864,000.

Mr. FLOOD. Now we have the National Cancer Institute. Dr. Kenneth M. Endicott, the Director, will be the principal witness.

Doctor, do you have anybody else we do not know here? Anybody's first appearance?

Dr. ENDICOTT. No first appearances.

Mr. Learmouth, the executive officer; Dr. Steinfeld, associate director for program, and Mr. Browning, our finance officer.

Mr. FLOOD. You have a statement here, Doctor. What do you want to do about it?

Dr. ENDICOTT. I would be happy to read it.

Mr. FLOOD. Whatever you wish.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

We will place your biographical sketch in the record and then you may proceed.

(Biographical sketch follows:)

BIOGRAPHICAL SKETCH

Name: Kenneth Milo Endicott, M.D.: Position: Assistant Surgeon General, Public Health Service; Director, National Cancer Institute; Birthplace and date: Canon City, Colo., June 6, 1916: Education: A.B., University of Colorado, Boulder, 1936; M.D., University of Colorado, Denver, 1939.

Experience: Director, National Cancer Institute, National Institutes of Health, U.S. Public Health Service, Department of Health, Education, and Welfare, July 1960; appointed Assistant Surgeon General, U.S. Public Health Service, January 1960; Associate Director, National Institutes of Health, 1958–1960; Chief, Cancer Chemotherapy National Service Center, National Cancer Institute, 1955–1958; Scientific Director, Division of Research Grants, National Institutes of Health, 1951–1955; Chief, Section on Metabolic and Degenerative Diseases, Division of Pathology, National Institutes of Health, 1942–1951; Medical Center for Federal Prisoners, Springfield, Mo., 1942; Maritime Quarantine Station, San Francisco, Calif., 1941–1942; U.S. Public Health Service Relief and Quarantine Station, Portland, Oreg., 1940; Commissioned in U.S. Public Health Service, 1939.

Association memberships: Diplomate, American Board of Pathology; American Medical Association, fellow; American Association for the Advancement of Science; American Association of Pathologists and Bacteriologists; Society for Experimental Biology; International Association of Medical Museums; Society for Experimental Pathology; Washington Academy of Sciences; Alpha Omega Alpha; Phi Rho Sigma; Theta Xi.

Special awards, citations, or publications: Distinguished Service Medal of the Public Health Service Commissioned Corps, awarded 1964: For his outstanding and distinguished leadership in Medical Research Administration and National Cancer Research Programs.

GENERAL STATEMENT

Dr. ENDICOTT. Mr. Chairman and members of the committee, the problem we confront in dealing with cancer is formidable and the research task demanding and challenging. Every step of significant progress is therefore of utmost importance, and every opportunity to reach out for new gains is of utmost urgency.

The wide range of malignant diseases called cancer will claim 615,000 new victims and 325,000 lives in the United States this year. Close to a million Americans are suffering from cancer today—a toll exceeded only by the ravages of heart disease and related conditions.

Over the years the National Cancer Institute has advanced the research attack on cancer as rapidly as scientific progress would permit. In doing so the Institute has elaborated a pattern of positive approaches to different aspects of the problem—a pattern that recognizes and follows the most promising leads toward the ultimate control of cancer in man.

Mr. FLOOD. Control?

Dr. ENDICOTT. Yes, sir

Mr. FLOOD. Just control?

Dr. ENDICOTT. By that I mean eliminating it as a serious health problem either through prevention or cure or a combination of both.

Thus, the Institute has achieved a balanced program encompassing fundamental studies of the biology of cancer, investigation of causitive factors that may be clues to prevention, and a constant effort to improve treatment. The objective is to reverse the continuing unfavorable balance of occurrence over cure, and ultimately to eradicate cancer as a major health threat.

The program is likewise balanced between project type research and so-called target research. Project research, which is devoted mainly to fundamental studies in various scientific fields or disciplines, is carried on both in the Institute's laboratories and at universities and other research institutions that receive grant support. Large scale research in areas recognized as being especially promising is accomplished through contracts as an extension of our direct operations.

All of these research activities have the backup of laboratory and clinical training programs supported by the Institute to increase and improve the Nation's pool of scientific manpower in the biomedical field.

Many of the most important advances in research are in the areas of etiology, or cancer causation; and chemotherapy, or drug treatment. Recent findings in both of these areas are of great significance scientifically, and of great promise for the prevention and cure of cancer.

VIRUS AND CANCER

As evidence of the viral causation of cancer in experimental animals continues to mount, the possibility that viruses cause human cancer become stronger. Although positive identification of a cancer-causing virus in man is still lacking, particles resembling animal cancer viruses have been observed in leukemia patients and are being closely studied. One type of particle is identical with those that cause leukemia in laboratory animals. Another is similar to the herpes virus that causes fever sores and shingles. Human cancer of the uterine cervix, or neck of the womb, has also been found to be associated with a herpes-type virus.

An effective way to deal with a cancer-causing virus would be to stimulate the body's reaction against the agent as a foreign substance. Our bodies have a built-in immune mechanism, but it is often not quick enough or strong enough to overcome an invading bacterium or virus. This mechanism can be strengthened by inoculating a subject with a weakened or killed virus that acts as an antigen and stimulates the production of antibodies against that type of virus.

Mr. FLOOD. You are taking quite a chance, are you not?

Dr. ENDICOTT. It is probably going to be more complex than the problem which Dr. Murray was just discussing in connection with whether or not to use rubella vaccine in adult women. It is not a simple problem, but I am personally convinced that if there is one area which offers great promise for wide-scale prevention of cancer, it lies in this direction.

Another way of stimulating the immune mechanism has been discovered recently. The cells of the body produce a protein called inter-

feron as a defense against attacking viruses and certain other disease agents.

Mr. FLOOD. How many types and kinds of cancer are there, about?

Dr. ENDICOTT. It depends on who is classifying them.

Mr. FLOOD. You classify them.

Dr. ENDICOTT. I would say somewhere between one and 200 varieties. That is, in man. And some of these may be simply the same disease but manifested in a different organ or something of that sort.

Often, however, this process fails to give protection, possibly because it is either too slow or triggered too late. Interferon production can be stimulated by certain nonliving materials, including natural and synthetic biologically related substances. One of these is a drug called Poly I:C. Laboratory animals with several types of cancer, including some induced by human adenovirus, were treated with this drug and showed regression of tumors, decreased rates of tumor growth, and increased survival time.

CAUSES OF CANCER

Mr. FLOOD. Do you think cancer can be induced by trauma of any sort?

Dr. ENDICOTT. Yes, sir; certainly.

Here I would include as the most important one, trauma from radiation, sunlight, X-ray, this sort of thing. Whether a single instance of physical trauma like a blow to the breast or something ever has caused cancer, I personally seriously doubt. But trauma, if you will include radiation, clearly does cause cancer.

Preliminary studies are now being made preparatory to evaluating Poly I:C in cancer patients. Information must be obtained on the mechanism of the drug's action, and the dosages required, before the material can be evaluated in man.

I might add parenthetically, we have run into some unexpected toxicity which is sufficiently serious that the manufacturer feels that about the only condition in which this drug should be tested clinically at the present time is a life-threatening disease like cancer.

Mr. FLOOD. What produces a tumor? Where does a tumor come from?

Dr. ENDICOTT. The word "tumor" is broader than the word "cancer."

Mr. FLOOD. I know that.

Dr. ENDICOTT. And it includes a number of growths which are not malignant. Literally the word means a swelling.

Mr. FLOOD. What produces it?

Dr. ENDICOTT. A variety of things, many of which we probably do not know.

Mr. FLOOD. External things?

Dr. ENDICOTT. Certainly they can be produced by viruses, they can be produced by trauma, especially radiation, they can be produced by a great variety of chemicals, heredity certainly has something to do with it.

Mr. FLOOD. What is the cellular activity?

Dr. ENDICOTT. The cells in a tumor divide in essentially the same way as normal cells divide, one cell just divides into two and each of them in turn divides into two more, and so on and they begin to accumulate and they produce a mass.

Mr. FLOOD. Proceed, Doctor.

Dr. ENDICOTT. For many years efforts have been made to find tests for early cancer or even a susceptibility to cancer. A technique for identifying persons with a high risk of cancer because of certain abnormalities, such as inborn immunological defects, chromosomal disorders——

Mr. FLOOD. Is that hereditary?

Dr. ENDICOTT. Yes, sir. Or other congenital conditions now being studied. These individuals can be identified by the response of certain of their cells in tissue culture to a known animal cancer-causing virus. The efficacy of the technique must now be assessed through further studies of cells from persons with these abnormalities, their close relatives, persons exposed to environmental cancer-causing agents, and patients with untreated leukemia or other cancers.

Mr. FLOOD. Does the law of Mendel apply there?

Dr. ENDICOTT. We have thought so for a long time, but the deeper we get into the virus business, the more we are beginning to think that perhaps the law needs amending.

Mr. FLOOD. Very clever.

DRUG THERAPY

Dr. ENDICOTT. In the treatment of cancer with drugs, important gains have been made by exploiting differences in the reproductive cycles of normal and malignant cells. Because of their more rapid cycling, cancer cells are harder hit by drugs than normal cells with their longer resting and recovery periods. The greatest improvements have consequently been made in treating such fast-growing tumors as leukemia, with 85 to 100 percent of patients achieving complete remissions lasting from 23 to 40 months when given combinations of drugs in intensive, intermittent courses. Studies are being made to match the techniques to the unique biology of slow-growing tumors such as those of the breast, colon, and lung.

Mr. FLOOD. Is there a chain reaction on these cells, a violent chain reaction?

Dr. ENDICOTT. In the process of cell division, after the cells divide into two, there is a period actually during which they grow to normal size, and what might be called a resting period. Then as they begin to prepare to divide again something turns on a chemical process which produces increased amounts of DNA in order to provide the necessary genetic material so that each new daughter cell will have the total genetic information.

It is during the period when the DNA is being rapidly synthesized and during the period of actual cell division that most of our present cancer drugs act. So if you have a tumor which is growing rapidly——

Mr. FLOOD. That is the point to hit.

Dr. ENDICOTT. There are more cells that are in the process of division, so you hit.

Mr. FLOOD. Do you know that point, the Achilles heel? Do you know where it is within reason?

Dr. ENDICOTT. Actually, it varies from one drug to another. There is a very complex chemical process involved here.

One drug will hit at one point in the process and another drug at another. With each new drug that comes along one of the problems is

really to find out where it hits the chemical process that results in the production of DNA.

I think the success of combination therapy rests largely on the fact that there are different points of attack, and also that there are different types of toxicity so that you can increase oftentimes the effectiveness of the drug without toxicity being added.

Mr. FLOOD. One thing will be as bad as the other?

Dr. ENDICOTT. Cancer drugs almost without exception are extremely toxic, and it has always been a very close touch and go proposition.

Mr. FLOOD. The demarcating line is very thin?

Dr. ENDICOTT. Yes, sir; it is like walking a tightrope oftentimes.

Mr. FLOOD. Good trick if you can do it, like walking across Niagara Falls on a rope.

Dr. ENDICOTT. Yes.

Continued improvement has also been made in the treatment of advanced Hodgkin's disease with intensive intermittent combinations of drugs.

We have a special report on chemotherapy research if you would like for the record.

Mr. FLOOD. We will place it in the record at this point.

(The report follows:)

SPECIAL REPORT: CHEMOTHERAPY RESEARCH

Even with the earliest diagonsis possible and treatment by surgery and radiation by the best doctors in the best medical centers, sufficient knowledge is not available to keep 300,000 Americans from dying of cancer this year. Lack of knowledge of the causes and lack of means for preventing cancer will result in development of the disease in hundreds of thousands more people; 600,000 new cases will be diagnosed for the first time during the year.

But, one by one, the number of different types of cancer successfully treated by drugs is steadily increasing. Under the stimulus of the National Cancer Institute's chemotherapy program, new chemical agents are being discovered and developed into cancer drugs. New techniques of administering them are producing long remissions (absence of signs and symptoms of disease) and even cures. In some instances, these results are being obtained with drugs previously found effective against some types of cancer but not against others when given by older, conventional methods.

One of the key factors in the new techniques is the use of combinations of drugs or of therapies, such as drugs and surgery or radiotherapy. Use of drugs in combination takes advantage of the fact that different ones produce different types of toxic side effects, so that there is increased anticancer action without additive toxicities. Another important factor in the new treatment schedules is the timing of the administration of drugs. Increasing knowledge of the cancer cell and its behavior will permit giving a drug at a time in the life cycle of the cancer cell when it is most vulnerable to drug action.

DEVELOPMENT OF THE PROGRAM

The National Cancer Institute began its activities in drug research with the formation of a section of chemotherapy in 1946. By 1955, when the Congress asked the Institute to undertake a large-scale attempt to find new and better antitumor drugs, studies in experimental and clinical pharmacology of cancer drugs and some clinical trials were in progress at NCI, while work throughout the country was being conducted in a few small clinical studies and scattered drug development programs. During the years 1955–65, NCI leaders forged a complete national program for the discovery and development of anticancer drugs. This coordinated, cooperative and successful program includes sources of new drugs from chemists and from natural products, animal tumor systems for screening the chemicals, rigorous animal studies for the toxicity and safety of new drugs, resources for the study of how the new drugs behaved in animals and man, formulation of a drug into a product safe and appropriate for use in patients,

and, finally, the clinical trial itself. So little was known and available in 1955 that each of these resources had to be created almost in its entirety.

Continuing analysis of the 10 years of effort permitted identification of all the key steps for even more rapid drug development under the leadership of a strong coordinated central management group. All activities concerning drug development have been grouped under the chemotherapy program. These included the Institute's laboratory and clinical research at Bethesda, contracts for working with industry and some grants for carrying out clinical research in the universities. The program also made extensive use of small working groups, such as task forces, wherein scientists, physicians, contractors, and grantees analyzed their results and together worked out better ways of accomplishing given tasks.

Analysis and review of the program continue. Results and planned use of resources in NCI's research and that of contractors and grantees are evaluated constantly on the basis of their contribution to the ultimate chemical control of cancer. The program's two general objectives are: (1) to identify chemical compounds for best control of cancer and (2) to study the best ways for most effective use of drugs in man. Progress in developing and accomplishing these objectives is evident in results from a number of studies.

SEARCH FOR EFFECTIVE DRUGS

The program is revealing active compounds from a wide spectrum of sources. They include natural products from plants, antibiotics from bacterial sources, enzymes, and simple and complex synthetic compounds. Some are related to theoretical concepts of chemotherapy derived from past experiences; some represent entirely new classes of compounds. Studies of their modes of action are producing new biochemical information on the synthetic pathways in cancer cells susceptible to attack by effective drugs.

The systematic search for cancer-controlling drugs consists of a wide variety of probing efforts, both empirical and theoretical, for clues to compounds that can selectively destroy cancer cells. The usefulness of experimental efforts to select such drugs rests upon the demonstration that they can bring about complete disappearance of clinical cancer and substantially prolong life expectancy of patients.

Empiric testing of natural and synthetic products continues to be a productive approach to the identification of active drugs. While random sampling must continue, especially in the search for chemical compounds now unknown but existing in nature, such as in bacteria, plants, and animals, the scientific selection of materials for screening is playing a larger and larger role. The availability of a sufficient number of chemicals that cause regression of clinical cancer permits study of the relation of chemical structure to anticancer function. Results have shown that the choice of compounds for introduction into the screen will progressively be determined by structure-function considerations, so that directed synthesis may gradually displace much of the empiric screening. In addition, the establishment of the structure of active antitumor compounds from natural products is so rapid that these randomly determined new structures soon add their contributions to the total structure-function mosaic.

Experience during the past year showed that for initial screening of candidate compounds L–1210 leukemia of the mouse is by itself adequate for selection of agents active in fast growing tumors, such as acute leukemia. The L–1210 mouse leukemia model has been studied quantitatively to show that active drugs given in their most efficient regimen can reduce the leukemic cell population from 100 million to zero with cure of the leukemia in the mouse. As a consequence of the further study of the past year, the Walker 256 tumor of the rat, which had been the other part of the primary screen since 1965, was dropped from the system. The new primary screen permits a biological material of high potential activity to move at a rapid pace through the various preliminary stages and into clinical trial.

Another change introduced in the past year was in the dosage schedules administered in the L–1210 primary screen. Utilizing a wide dosage range for each schedule, both single doses, and daily doses for 9 days, are tested in the screen. All drugs active in the primary screen are immediately studied in a variety of dose schedules both in L–1210 and in normal mice. This leads to solid knowledge of the best way to use the drug and also gives important information as to the dose schedules that should be used in toxicologic and pharmacologic studies.

Pharmacologic studies of active compounds continue to provide improved correlations between drug effects in animals and man and lead to stronger confidence in the ability of animal studies to predict safe posage and possible side effects in patients. A study reported during the past year indicated that sheep may be especially valuable in predicting hair loss due to drugs and in development of ways to overcome it. Administration of a cancer drug, cyclophosphamide, to Suffolk sheep was followed by a loss of wool that is comparable to hair loss in drug-treated cancer patients. This happened because the growth of sheep's wool, like that of man's hair, is more or less continuous. In contrast, the hair coats of the usual laboratory animals, such as mice or rats, are replaced seasonally or cyclically. Examination under a microscope of skin specimens from the sheep showed death of hair root cells in less than 24 hours after administration of the drug; however, the growth of new hair could be detected within 2 weeks. Other toxic effects frequently associated with the use of cyclophosphamide in patients, such as damage to bone marrow and to liver, were also detectable in the sheep.

The search for effective drugs includes another dimension, which is assuming increasing importance in the efforts to build a firm theoretical base for cancer chemotherapy. Studies of cell kinetics, the growth characteristics of populations of cells, have suggested that the sensitivity of cancers to drugs is related to the rate at which they grow.

Laboratory findings, obtained with cancer cells growing in mice, were applied to studies of clinical cancer. The results suggested that the types of malignancy in which the major successes in drug control have occurred are rapidly growing tumors, such as acute lymphocytic leukemia; Burkitt's lymphoma, a type of cancer seen most frequently in African children; choriocarcinoma, a highly malignant cancer that arises from the placenta; and Wilms' tumor, a type of kidney cancer in children probably of congenital origin. The types that are poorly responsive to drugs, such as cancers of the lung, breast, and colon, are slowly growing tumors. A major question that must be answered concerns the reasons for the differences between the drug sensitive tumors and the drug insensitive ones.

Additional studies in experimental systems seem to suggest an important difference between the cell populations of tumors that grow rapidly and those that grow slowly. It appears that the fraction of tumor cells dividing at any one time is as high as 90 percent in the fast growing tumors, but may be only 1 percent in the slow growing ones, with 99 percent of the cells of the latter tumors in a nonproliferative state.

A hypothesis has been developed based on the possibility that susceptibility to cancer drugs may be determined by the fraction of cells dividing at any one time. Three different tumor cell types, in a functional sense, are postulated: dividing cells, cells temporarily not dividing but retaining a full capacity to return to the dividing state, and cells permanently removed from the possibility of dividing. Such cells comprise three hypothetical compartments within a tumor: compartment A—cells in active cell division; compartment B—cells temporarily out of the division cycle but fully able to return to active cell division; compartment C—dying and end-stage differentiated cells.

Experience has shown that most of the highly active cancer drugs, such as methotrexate and vincristine, affect only cells during the division cycle. Hence, tumors with a large fraction of cells actively dividing would be fast growing and drug sensitive. Tumors with small fractions of dividing cells and large fractions of nondividing cells would be both slow growing and drug insensitive. Cells in compartment C are not of concern in this context.

To date, the major practical result of this concept has been among the rapidly growing tumors, where it has been shown that the rapidly growing animal tumor models predict drug schedules and drug combinations of great effectiveness. From such models have come the dosage regimens and drug combinations so highly effective in the treatment of leukemias, lymphomas, choriocarcinoma, and Wilms' tumor. Investigators in the field believe that in the drug sensitive tumors a considerable opportunity exists to use present knowledge to attempt cure of patients with these types of cancer.

The situation for the slow growing tumors is very much different. The average doubling time of drug insensitive tumors is measured in weeks to months. The rate of decrease of tumor size is not a measure of the extent of drug-induced killing of tumor cells. The fast growing animal screens have not selected active drugs for tumors of the slow growing type in the clinic. Optimum drug schedules useful in rapidly growing tumors are not suitable for the slow ones.

Attempts are being made to extend to the slowly growing tumors what has been learned from successful chemotherapy in animals and man. Hypothetically, one approach involves manipulation of temporarily nondividing cells in animal tumors, so that they will revert to actively dividing stages where they will be sensitive to drugs. The research has included measuring factors that will define the reason for slow growth of tumors; finding an animal tumor with similar biologic characteristics and studying the effects of drugs; applying in man those drugs and drug schedules that can be found effective in the animal model for slowly growing tumors; and extending the mathematical model so as to predict on the basis of present hypotheses the drug schedules of present drugs most likely to be effective in tumors of the slowly growing type.

EFFECTIVE USE OF DRUGS

Several new drugs are in clinical trial or final preclinical stages. Two compounds have come into use entirely through the empiric screening system of the chemotherapy program: BCNU [1,3-bis(2-chloroethyl)-1-nitrosourea] and dimethyl triazeno imidazole carboxamide. Two others represent new types of active antitumor compounds; they are L-asparaginase and polyI :C.

BCNU was established in the last several years as an additional, effective drug in the combination treatment of acute leukemia of childhood. Although not active by itself in inducing complete remission (absence of all signs and symptoms of disease), it is of great value in maintaining remission. Its ability, in contrast to that of most other cancer drugs, to cross the blood-brain barrier suggests its possible usefulness in treatment of meningeal leukemia (leukemia that has spread into the central nervous system).

NCI grantees cooperating in the Southeastern Cancer Chemotherapy Study Group have this year reported activity of BCNU in temporarily controlling advanced Hodgkin's disease generally resistant to standard drug treatment with alkylating agents. The group of 15 cooperating clinical investigators at eight medical centers reported responses by about half of 31 patients; medium duration of maintained remissions was longer than 4 months.

Preliminary results from investigators working in the central drug evaluation program showed a response to dimethyl triazeno imidazole carboxamide among 15 percent of a group of almost 200 melanoma patients. The best responses were observed in skin lesions; others were noted also in nodes, lungs, and the liver.

The speed with which research is demonstrating the clinical activity of the new drug, L-asparaginase, can be attributed to the intense interest and generous collaboration among scientists of the National Cancer Institute, Sloan-Kettering Institute for Cancer Research, Cornell University Medical College, and the pharmaceutical industry. These studies have shown that L-asparaginase has wide metabolic effects and have opened new areas of biochemical exploration related not only to cancer but other ailments. The compound is now available in large amounts and it will be studied in a great many patients in this country. Starting early in 1969 a majority of patients with acute lymphocytic leukemia, the form of the disease occurring primarily in children, will be receiving it. Preliminary studies show that some patients with acute myelocytic leukemia, the adult form of the disease, respond to L-asparaginase when it is given in large doses.

L-asparaginase, an enzyme, exerts its anticancer effect by destroying asparagine, an amino acid essential for all cells, whether normal or cancerous. It is hypothesized that tumors that are sensitive to L-asparaginase lack an enzyme called asparagine synthetase, which is necessary for the production of asparagine. Such sensitive tumors must therefore obtain asparagine from the body's extra-cellular fluids, such as the blood, in order to survive. The drug L-asparaginase breaks down this extracellular asparagine and stops the growth of the tumor. Tumors that do not respond to treatment with L-asparaginase, and all normal cells, contain asparagine synthetase and are independent of outside sources of asparagine.

The taxic side effects of L-asparaginase are being intensively investigated. These include hypersensitivity reactions, such as hives and/or fever; liver involvement; pancreatitis; abnormalities in the clotting proteins in the blood; and central nervous system toxicity. Particularly when large doses of the drug are given, CNS toxicity is shown by personality changes, abnormal electroencephalographic patterns, and even lapse into coma. The effects are similar

to those seen in acute alcoholism and they raise questions requiring further biochemical research to determine, for example, why these effects occur, whether they occur with other enzymes, and whether other enzymes may destroy specific amino acids.

Collaboration of NCI scientists with those of the National Institute of Allergy and Infectious Diseases has yielded an opportunity to study an entirely different kind of potential cancer drug. Called polyI : C for short, the compound results from research on viruses and interferon, a protein produced by cells as a defense against attacking viruses.

The protective action of interferon is not limited to attacks by viruses but extends to certain other disease agents. Interferon gives some protection to cells infected with organisms causing psittacosis and trachoma ; and in the past year it has been shown that use of interferon inducers protects mice and mouse tissues against toxoplasma and malaria.

Certain nonliving materials also induce the production of interferon by cells. These include natural and synthetic biologically related substances. PolyI : C is one of these interferon inducers; it is a synthetic double-stranded RNA (ribonucleic acid) formed by mixing two chemical compounds, polyinosinic and polycytidylic acids.

It is believed that interferon acts by inducing an infected cell to produce another intracellular protein, which is thought to combine with ribosomes (the protein manufacturing sites) in the cell. The altered ribosomes then no longer continue to make the proteins essential for continued support of the attacking disease agent but do continue to make the host cell's proteins in a normal fashion.

Since effective treatment of cancer is thought to involve interference with the life processes of cancer cells, it was reasonable to suggest that interferon may inhibit the growth of tumors without affecting normal cell growth. In a series of experiments carried out by scientists of the two Institutes, treatment with the interferon inducer polyI : C resulted in regression of tumors, decreased rates of tumor growth, and increased survival time of laboratory animals bearing several different types of transplanted tumors. These included leukemias, reticulum cell sarcomas, lymphatic lymphomas, fibrosarcomas, plasma cell tumors, human adenovirus 12 induced tumors, and Bittner mammary tumors in mice; and a sarcoma in rats. Originally some of the tumors were virus induced and others were spontaneous tumors. In general, the leukemias studied have been more resistant to the action of polyI : C than the slower growing tumors.

The drug is under test now in the L1210 mouse leukemia screen in the NCI's chemotherapy program and it shows significant activity. Toxicity and other studies will be the next step preparatory to introduction of the drug into studies of cancer in patients.

The mechanism of the drug's antitumor activity is being studied. The investigators now think that the antitumor effect of polyI : C is more complex than that related solely to the antiviral action of the interferon induced.

A synthetic plastic, pyran copolymer, has also been found to be a potent stimulator of interferon production in man and experimental animals. It is being tested in preliminary studies in patients under the sponsorship of the NCI's eastern solid tumor group.

Further clinical evidence of the increasingly effective use of drugs has been obtained in the past year. Reports from the various clinical studies indicate that 85 to 100 percent of patients with acute lymphocytic leukemia, given combinations of drugs in intensive, intermittent courses, are achieving complete remissions and that the durations of remissions range from 23 to more than 40 months among the various groups. The latest report from the acute leukemia cooperative group B on survival of patients under 20 years of age with acute lymphocytic leukemia shows that about 60 percent of the children are surviving 24 months from diagnosis of their disease. Currently, nine effective drugs are in use in various combinations: methotrexate, mercaptopurine, prednisone, cyclophosphamide, vincristine, cytosine arabinoside, daunomycin, BCNU, and L-asparaginase.

Children with acute lymphocytic leukemia who have begun treatment in the last few years have an estimated median survival (survival of 50 percent of the group) of about 3 years. With improvements in therapy resulting from introduction of new drugs and better care, it is not too much to hope that a median survival of 5 years can be reached. This is an important milestone, since it has been shown that those who survive 5 years have a 50 percent chance of being alive and well at 10 years.

Successful and safe combination drug treatment of acute lymphocytic leukemia has been possible only in those few centers where there is an experienced group of physicians and nurses trained in chemotherapy, backed by equally well trained pathologists and pharmacologists. They have had available extensive resources in diagnostic facilities in clinical pathology and radiology and the means for protecting patients against the two dangers of hemorrhage and infection. Hopefully, further experience will enable a simplification of therapy, but in the meantime there is a need to make available to all leukemia patients the resources and medical skills assembled at the major research centers.

Acute myelocytic leukemia has not responded to drug therapy in the same manner as the lymphocytic form of the disease. In the last few years drugs active against acute myelocytic leukemia have been developed and the study of effective combinations has begun. The active drugs are: methotrexate, mercaptopurine, methylglyoxal-bis-guanylhydrazone (methyl GAG), cytosine arabinoside, daunomycin, and 6-methylmercaptopurine riboside (MMPR).

Intensive, intermittent combinations of bincristine, nitrogen mustard, ibenzmethyzin, and prednisone have been studied in far advanced stages of hodgkin's disease. Eighty percent of the patients in one study achieved complete remissions and 50 percent remained in remission longer than 2 years. Combination drug therapy then makes available a degree of drug control of advanced hodgkin's disease not previously possible. Another lymphoma, Burkitt's tumor, is being studied with more intensive chemotherapy than previously used. Some patients with early disease have responded well to single doses of drug and others with advanced disease to high dose combinations of agents.

Long term survivals, measured in periods of 3 to 4 years, have been reported in the past year in patients with Ewing's sarcoma, which usually occurs in the long bones and pelvis and spreads rapidly to the lungs and other organs. Treatment of these patients consisted of doses of drug (cyclophosphamide alone or in combination with vincristine) in addition to localized irradiation of the primary tumor.

Studies are underway in the clinic on cancer of the breast, colon, and lung in attempts to match the administration of drugs to the unique biology of these slowly growing tumors. These will include studies of both new drugs and new dose schedules. In the absence of a reliable chemical measure of the size of the total tumor cell population, such as the measurement of the hormone chorionic gonadotropin produced by choriocarcinoma, empirical design of surgical adjuvant studies is planned. Promptly after surgical removal of a tumor, drugs such as 5-florouracil, methotrexate, cyclophosphamide, or cytosine arabinoside will be started and given intermittently for a period of 1 to 2 years. This will show whether there will be an improvement in percent of patients remaining without symptoms of disease and in length of survival. This determination will be slow, but with the slowly growing tumors there is a strong likelihood that recognition of success will take a long time.

THE OUTLOOK FOR PROGRESS

Under the leadership of the chemotherapy program, collaborative efforts among NCI scientists and those of other Institutes of the NIH, other Government agencies, pharmaceutical industry, research institutions, and universities have been expanded. These efforts in basic research and in the clinic continue to be fruitful and to produce new ideas, new test materials, coordinated use of resources, and more rapid answers to questions posed in research.

Only within the last several years have investigators been able to report without reservation that the goal of drug therapy to reach tumor cells wherever they are and selectively destroy them has been reached for a few types of clinical cancer. Generally, these are recognized as rapidly growing tumors; the slowly growing ones are not responsive to drugs. It is believed that growth rate and drug sensitivity are related and that the determining factor in responsiveness to drugs may be the fraction of tumor cells actually dividing.

An understanding of some principles of successful chemotherapy has strengthened the hope of drug cure of the fast growing tumors and provided opportunity to search for clues to the effective drug control of those that grow slowly. Attempts to reach new successes in the clinic will follow the twin approaches of empirical and theoretical research both in the search for new drugs and better ways to use them. Such a drug research and development program in all its complex aspects requires the continued coordination and utilization of the resources of the Federal Government in collaboration with private segments of biomedical research endeavors throughout the country.

REMISSION AND RECURRENCE

Mr. FLOOD. How do you use recurrence and remission?

Dr. ENDICOTT. Let me see if I can explain it. The term "remission" is used to describe a situation where the tumor disappears, the symptoms go away, and to all intents and purposes the patient has recovered.

Mr. FLOOD. What is recurrence?

Dr. ENDICOTT. Recurrence is when you find out it was a remission instead of a cure because the disease comes back.

The doctors like to use the term "remission" in cancer because it takes a long time to be sure whether it is going to come back or not.

Mr. FLOOD. What is longtime?

Dr. ENDICOTT. In the case of acute leukemia longtime for a remission is a year. In the case of a slow-growing tumor like cancer of the breast, they have been known to recur as long as 25 years after the original surgery. So you can see it depends on what kind of cancer you are talking about as to what is a long time.

Mr. SHRIVER. May I ask a question?

Mr. FLOOD. Mr. Shriver.

Mr. SHRIVER. Does that mean the tumor itself is not the disease but it is just a symptom of it.

Dr. ENDICOTT. What it means I think, sir, is that for some reason, at the time let's say of surgery for cancer of the breast, a few cells——

Mr. FLOOD. Removal of the entire breast or just an operation on the breast, which?

Dr. ENDICOTT. Almost always in the case of cancer of the breast, they remove the entire breast and in addition make a radical dissection of the armpit and so on. But either at the time of surgery or before the time of surgery, when cancer cells have gotten into the bloodstream and floated off to somewhere else and lodged and managed to survive but not managed to grow, or at least to grow very rapidly, and then something happens. We are not sure what. But something happens at some interval and the growth rate picks up and enough cells are produced to produce a visible palpable tumor.

Mr. FLOOD. Are these cells what we used to call a sport?

Dr. ENDICOTT. I think that is an apt term perhaps. They are oftentimes anatomically, from the standpoint of their appearance, very much like the tissue from which they originate and yet they do not behave like the normal cells do.

For example, in leukemia the cells that one sees in the blood look very much like the cells in the bone marrow which produced normal leucocytes and red cells. But they are generally incapable of carrying out other functions that blood cells ordinarily would. So they are sports.

Mr. FLOOD. Sports, sure.

HODGKINS DISEASE

Dr. ENDICOTT. Continued improvement has also been made in the treatment of advanced Hodgkins disease with intensive——

Mr. FLOOD. What is Hodgkins disease?

Dr. ENDICOTT. It is a malignant disease which affects the lymph nodes, thymus, and the spleen primarily.

Mr. FLOOD. What is the spleen?

Dr. ENDICOTT. A spleen is a rather vascular organ in the abdomen, the precise function of which is not entirely known. Clearly it is partly involved in cleaning up wornout red blood cells and breaking them down. It also is involved in the production of lymphocytes. It may have something to do with immunity and, to some extent, it is kind of a reservoir in which blood can stagnate or be stored and then pushed rapidly into circulation by contraction.

Mr. FLOOD. It could be diseased in itself?

Dr. ENDICOTT. Yes, sir. There are a number of diseases of the spleen itself and one of them is Hodgkins disease.

It may be primary there. It may begin there. The latest results show that 80 percent of the patients achieved complete remissions and 50 percent remained in remission longer than 2 years.

Mrs. REID. Mr. Chairman?

Mr. FLOOD. Yes.

REMISSION

Mrs. REID. I don't understand your explanation of remission. How do you know that 80 percent achieved complete remission?

Dr. ENDICOTT. All of the signs and symptoms of the disease disappear. One of the signs is an enlargement of the spleen, and in a complete remission in the spleen it returns to its normal size. There are other symptoms that go along with the disease. Dr. Steinfeld, an expert in this area, could elaborate on that. It includes a feeling of weakness, malaise, oftentimes weight loss, fever, and so on. All of these symptoms go away.

Mrs. REID. There could be a recurrence?

Dr. ENDICOTT. Yes. When you use the term "remission" you are not implying cure. All you are saying is that so far as you can tell there is no further sign of the disease.

Mrs. REID. Thank you.

Dr. ENDICOTT. Similarly, high-dose combination drug treatment of other forms of lymphoma produced remissions in 100 percent of patients with lymphosarcoma and 85 percent of those with reticulum cell sarcoma. A drug called BCNU, used in combination treatment of childhood acute leukemia, was found to be temporarily effective in some drug-resistent lymphomas.

LEUKEMIA

Mr. FLOOD. You seem to be obsessed with leukemia. Why leukemia? That is just one of 250.

Dr. ENDICOTT. Right. I think the reason that there is so much attention being given to leukemia at the present time is, first of all, it is a relatively acute form of cancer so that you can get answers in a reasonably short period of time which, hopefully, then you can apply to others.

Mr. FLOOD. There are many kinds of leukemia?

Dr., ENDICOTT. Yes, sir. And some quite different from the acute leukemia of children.

Mr. FLOOD. Why are you so obsessed with it today, March 1969?

Dr. ENDICOTT. I would answer it in this way: I think we are close,

both in prevention and therapy, to controlling acute leukemia which up until now has been a hundred percent fatal disease.

Mr. FLOOD. Progressive and terminal?

Dr. ENDICOTT. Right. It is very likely that this will be one of the first diseases in which we will pin down the virus etiology of cancer.

Mr. FLOOD. What makes you think that?

Dr. ENDICOTT. There are many reasons I think that.

Mr. FLOOD. You better have one good one.

Dr. ENDICOTT. One reason is that we know so much about the cause of leukemia in animals and we have proven it over and over again from species to species to species to species as the etiological factor in animals.

Mr. FLOOD. I see you have a special report on this subject. We will place that in the record.

(The special report follows:)

SPECIAL REPORT—LEUKEMIAS AND LYMPHOMAS—EVIDENCE OF VIRUS CAUSATION

During the last 60 years scientists have proved conclusively that viruses cause cancer in many species of animals. During the past year six new cancer-causing viruses were discovered, bringing the total number of known cancer-causing viruses to more than 60. There is good reason to suspect that viruses also cause some types of human cancer. When such cancer-causing viruses are identified, it should be possible to develop vaccines and/or other preventive measures to protect man against several types of cancer.

Since 1965 the National Cancer Institute, through its special virus-leukemia program and related activities, has developed an effective system for the conduct of major research efforts aimed at elucidating the human situation. During this same period the NCI has developed the means for controlling certain animal cancers induced by viruses. The system effectively combines the skills and efforts of in-house staff and scientists throughout the world. The effort has produced considerable progress, particularly in gaining knowledge of lymphomas and sarcomas.

Mouse and chicken leukemias are known to be caused by viruses called C-type particles. Viruses similar to these in appearance can be found in human leukemia patients, yet, unlike the mouse and chicken type C particles, they have not yet been grown successfully outside the body nor have they yet produced cancer when injected into experimental animals. Another virus—herpes-type virus (similar to but not the same as the fever blister virus)—has been shown to be associated with Burkitt's lymphoma, a common childhood tumor in tropical Africa. This virus apparently also causes infectious mononucleosis, and still another herpes-type virus has recently been shown to be associated with cancer of the uterine cervix in women. Evidence has been developed that some types of virus are unable to produce cancer without the aid of a second "helper" virus. The evidence and the questions accumulate at an exciting rate, and this report will touch on these at some length.

Three groups of staff scientists share the responsibility for planning, implementing, and managing all programed research of the National Cancer Institute on viruses in relation to cancer. The viral biology, viral carcinogenesis, and viral leukemia and lymphoma branches represent the scientific disciplines necessary for the broad operational management and in-depth study essential to the attainment of program objectives.

A special $10 million appropriation by Congress in 1965 launched the intensified special virus-leukemia program. Its main objectives are: (1) to determine whether viruses comparable to those known to cause leukemia or lymphoma in many laboratory and domestic animals are causative agents of human leukemia or lymphoma, and (2) to develop a vaccine or other means of control of human leukemia and lymphoma when such agents are found. The overall program is based on the assumption that at least one virus is an indispensable element for the induction of at least one kind of human leukemia or lymphoma and that the virus, or some derivative of it, persists in the diseased individual.

C-type particles

When the special virus-leukemia program was initiated, highest priority was given the search for viruses in human acute leukemia comparable to the C-type particles associated with chicken and mouse leukemias. Electron microscope studies of blood plasma-pellet fractions from leukemia patients revealed virus-like entities resembling C-type particles. Electron microscopy remains the chief tool in the continued search for these particles. Examination of plasma and tissues of human leukemia and lymphoma patients has shown C-type particles in almost a third of those studied. However, since relatively high concentrations of virus are needed to give a reasonable chance of their detection by electron microscopy, this method is less likely to detect small quantities of mature virus than immunological methods.

Drs. Mary A. Fink and Richard A. Malmgren of NCI improved and developed methods for determining whether human leukemia patients had been exposed to viruses similar to those that cause animal cancers. They found that of 72 leukemia patients, 49 (68 percent) had antibodies to human C-type particles derived from leukemic plasma, suggesting that a virus is concerned with the leukemic process.

Unfortunately, it has not yet been possible, despite extensive efforts, to induce these C-type particles to persist or reproduce in an identifiable form in tissue culture, an essential step for future work. However, with new techniques and approaches in the special virus-leukemia program, several promising new avenues of investigation to bring forth "hidden" viruses have recently been opened. These include:

1. *Enhanced Response to Sarcoma Virus.*—Leukemia viruses can hinder or enhance responses to sarcoma (solid tumor) viruses in both chickens and mice. Recently it was found that co-infections with leukemia viruses, or superinfection following infection with sarcoma viruses, may result in enhancement of response to the sarcoma virus. These are potentially sensitive techniques for the detection of human leukemia-causing viruses, provided the necessary indicator strains of human sarcoma viruses can be found. A search for such agents is now under way.

2. *Defective Viruses and Helper Virus Activity.*—Several years ago some strains of Rous sarcoma virus (RSV—a chicken tumor virus) were found to be "defective"; that is, they were incapable of producing new virus particles to infect other cells without the aid of a second virus, called Rous associated virus (RAV). The "helper" virus apparently supplied the genetic information, lacking in the RSV particles, necessary for production of the outer protein coat of the infectious virus. More recently the Moloney strain of mouse sarcoma virus was found to be "defective" and also dependent upon coinfection with a leukemia virus for its reproduction in infectious forms. As in the chicken system, the defective virus can be used as an indicator agent for the detection of leukemia viruses.

3. *Persistence of Cancer-Inducing Genetic Material in Transformed Cells and Rescue from Noninfective Tumors.*—Two recent fundamental discoveries of far-reaching significance to the search for tumor viruses are: (a) that the viral genetic material, or some noninfective form of the virus, persists in cells that have been transformed by chicken and mouse sarcoma viruses; and (b) that these noninfective forms can pass between cells in close physical contact, both in living animals and in tissue culture, in the absence of an infectious process.

Cells of tumors induced in other species of animals by some chicken and mouse sarcoma viruses usually do not release the virus in infectious or mature form, probably from lack of some enzymatic or other biochemical capability. However, when such cells are transplanted back into natural hosts (or placed in close physical contact with natural host cells in tissue culture), the viral genetic information passes into the natural host cells, which then produce and release infectious virus. If the genetic material is defective, the addition of a helper virus is required. Efforts are now under way to apply these new techniques and purinciples to the search for cancer-inducing viruses in human leukemias and sarcomas.

4. *Studies on Low-Dose Virus-Induced Cancers as an Approach to the Natural Diseases.*—A certain minimum dose of virus is necessary to induce cancer. In some experiments, a clear relationship of mature virus yield to amount of original infecting dose has been observed. Cancers induced by a high dose of virus produce large quantities of mature virus. But mature virus cannot be recovered from many of the cancers induced by the lowest effective doses of laboratory strains of leukemia and sarcoma viruses. Such low doses present in

man may account for the lack of success in detecting and growing in quantity the virus seen as C-type particles in electron microscopy. Such laboratory cancers are considered as possible models for the development of methods applicable to naturally occurring cancers from which virus likewise cannot be recovered. Program activities are now under way for producing such noninfective cancers in germfree animal hosts, to develop techniques for recovering "hidden" virus from low-dose interactions. It appears likely that some human cancers are induced by such low-dose infections of virus, and techniques developed will be vigorously applied in the human situation.

Herpes-types viruses

A type of virus associated with some forms of chronic leukemia and lymphoma is the herpes-type virus (HTV), similar in size and shape but not identical to those herpes viruses known to cause fever sores or shingles. HTV has been seen in at least 80 of the cultures of tumor cells that have been established from 180 leukemia and lymphoma patients. Unlike C-type particles, HTV grows well in tissue cultures. It is now possible to grow the cells in large quantities and recover large quantities of purified and concentrated HTV. Currently, the most active and apparently most productive area of viral oncology is that concerned with definitive characterization of the HTV.

A certain type of HTV, Epstein-Barr (EB) virus, has been recovered from cultured lymphocytes (white blood cells) derived from patients with Burkitt's lymphoma.

Until fairly recently, infectivity or other kinds of biologic activity had not been shown with the EB virus. Recent developments, however, have shown that cells growing in tissue culture infected with EB virus will grow much more rapidly than their uninfected counterparts. Also studies by Dr. Victor Zeve, NCI, have shown that cells could be infected in tissue culture by the virus passing through a membrance with appropriate pore size. This year, Drs. Gertrude and Werner Henle and a colleague at the University of Pennsylvania presented convincing evidence that the EB virus is causally related to infectious mononucleosis. Also, Dr. James T. Grace, Jr., and associates at Roswell Park Memorial Institute, also obtained clinical evidence that EB virus is capable of inducing infectious mononucleosis. These important findings show that a virus repeatedly isolated from human cancer patients is capable of inducing rapid and, for a time, uncontrolled growth of the same kind of human cells that are involved with leukemia. It should be noted, however, that infectious mononucleosis is a self-limited, nonmalignant disease.

Antibodies to EB virus are found in 100 percent of individuals who have had infectious mononucleosis. In an attempt to discover whether the antibodies give protection against leukemia, the Epidemiology Branch of the National Cancer Institute is conducting a 3-year study with the National Academy of Sciences-National Research Council of 2,600 of the 30,000 American soldiers who had infectious mononucleosis during World War II. Followup data on them have been collected and are now undergoing analysis.

Of high interest is a corollary report during 1968 by Drs. Henle and an associate that 100 percent of African children with Burkitt's lymphoma have high levels of antibody to this virus, whereas less than 50 percent of control children, living in the region where Burkitt's lymphoma is common, show these antibodies and at lower levels. Similar tests of the blood serums of large numbers of leukemia and lymphoma patients in the United States are being conducted to determine whether HTV antigen or antibody is found with high frequency.

In another study of Drs. Henle and associates, chromosomal abnormalities characteristic of Burkitt cells were found in normal human leukocytes (white blood cells) that were stimulated to grow in mixed culture with the Burkitt cells. They also demonstrated the transmission of the HTV from the Burkitt cells to normal cells, a significant step in establishing capability of transmission and replication in the human species. In these studies, EB virus stimulated the long-term growth of normal human white blood cells, a phenomenon which mimics the growth of tumor cells in cancer patients.

During 1968 Dr. Sarah E. Stewart, NCI, presented further evidence of biologic activity for the EB virus. In earlier studies, she had established that when cells known to contain large quantities of EB virus were inoculated into the brains of newborn hamsters, the animals later developed a progressive form of encephalitis. To prove that this was caused by a human EB virus and not a latent hamster virus, she inoculated a human white blood cell culture with the virus.

now in its 60th passage in hamster brains. Electron microscopy and immunofluorescence tests of the inoculated culture confirmed than the virus from infected hamster brains was indeed EB virus, and thus proves its biological activity in this animal system.

Herpes-type virus is also found in subhuman primates. Scientists at the NCI contract-supported Bionetics Research Laboratories, Kensington, Md., recently established blood cell lines from three uninoculated chimpanzees, all of which were found to contain a herpes-type virus. This virus is similar to EB virus derived from human Burkitt lymphoma cells. Other investigators have reported high levels of antibodies to EB virus in four species of primates. Subhuman primates thus may constitute a reservoir of virus from which transmission to the human by mosquitoes or other bloodsucking insects may be possible. Studies by Dr. Grace and colleagues at Roswell Park Memorial Institute indicate that only a certain type of human and monkey white blood cells have the ability to absorb EB virus, or that the virus has an affinity for these particular cells.

The data being accumulated on C-type and herpes-type viruses bring scientists closer each day to the potential of developing vaccines against certain human leukemias and lymphomas. The research is time consuming, and several more years' work may be needed before the outcome is certain. Comparisons with the timetables of the development of certain other virus vaccines may provide perspective.

TARGET DATE

Mr. FLOOD. Any target date on cancer? What year?

Dr. ENDICOTT. I wish it were 1946.

Mr. FLOOD. So do I, but what do you think?

Dr. ENDICOTT. I would probably lose my scientific reputation if I gave you a date.

Mr. FLOOD. Would you mind giving us a time range, and losing only part of it.

Dr. ENDICOTT. I am very hopeful that we will have pinned down a viral etiology of cancer in at least one form of human disease within the next 5 years.

Mr. FLOOD. I realize this is not really a fair question to ask you. Please proceed with your statement.

DRUG THERAPY

Dr. ENDICOTT. One of the most promising new anticancer drugs is L-asparaginase, an enzyme that cuts off the supply of an essential amino acid, asparagine, to cancer cells that cannot manufacture it.

L-asparaginase has been effective in treating some children with acute leukema. The possibility that its anticancer effect can be enhanced in combination with other drugs is being studied by several centers cooperating in the National Cancer Institute's chemotherapy program. It is encouraging to note that the end results of cancer management are improving. A National Cancer Institute study of nearly 400,000 patients in more than 100 scattered hospitals reveals an upward trend in survival of patients with a cancer of some 50 different body sites, including the colon, rectum, breast, uterine cervix, and prostate gland. The outlook for the lung cancer patient, however, remains very grim.

GEOGRAPHIC DIFFERENCES IN INCIDENCE OF CANCER

Information is needed on the impact of cancer not only in this country but throughout the world, particularly in unique populations in different countries. For example, we need to know more about Bur-

kitt lymphoma and why it selected its victims from a relatively restricted area of Africa. We need data on the unusual prevalence of cancer of the nasopharynx in Hong Hong and Singapore. In Japan, breast cancer has a lower incidence and stomach cancer a higher incidence than in the United States, and we should know why. We have been carrying out studies of Japanese in Japan, in the Hawaiian Islands, and on the west coast. The incidence of cancer of the stomach is progressively lower as you go from the home islands to the Hawaiian Islands to California. These are among Japanese who have not married outside the Japanese race. Clearly this is not a genetic thing. This is something in the environment. The changes in breast cancer are much less impressive. This would lead one to guess that it same some strong heredity overtones. We can guess, and I think we are in the process of pinning this sort of thing down.

Mr. FLOOD. Did you ever hear the theory about the Chinese woman as opposed to the men with cancer of the stomach because the men eat the hot food first and the women get the second round; do you know that one?

Dr. ENDICOTT. Yes, I have heard that.

Mr. FLOOD. What about it?

Dr. ENDICOTT. I think probably, sir, that the difference we are talking about here has to do with food.

Mr. FLOOD. Sure it does.

Dr. ENDICOTT. Over the years that has been one of the explanations. Another one is because stomach cancer tends to be quite high among the races that consume a great deal of smoked food, especially smoked fish.

Mr. FLOOD. Especially the males.

Dr. ENDICOTT. There has always been a preponderance of gastric cancer amongst males whether they ate with the women or before the women.

Mr. FLOOD. They always eat before.

Dr. ENDICOTT. This has always been true. Men are apparently more susceptible to cancer of the stomach than are women. The same thing appears to be true in the cancer of the lung.

Mr. FLOOD. Because of sex hormones?

Dr. ENDICOTT. I dare say the effect of the sex hormones is indeed important in this area.

Mr. CASEY. Mr. Chairman.

Mr. FLOOD. Yes.

Mr. CASEY. I heard someone say that eating charcoal-broiled steaks was bad for you and might create cancer. Is there any foundation to that?

Mr. FLOOD. He is from Texas. Be careful.

Dr. ENDICOTT. I am from Colorado and I feel the same way about steaks that you do. Cattle, too.

There were some studies completed several years ago in which they compared steaks cooked over a charcoal fire to those cooked underneath an electric oven. What they found out was that the amount of chemicals that known to cause cancer in animals is greater in the charcoal-broiled steak than it is in the one that is cooked underneath an electric broiler. The significance of this for man is unknown. There is no statistical evidence to suggest that you and I who eat charcoal-

broiled steaks are in any greater danger than the ones who cook them in the house in the electric range.

Mr. CASEY. I feel better, thank you.

Mrs. REID. Mr. Chairman.

Speaking of hot foods, do you mean highly seasoned foods?

Mr. FLOOD. No, temperature. I was speaking of temperature only.

Mrs. REID. Not the seasoning?

Mr. FLOOD. The seasoning is the same. It is said the temperature, with the men eating the hot food first.

Dr. ENDICOTT. There should be some explanation for the relatively high incidence of cancer of the uterine cervix in Puerto Rico compared with other areas.

Even the information available on cancer in the United States is hardly adequate for good biostatistical studies and much of it is out of date. This will be largely corrected by the Third National Cancer Survey to be inaugurated in 1969 by the National Cancer Institute with the cooperation of health authorities in 10 large cities and two States. Complete coverage of the population groups in this new 3-year study will provide physicians and public health officials reliable information on variations in the incidence and prevalence of specific forms of cancer and the economic cost to a community.

The activities and plans of the National Cancer Institute are largely in the areas of etiology and chemotherapy because progress in these areas has been relatively rapid and the opportunities are compelling. Prevention of cancers caused by viruses or other presently unaccounted but suspected organisms and chemical agents is a likely possibility in the 1970's. Among these agents are the substances that make cigarette smoking a major factor in lung cancer, which will take nearly 60,000 lives this year. The Tobacco Working Group, formed as an offshoot of the lung cancer task force, is now drawing up a program of research and development out of which it is hoped that a less hazardous cigarette can be produced.

Progress against cancer is being made through research and training; yet, progress will have little meaning unless the benefits of improved diagnosis and treatment can be made available to people everywhere. The successes achieved in treating childhood leukemia, thereby increasing remissions and life expectancy for these patients, are impressive. But it should be realized that these results have been achieved only in a few specialized centers where patients are in the hands of teams of highly trained specialists in cancer chemotherapy.

Only a few institutions situated mainly in the northeastern part of the country, now approach the cancer center ideal to one degree or another. Superior management of cancer—not only leukemia, but other forms as well—can be constantly improved and more widely applied by developing, throughout the country, centers where research, treatment, and training can be combined for the advancement of knowledge and the improvement of therapeutic proceduers and techniques. This is unquestionably the direction in which we must go to increase patient care capability.

Scientific research is a cumulative process in which knowledge begets knowledge. The process can go on so long as scientists are provided the necessary resources with which to work. This has been borne out no less in the cancer field than in others.

Mr. FLOOD. Just dollars? Mere money?

Dr. ENDICOTT. Money, bricks, and mortar, equipment, some feeling of security as discussed this morning, and I think in the cancer field especially it takes a peculiar type of personality who can stay with a problem for a long time without achieving spectacular success. This is a difficult field, especially for the young man.

Mr. FLOOD. It is an exciting and dramatic field?

Dr. ENDICOTT. It is becoming that way. It has not been in years gone by. It has not been an attractive field to the young investigator but it is beginning to be. It is beginning to be exciting. We are really making progress and many, many young people have become interested in it. I think it is significant that 20 years ago a very much higher proportion of the NIH research funds were available for cancer research than there is now proportionately. This created some pressure on the young man to go into the cancer field. Now that funds are available for a much wider variety of research, in order to get the man into the cancer field now he has to feel that he is going to be able to get something important accomplished in his lifetime, or hopefully next week. It was very encouraging to see a steady increase in the number of young physicians and young scientists who are seeking careers not only at the National Cancer Institute but in a number of other organizations around the country.

Looking back over the decade of the sixties, we see that more than three-fourths of the funds provided to the National Cancer Institute since its establishment in 1937 have been appropriated in that period. Looking ahead to the seventies, it can only be assumed that the accelerated rate of progress in cancer research will continue to require a doubling and redoubling of effort if the return from past endeavors are to be wisely and profitably invested in the future.

Mr. Chairman, the request of the National Cancer Institute for 1970 is $184,402,000, compared with the 1969 operating level of $181,418,500. The 1970 budget contains a net increase of $2,983,500. The increases are as follows: $436,000 for research grants and $3,175,500 for direct operations. These increases are offset by decreases of $173,000 for fellowship grants and $455,000 for training grants.

LUNG CANCER TASK FORCE

Mr. FLOOD. Last year you recall you and I talked about this at some length. I made a point to have the report show it. The committee expressed its strong interest in the lung cancer task force. What happened since you sat in that chair a year ago? We made quite a thing out of that.

Dr. ENDICOTT. Yes, sir. We are trying to do the same thing. We have initiated projects in three areas: One is an attempt to diagnose the disease earlier when it is operable. If you can detect a disease when the lesion is small and before it has spread——

Mr. FLOOD. As distinct from a tumor?

Dr. ENDICOTT. Yes, sir. Usually you detect it with an X-ray picture.

Mr. FLOOD. You can do that?

Dr. ENDICOTT. Yes, sir.

Mr. FLOOD. You are sure of that?

Dr. ENDICOTT. Only after it reaches a certain size. It can also some-

times, depending on its location, be actually directly visualized by passing a tube down through the windpipe and actually seeing the tumor. If it can be identified at an early stage, then surgical treatment may result in cures of perhaps as many as 25 percent of the patients.

Mr. FLOOD. What progress have you made since last year? What happened in the last year on this Lung Cancer Task Force?

Dr. ENDICOTT. As I say, we have gotten the program planned for a combined assault using a variety of techniques to improve early diagnosis. One approach is——

Mr. FLOOD. Is that the first important thing in lung cancer especially? Any cancer, but especially lung?

Dr. ENDICOTT. In terms of cure, it is certainly the most important. Early diagnosis, because the cure rate can be as high as 20 percent.

Mr. FLOOD. No more than that?

Dr. ENDICOTT. In early detection.

Mr. FLOOD. Twenty percent?

Dr. ENDICOTT. The average for all cases is 5 percent.

Mr. FLOOD. Only 20 percent when it is diagnosed early?

Dr. ENDICOTT. Yes, sir. The highest figures on cases diagnosed early I have seen are 25, 26 percent.

Mr. FLOOD. I thought it would be at least twice that.

Dr. ENDICOTT. This disease tends because of the very vascular nature of the lung, tends to get into the blood vessels, single cells, and be swept away and carried off to another part of the body when the tumor is still so small that you can not see it. Therefore, even with——

Mr. FLOOD. There is no such thing as a localized tumor, it could appear anyplace?

Dr. ENDICOTT. As I say, in the best series of early diagnosed cases, as many as 25 percent are still living without any evidence of reappearance of the disease in the period of 5 years. If you lump them all together, though, all lung cancers, early and late, the overall survival rate is only 5 percent. That is, five out of 100 that live for 5 years.

Mr. FLOOD. What is magical about 5 years? Why five? Why not 10 or three?

Dr. ENDICOTT. I wish I had some of my surgical colleagues here to take the rap for this because this is a term which I think the surgeons generated some years ago because they had to have a cutoff point somewhere. They talk about 5-year cures.

Mr. FLOOD. I am a statistic. Mine was 7 years ago. What about five?

Dr. ENDICOTT. Seven is better than five.

VIRUSES AND CANCER

Mr. FLOOD. The report last year also showed our interest in the virus research, with the long-term prospects of a vaccine or vaccines.

If they proved to be caused by viruses, and apparently many scientists now think they are, what about that? What progress have we made in that field? Ten years ago they would have thought you had been drinking if you talked about viruses like you do today.

Dr. ENDICOTT. This is one of the curious things about cancer research. Every two or three generations they rediscover something that

had already been discovered. I think that it is worthy to note that last year, or the year before last, a Nobel Prize was awarded for the demonstration that virus was capable of causing cancer. That research, sir, was done in 1911. It happened to apply to chickens, and scientists at large said, "Well, it may be true about chickens but it does not apply anywhere else." There was only scattered work in this field by a few hardy souls until the fifties, when Dr. Ludwig Gross, a research investigator in the Veterans' Administration, demonstrated that he could pass cancer with cell-free filtrates, a criteria for viruses, by inoculating material from one mouse into a newborn mouse of the same strain. For several years after that, people were unable to repeat his work because they didn't do it exactly the same way. They still pooh-pooh'd the virus theory. Then several individuals, including investigators at the National Cancer Institute, also succeeded in transmitting cancer by using this new technique of the newborn mouse and the field came awake again. That is a long time.

I would have to agree with you that from the initial observation to an intensive attack, 50 years is a long, long time.

Mr. FLOOD. You have finally been sold on it as of this afternoon?

Dr. ENDICOTT. Yes, sir; I certainly have. I am a convert.

DRUG THERAPY

Mr. FLOOD. What about the treatment of cancer with drugs; what do you think about that?

Dr. ENDICOTT. There has been only one disease in which surgical or radiation therapy was a reasonable alternative in which treatment by drugs has become the treatment of choice. This is chorio-carcinoma in women. This disease occurs in connection with childbearing and it occurs, therefore, mostly in young women, many of whom would like to have more children. Until a few years ago the treatment was to remove the uterus and if the tumor has not spread beyond the uterus, then you could achieve a cure. Now the treatment of choice is no longer surgery. The treatment of choice is drugs. Most of the women are cured with drugs and now a number of them have had one or two children since treatment.

RESULTS FROM INVESTMENT IN RESEARCH

Mr. FLOOD. Suppose somebody said to Mr. Natcher when he is on the floor making a speech in a couple of months, "We are spending almost $200 million a year on cancer research. What do we get for the $200 million?" What is Mr. Natcher going to say, $200 million on cancer research; what did you buy for it?

Dr. ENDICOTT. I hope he would say that we are getting a massive effort to solve one of mankind's most serious problems where progress is slow. The death rate is going up, the incidence is going up, but the cure rate is going up, too. It has gone up from one in four when the Cancer Institute was created, to one in three. If through effective application of what we know now, if what we know could be actually applied at every crossroad in the United States, there have been various estimates, but one of the most commonly used is that even right now one in two could be cured. This implies——

Mr. FLOOD. That is a long way from one in 10, is it not?

Dr. ENDICOTT. Yes, sir. If you want us to go from one in three to 10 in 10, it is going to take a lot of money and it is going to take quite a lot of time. I am acutely aware, sir, of the fact that since I took this post the Congress has appropriated over $1 billion and I have been responsible for its expenditure. What this means since the research is so slow is that an experiment may take 5 or 10 years so that what you appropriated last year we won't really know what that means for quite a while. The payoffs we are getting now represent investments that were made perhaps 6, 8, 10, or more years ago. We are really making progress. This field is getting hot. We may have invested right now what you might call a critical mass necessary to solve this problem. I think it is capable of being speeded up or slowed down but, in my opinion, we have now in operation a program capable of solving the cancer problem. I don't know how to put a value on that.

Mr. NATCHER. Mr. Chairman, would you yield at that point?

ABILITY TO USE $1 BILLION IN 1970

Dr. Endicott, in order for me to answer the question that the chairman just talked about a little better on the floor, just assuming now that we have the money to appropriate and in this bill we approved a billion dollars for the National Cancer Institute, what changes would you make not only in the number of grants but what changes would you make and how would you speed this up as far as time is concerned? What would you do with it?

Dr. ENDICOTT. Well, sir, first of all, one of our most serious limiting factors at the present time is the ability to construct facilities. The cancer research facilities around the country are pretty well filled. There is not very much room to crowd in more people and we don't have construction authority any more in the Cancer Institute. This is one of our serious limiting factors.

A second one is availability of a number of people. If you were to appropriate $1 billion of 1-year money in the existing circumstances, I would probably have to lapse about something on the order of $800 million of it.

Mr. NATCHER. In other words, you could not use any more than you are requesting now?

Dr. ENDICOTT. I could use more than I am requesting now, sir, because it is not $200 million, it is $184 million.

Mr. NATCHER. Approximately?

Dr. ENDICOTT. I couldn't in the existing circumstances. To appropriate $1 billion on a 1-year basis would simply result in a lapsing of, I would say, perhaps $800 million of it. I don't know exactly the amount.

Mr. NATCHER. Are we down to bricks and mortar? Is it a matter of structures? Hasn't this been one of the objections that we hear in the medical profession down through the years in regard to the amounts that we have expended in cancer research—too much duplication, too much in buildings, too much in structures? Why not select outstanding people in existing facilities? Isn't that possible? I don't know, I am just asking this question. You know.

Dr. ENDICOTT. I would like to answer that by saying that I believe

we have identified outstanding people in outstanding institutions and are supporting them, perhaps not supporting them as much as we should, but there are very few outstanding investigators interested in the cancer field, really outstanding ones not getting some support. There are other reasons why I said we would probably lapse that kind of money; that is, with attrition that is built into the Revenue Act, I have fewer and fewer people with which to mount new programs.

Mr. NATCHER. With $1 billion——

Dr. ENDICOTT. You can only do so much with so many people.

Mr. NATCHER. With $1 billion, instead of lapsing it couldn't you get people?

Dr. ENDICOTT. No.

Mr. NATCHER. Couldn't get them?

Dr. ENDICOTT. The attrition which is imposed by the Revenue and Expenditure Control Act——

Mr. NATCHER. We are going to forget that. Forget the Revenue and Expenditure Control Act. We don't have any hindrances of that type at all. You have $1 billion.

Dr. ENDICOTT. I am impatient about the speed with which we are moving forward with the Lung Cancer Task Force. I have a group of experts and they have worked hard and met frequently to try to lay out a battery of biological and chemical tests. You appropriated funds for this effective July 1st. The committee has only just now come forward with enough specifications that we could invite contract proposals so that I will be lucky if I get the contracts let and the actual work started by the end of this year.

Cancer is a slow business. If one had $1 billion without the 1-year part on it, then I could move up quite rapidly. The sudden injection of $1 billion into the system under the present circumstances of 1-year money would, as I say, result in a lapsing of a substantial part of it.

Mr. NATCHER. If it were not 1-year money, Doctor, assuming it is not 1-year money and you had an additional $1 billion, what would you do with it? "Here it is, Doctor. What are you going to do with it?"

The war in Vietnam will be over one of these days and our people will demand more in the field of cancer research and achievement.

Dr. ENDICOTT. There would be the following areas that I would concentrate on from the scientific standpoint. One, clearly would be virus. I would give this quite heavy emphasis. I would undertake a major expansion of the efforts in the field of chemical carcinogenesis. I would supplement the chemotherapy efforts but this would not require additions in terms of money that the other two do.

I would create a number of new cancer centers, especially in the South, the Middle West, and the Far West, and I would launch an intensive training program. These are the five main areas in which I would really push hard and then try to keep good basic research supported as it comes along. More specific data on use of an additional $1 billion for the National Cancer Institute will be supplied for the record if you would like.

Mr. NATCHER. Whatever you would like to do.

(The additional information follows:)

USE OF ADDITIONAL $1 BILLION FOR NATIONAL CANCER INSTITUTE

Assuming that the National Cancer Institute was given an additional $1 billion over normal appropriation levels to be available until expended and with restraints on employing personnel and in construction removed, the general plan for use of these funds is as follows in order for NCI to speed the day when cancer will be prevented or cured:

(1) Invest $80 million over a 5-year period in basic research carried on in universities and medical schools much of it under a modified project system that would provide funds in large blocks to these institutions whose top staff and advisers would determine how these funds would be utilized for cancer research. Construction funds to facilitate this research are estimated at $50 million.

(2) Invest an additional $15 million a year for 5 years in virus research with the expectation of eventually producing an anticancer vaccine. Includes field trials at the end of 5 years.

(3) Gradually increase funds for research in chemotherapy, particularly in the clinical area, and with increasing emphasis being placed on the chemotherapy in solid tumors. We would start with an increase of $3 million a year and reach an increase of $15 million a year by the end of 5 years. In addition, we would expand the network for clinical trials of cancer drugs carried on in medical schools and hospitals to reach a level of $15 million annually.

(4) Greatly increase targeted research designed to identify and eliminate cancer causing chemicals from our environment. This would involve establishing bioassay systems and a screening network capable of assaying thousands of chemicals a year. A part of this effort would be to produce a less hazardous cigarette. This effort would start at $10 million a year to reach a total of $50 million a year within 5 years for a total cost of $150 million.

(5) Start a target effort in cancer immunology at $1 million annually gradually increasing to a level of $10 million within 5 years for a total cost of $25 million.

(6) Establish 10 new cancer institutes or expand existing small ones in the South, West, and Midwest. The goal would be to reach a level of Federal investment in operating budgets which would permit each center to operate at an $8 million annual budget. Each of the new ones would require construction funds of $10 million and the established ones substantial funds for improvements and extensions of existing facilities. Also involved would be expansion of existing clinical centers for related clinical and laboratory research. Construction—$150 million. Operating cost—$310 million.

(7) Support training for these new ventures over that included above as a part of the research effort—total $30 million over 5 years.

(8) Construct and equip a Government-owned facility to be operated under contract funds already provided above—$15 million.

(9) Provide special-purpose facilities for new ventures and special instrument development at an average cost of $2 million a year—total $10 million over 5 years.

POSSIBLE CHANGES IN METHODS OF RESEARCH SUPPORT

Mr. NATCHER. Would you change your system at all that you are now using in regard to selecting the people who would use this money, the research people? Would you change your system at all there?

Dr. ENDICOTT. Yes, sir, I would.

Mr. NATCHER. To what extent?

Dr. ENDICOTT. In terms of self-sponsored research carried out in an academic-type institution, I would try to move away from the small project system into either departmental support or institutional support, so that the decisions on small projects could be made at the local level. I would watch this to be sure it was being done carefully, but I would try to get the detailed decisionmaking on self-sponsored research out of Washington and back into the institutions. That is, in fact, what we are doing with the single instrument of support at the Sloan-Kettering Institute.

In the areas of target research, which require a strong central staff

not only to plan but also to monitor and to interpret, I would try to put this in bigger and bigger packages; in other words, to farm out bigger and bigger pieces of the problem.

Mr. FLOOD. You are talking about the Sloan-Kettering——

Dr. ENDICOTT. No.

Mr. FLOOD. Single-instrument plan?

Dr. ENDICOTT. No. Here I am talking more in terms of——

Mr. FLOOD. This sounds like the Sloan-Kettering single-grant system?

Dr. ENDICOTT. Yes, sir, but that is a cancer institute which has a primary orientation toward fundamental research. They have clinical research there. They have a little bit of everything. I am talking about the kind of an approach in which—this is more familiar in the defense area—in which you take something like a supersonic transport or some kind of a missile and you farm out the problem to a prime contractor with specifications as to what you want the performance to be and then it is his problem to lay out the plans, to subcontract, to carry the thing through to completion. A big problem, in other words, instead of acting as the prime contractor ourself on all of these areas; for instance, the whole chemotherapy program conceivably could become——

Mr. FLOOD. Isn't the single instrument grant like the one to Sloan-Kettering?

Dr. ENDICOTT. No; I disagree.

Mr. FLOOD. You do?

Dr. ENDICOTT. Yes, sir. I disagree, Mr. Chairman. Sloan-Kettering has a little effort, it is more than that, but a substantial effort in chemotherapy. Their concern is only with the management of what goes on at the Sloan-Kettering Institute. The thing I am talking about is literally farming out the management responsibilities of good-sized segments of problems to reliable prime contractors. If you are worried about their reliability you can contract with somebody else to watch them. You know more about this than I do.

Mr. FLOOD. Like a missile system.

Mr. NATCHER. Mr. Chairman, thank you very much.

Mrs. REID. In your discussion of this plan, it seemed to me that you indicated the time element really is a greater factor than the money element. In the plan you described, if you were to follow this plan, would we come to a cure more quickly?

Dr. ENDICOTT. Well, I would say time is certainly a factor, Mrs. Reid. One of the inescapable things is that—well suppose that we take childhood leukemia as an example? We have talked about it a lot today. This has its peak incidence at age 7. If you treat the child and apparently the disease goes away, and it goes away for 5 years, you speak of a 5-year cure. The 5-year cure does not really mean a cure. In order to achieve a cure, that child must have the same life expectancy as if he never had had leukemia. So you are really talking about a 70-year experiment. I don't know any way to escape this. You are confronted with a situation in which even after you have come up with a way to prevent a form of cancer, it is going to take perhaps two generations before you can be actually sure that you have done that. When I am talking in terms of rapid progress in the next decade, we are going to make rapid progress in the next decade but

probably it will be our grandchildren, our great-grandchildren who will really know for sure that we did it.

When you mentioned $1 billion, I have already spent $1 billion in this job, more than $1 billion in this job in 9 years, so I think that I could probably figure out how to spend more than $1 billion if you take the 1-year limitation off. This is expensive research. We know it.

Mrs. REID. Thank you, Mr. Chairman.

NATIONAL CANCER SURVEY

Mr. FLOOD. We talk about this national cancer survey. That is the third national cancer survey. How much is that going to cost? I got the impression it is $185,000 from page 24. On page 46 it looks like it is $1,040,000.

Dr. ENDICOTT. On the contract portion that is $1,040,000. In addition to the cost of the contracts, there is the cost staffwise and travelwise. That is the in-house costs.

Mr. Learmouth?

Mr. LEARMOUTH. The $185,000 on page 24 refers to in-house staff. The reference on page 46 is to contracts needed to carry out the program.

Mr. FLOOD. In metropolitan areas? Ten or a dozen or so?

Dr. ENDICOTT. Yes, sir. It is 10 cities and two States.

Is that responsive to your question?

Mr. FLOOD. I think so. Yes.

What will this survey be? Is it worth that much money? That is a lot of money even for you.

Dr. ENDICOTT. This is in lieu of something that would cost a lot more. It surely would not be in here if I did not think it was worth it.

Mr. FLOOD. I believe that. What about it?

Dr. ENDICOTT. Cancer is not a reportable disease. Therefore, the only statistics that are available, vital statistics with regard to cancer, are the statistics that are collected from death certificates. We need to know more than how many people are dying of it. We need to know how many are getting it, how many are getting cured and what the changes in the incidence are.

Mr. FLOOD. A death certificate is a very impressive certificate, is it not?

Dr. ENDICOTT. Yes, sir; but it is a little late. We can go about this by making cancer a reportable disease.

Mr. FLOOD. We tried that, it would not work.

Dr. ENDICOTT. This is expensive and in most States it has not worked where they have tried it. We missed one census, the 1960 census. I hope we will never get this far behind again. We have not done this for 20 years so we are trying to interpolate and extrapolate from the death certificates.

Mr. FLOOD. Extrapolate. I love that word.

Dr. ENDICOTT. They were collected 20 years ago and they are outdated and we need to do it again. This involves a lot of visits to doctors' offices, hospitals, patients, patients' families.

Mr. FLOOD. Is this a 1 year job?

Dr. ENDICOTT. Most of the actual work, survey work will be done at the same time as the 1970 census or immediately after the census,

so that we can tie our data into the data that is collected for the census tract. But the last one, which was done 20 years ago before all of the analyses had been completed, I think some 6 years went by from the beginning to the end.

The big cost of this of course comes at the time you are doing the house-to-house survey. This is not unlike the problem of the Bureau of the Census.

SLOAN-KETTERING SINGLE INSTRUMENT GRANT

Mr. FLOOD. Suppose for the record you tell us about the Sloan-Kettering system.

(The information follows:)

SLOAN-KETTERING SYSTEM

The Sloan-Kettering Institute in New York City was organized for, and is engaged solely in cancer research. Because of this and the high quality of its scientists, it has since its creation in 1945 been one of the largest recipients of National Cancer Institute (NCI) grants approved by study sections and the National Advisory Cancer Council. In addition it has a large endowment and devotes its income from this and funds from other granting organizations to cancer research. This research is all interrelated.

Over the years many attempts were tried to consolidate support for large cancer institutes including the Sloan-Kettering Institute (SKI), so that one could better appraise the research endeavor being supported. Immediately prior to the adoption of the single instrument in 1966, the SKI was principally supported through a system of divisional grants.

At the time this plan was adopted the SKI's total budget was $9,160,306 and the NCI share was set at 47.1 percent of the total budget, and amount somewhat less than the amount which NCI had been granting to the SKI.

The SKI has an excellent system for management and its groups of external advisers on research projects to be carried on within the Institute are of the stature of NIH's own advisers on grants to be approved. The plan was entered into as an experiment and the Director of NCI outlined in a memorandum to the Director, NIH, some of the expected advantages of this system of support as follows:

"Supporting SKI by a single cost-sharing instrument would strengthen its excellent management, enabling it to plan and conduct its research as an integrated program, rather than as a group of separately presented, variously supported individual projects; and to deploy its total resources for this purpose according to its own judgment of program needs, free from the inflexibilities of individually funded projects.

"As for the NIH, we would be reviewing the SKI program at one time, as a totality, thereby obtaining a more comprehensive understanding of its scope and direction than is possible under the present system of review of isolated segments, by each of five Institutes, five councils and many study sections, at long time intervals. We recognize that the change involves problems (for instance, the need for great care in the definition of a research "project"), but we believe that they are solvable and, in fact, offer challenges to develop and enlarge our own capacities. For example, the reviewers of research programs will have to devise criteria for evaluation of the overall performance of an institution, in place of the traditional review of experimental design and estimates of individuals' scientific potential or achievement.

"Thus, we count it an advantage of the single instrument of support, that it would foster the integration of research planning by SKI and of its review by NIH. Moreover, there would also be certain administrative advantages. The reduction of numerous applications for support to a single document, (however complex) would relieve the paper-preparation load of the SKI and, in turn, the paper-processing of the NIH. Other advantages, such as greater flexibility in handling of funds and utilization of staff by SKI, are discussed in the attachments."

The NCI designated a group of outside advisers to monitor this grant. These advisers report to the National Advisory Cancer Council frequently. At the last

meeting of the Council they gave enthusiastic approval to the concept and recommended that the 5-year grant be renewed for an additional 2 years so that 5 years of operations could be observed and still leave 2 years of the 7-year grant period in which to modify the method of support if the SKI or the NCI should wish to do so.

The current level of support is 42.8 percent of SKI's total budget or somewhat less percentagewise than under the original plan. The dollar level for 1969 is $4,377,448 out of a total SKI budget of $10,209,329.

REPORTING OF CANCER

Mrs. REID. Will the gentleman yield?

Mr. FLOOD. Yes.

Mrs. REID. You mentioned a few moments ago about having tried something twice and it did not work. I did not understand. You mean being reportable?

Dr. ENDICOTT. Yes. This has been tried in several States.

Mrs. REID. What do you mean?

Dr. ENDICOTT. For some reason the doctors do not report it.

Mrs. REID. The doctors do not?

Dr. ENDICOTT. The doctors. There has been very poor response in general.

Mr. FLOOD. It is like venereal disease. If you have a regular patient who has a venereal disease, they usually will not report it.

It is a very, very difficult problem.

Mrs. REID. But with cancer, is not the attitude changing?

For instance, we discuss the disease now and I can remember, a few years ago, no one even wanted to talk about it. It seems to me it is discussed more freely. I cannot understand doctors not reporting it.

Dr. ENDICOTT. I think, Mrs. Reid, this is changing, and——

Mr. FLOOD. What she means, it is no longer a bad word.

Dr. ENDICOTT. Yes. The attitudes of the physicians are changing, but to some extent it has depended on the diligence with which the central office really tried and worked at it. It has been a reportable disease in Denmark, for example, for a long while and they have some of the world's best figures in this area. It is reported on a nationwide basis in Denmark. That is a small country.

Connecticut has done a remarkably good job over a 30-year period. Puerto Rico started at least 10 years ago and they are doing a good job. I think one of the impacts is the regional medical program——

Mr. FLOOD. I know exactly what you mean. I had cancer 7 years ago. Now, Senator Russell told a press conference the other day that he likely has lung cancer. I think that is being done more every day. It is not a bad word any more.

Dr. ENDICOTT. I agree.

Mrs. REID. You see it on TV.

Dr. ENDICOTT. I agree attitudes are changing.

Mr. FLOOD. You ought to know, it is your business.

Dr. ENDICOTT. From our standpoint it is less expensive to do it on the basis of a sample every 10 years than to set up a nationwide system for reporting.

RESEARCH CAREER AWARDS

Mr. FLOOD. Take a look at page 37 of your justification. What you call career awards fellowships; $30,000 each. How can Mr. Michel

justify that, a single fellowship, $30,000. Somebody is going to ask him.

Dr. ENDICOTT. These are career awards. These are senior people and in effect we have a commitment to them to provide their salary for the normal career. We have set some ceilings on what that can be. But actually, that is a low figure.

Mr. FLOOD. It is a what?

Dr. ENDICOTT. It is a low figure, sir. I know what I am talking about here because I am losing men all the time. I have lost in the field of radiation therapy recently two men, both going to academic posts which would be comparable to these, and they are just barely out of their residency. One is going for a salary of $35,000 and the other $45,000.

Mr. FLOOD. Where?

Dr. ENDICOTT. Academic institutions. University salaries. These are people by and large at the full professor level and university salaries—I am sure Dr. Marston could tell you more about this than I can.

In some of my recent recruitments, I have had to persuade university professors with total income of say $45,000 or $46,000 to come to the Institute where until very recently our top salary was $28,000, and that is the trick of the week.

Mr. FLOOD. How old are you?

Dr. ENDICOTT. I am 53.

Mr. FLOOD. Just a kid.

Dr. ENDICOTT. Thank you. I am going to take that home to my wife.

INCREASE FOR NIH MANAGEMENT FUND

Mr. FLOOD. Let's look at page 41. Your increase there is $988,000, that is the transfer to the National Institutes of Health Management Fund for centrally furnished services?

Dr. ENDICOTT. Yes, sir.

Mr. FLOOD. All of the rest of your increase, the whole shooting match you are asking for is less than $2 million, the whole works?

Dr. ENDICOTT. Yes.

Mr. FLOOD. Does not this increase for the management fund seem out of line? Why the big increase?

Dr. ENDICOTT. When I first saw that I was somewhat startled myself, but then I looked into the matter and what this represents is redistribution of the cost in the light of a major reorganization of the NIH.

We have brought in two major new activities. We have another one which is developing in North Carolina where it is not possible to provide most of these centrally furnished services because of distance.

Using the best techniques that they could to cost out the services that are supplied centrally, our share turned out to be more than they had originally calculated. So this is how the figure comes out.

I will admit on the surface it looks as though the overhead is going up pretty fast. That is not the case. It is simply recalculation of the cost of providing these services.

Mr. FLOOD. What is the percentage increase?

Mr. LEARMOUTH. Our share runs about 10 percent. As Dr. Endicott suggests, this is primarily an adjustment, some Institutes went up and some down, in order to make application of the formula more accurate between the various institutions. This is a complete readjustment.

Mr. FLOOD. We must ask that because somebody is going to ask us that.

Mr. SEGGEL. We will be glad to supply for the record a detailed statement on how this works. In other words, this is a central fund.

(The information follows:)

The increase of $1,060,000 in the appropriation of the National Cancer Institute for the central management fund reflects primarily a redistribution of the costs of this fund among the Institutes in accordance with an established formula, that is, number of occupied beds in the clinical center, number of positions, research grant overload, and so forth. Based largely on refinements in the application of the formula, the distributions to some Institutes, such as the NCI, were increased and those to other, such as the National Institute of Arthritis and Metabolic Diseases and to the National Institute of Environmental Health Sciences were decreased. For example, in the case of the NIEHS, it was determined that its appropriation should be allocated a much smaller portion of the total cost since its physical location in North Carolina required it to provide much of its own services rather than utilize the central services at Bethesda. Because of these internal redistributions, increases and decreases for the central fund in each of the Institute appropriations cannot be directly related to the program changes shown in those appropriations.

The fiscal year 1970 budget of the central management fund shows an overall increase of less than 2 percent, which is consonant with the overall rate of increases projected for the sum total of the research programs in all of the Institute appropriations. The budget of the central fund is separately prepared, reviewed, and presented to the Congress, but, for purposes of appropriations, is distributed as an addition to each of the Institute appropriations based on the aforementioned formulas. This procedure is in accordance with authority granted by the Congress in 1958.

INCREASING INCIDENCE OF CANCER

Mr. FLOOD. Mr. Michel?

Mr. MICHEL. Doctor, in your opening statement you made mention of cancer claiming 615,000 new victims.

Dr. ENDICOTT. That is new cases.

Mr. MICHEL. And 325,000 lives. And last year, during the course of my questioning, it appeared that we were holding our own in the cancer death rate over the past 10 years or so. While you say the death rate is going up, of course the population rate is going up, too.

If we were to draw a graph, are we catching up? Can you tell us with all of these hundreds of millions of dollars and even the billion that you say now you have spent in this one area since you have been responsible, are we falling further behind?

Mr. FLOOD. Ten years.

Mr. MICHEL. Yes.

Dr. ENDICOTT. The population is growing, the number of people in the cancer susceptible age is increasing, and all of this has to be taken into account in arriving at an assessment of where we stand.

If you correct for age distribution of the population, and then determine the incidence per 100,000, cancer incidence has been moving slowly, but steadily, upward. Cancer mortality has increased at a rate of something one the order of 1 percent, or slightly less than 1 percent per year.

Mr. FLOOD. This I do not understand.

Dr. ENDICOTT. This is incidence. It cannot be explained I think in terms of better diagnosis. It clearly cannot be explained in terms of age because it is age-corrected.

I myself attribute it primarily to increasing pollution in one way or another of our environment. The most spectacular area of increase, and if it were not for this one area the overall trend would be down, is the rapid increase in the incidence of cancer of the lung. If we could get incidence of that disease turning down the figures would begin to look better.

The cure, rate, we are not making any progress there. But even so, incidence is going up faster than the cure rate so that the mortality figures are going up. This is the one which provides the grimmest outlook in the whole area.

I would be happy to extend a chart for you.

Mr. MICHEL. This increase in the incidence of lung cancer is attributed to what, in your opinion?

Dr. ENDICOTT. It is attributable to multiple factors. One of them clearly is smoking cigarettes. Another one is a series of industrial exposures. Chromate dust, asbestos, this sort of thing.

Mr. MICHEL. I was rather shocked to learn in the testimony earlier in environmental control the rate of lung cancer is seven times the normal rate for those uranium miners, for example.

CANCER IN URBAN VERSUS RURAL AREAS

Dr. ENDICOTT. I do not think there can be much doubt that atmospheric pollution has something to do with it because the difference between the urban and rural rate, and the British cities where the pollution is worse, have even worse figures than we have in this country.

Mr. MICHEL. Have we got any comparative figures to show for the record, the difference between those out in the rural clean air areas?

Dr. ENDICOTT. Yes, sir; I could do that.

Mr. MICHEL. I think it would be a significant statistic, or figure, to show.

(The information follows:)

CANCER IN URBAN VERSUS RURAL AREAS

It has been long known that densely populated and industrialized areas have higher mortality rates for many causes of death than nearby rural areas. An association between urbanization and mortality has been found for heart disease, cancer of the respiratory and digestive systems, and many other diseases, but the reasons are not yet fully understood. Part of the urban-rural difference is attributable to self-selection and errors in reporting place of residence—many people who become seriously ill move to cities where they can obtain better medical and hospital care. Even when mortality data are classified by place of usual residence rather than by place of death, this does not entirely compensate for the inflation of mortality rates resulting from a tendency of people with chronic illnesses to move from rural areas to towns and cities, where they can find less demanding occupations and lead more sedentary lives.

Even when allowance is made for these factors, there remain sizable urban excess risks for certain causes of death. Some of these causes can be related to specific environmental, industrial, or sociological characteristic of cities. Examples are deaths of pedestrians struck by motor vehicles, certain occupational cancers, and cirrhosis of the liver. Urban air pollution may also prove to be an important cause of cardiorespiratory diseases. Other causes of death, including many forms of cancer, are closely associated with urbanization but have not yet been related to any specific factors in the urban environment. Elucidation of these factors is one of the important problems still facing cancer investigators.

Comparisions of cancer incidence for urban and rural populations have been

reported for Connecticut and Iowa, and the results are summarized in the table that follows. These findings will be updated in the ongoing morbidity surveys being conducted by the National Cancer Institute.

URBAN-RURAL[1] RATIOS OF AGE-ADJUSTED CANCER INCIDENCE RATES, BY SITE OF CANCER AND SEX, CONNECTICUT, 1947–51, AND IOWA, 1950

	Male		Female	
	Connecticut, 1947–51	Iowa, 1950	Connecticut, 1947–51	Iowa, 1950
All sites	1.36	1.40	1.28	1.34
Buccal cavity and pharynx	1.33	1.33	1.19	1.76
Lip	.96	1.10	.25	1.50
Digestive system	1.42	1.28	1.25	1.05
Esophagus	2.35	1.86	2.14	.50
Stomach	1.34	1.00	1.29	.93
Intestines	1.46	1.45	1.28	1.23
Rectum	1.30	1.31	1.03	.91
Other digestive organs	1.39	1.45	1.35	1.03
Respiratory system	1.72	2.71	1.38	1.43
Lung and bronchus	1.57	2.84	1.24	1.47
Larynx	4.14	2.07	1.33	[2]
Male genital organs	1.23	1.12		
Prostate	1.19	1.11		
Breast	1.75	2.00	1.21	1.25
Female genital organs			1.35	1.48
Cervix			1.47	1.77
Corpus			1.45	1.23
Ovary			1.15	1.23
Urinary organs	1.29	1.52	1.22	1.74
Kidney	1.37	1.37	1.24	1.18
Bladder and other	1.25	1.56	1.21	2.21
Skin	1.03	1.38	1.19	1.82
Lymphatic tissues	1.55	2.00	1.33	1.31
Leukemia	1.32	[3]	1.50	[3]

[1] For Iowa, "urban" includes all incorporated places of 2,500 and over, and certain other political subdivisions so classified by the U.S. Bureau of the Census under special rules relating to population size and density; for Connecticut, "urban" comprises 76 towns with high population density.
[2] No cases observed among rural residents.
[3] Comparable Iowa data are not available.

The composite data show higher incidence rates in urban areas for cancer of nearly every organ or system. Among males, an unusually large urban excess appears for cancer of the respiratory system and esophagus. A slightly smaller urban-rural difference is observed for women than for men, especially in the digestive and respiratory systems.

In Connecticut, where much of the rural population is engaged in nonfarm pursuits, the excess urban risks are smaller than in Iowa, where there are sharper contrasts between urban and rural populations. The Iowa rural population has a large representation of farmers and the Iowa experience probably provides a better contrast of populations living under widely different environmental conditions, including air pollution. Urban-rural comparisons for Norway, Denmark, Finland, and other countries yield results similar to those described for the United States. Systematic comparisons of cancer experience in urbanized and nonurbanized parts of various countries may produce epidemiological information of great value.

Discussion of the possible effects of air pollution should distinguish general pollution of the outdoor air by industrial smoke and fumes, automobile exhausts, and home heating, installations for pollution of the air in limited areas near mines or industrial plants, by specific substances. Many carcinogenic substances may, under certain circumstances, become dispersed in the air—for example, some organic chemical products, or chromate dust—and if they are inhaled or absorbed in sufficient concentration for a prolonged period of time result in cancer. However, such situations are uncommon and can often be controlled or eliminated when the hazard is recognized.

General pollution of the air we breathe is found in all large cities and in many nearby suburbs, and it is the association between the incidence of cancer and these exposures common to urban life that require study. There is widespread suspicion that this association is at least partly due to the contamination of urban air with a wide variety of substances, but the evidence advanced so far is

at best presumptive in nature. Further investigations to define and measure the effects of air pollution on the incidence of cancer, and other diseases as well, are urgently needed.

Dr. ENDICOTT. I cannot help but feel, although I do not have any evidence whatever to support it, that there may well be a common factor here that will turn out to be a virus and that these other things which are so unlike one another, uranium, asbestos, tobacco smoke, and so on, the common denominator may turn out to be a virus and these other things simply precipitating factors.

USE OF PAP SMEAR FOR DETECTING CANCER OF THE CERVIX

Mr. MICHEL. Isn't the best opportunity and chance for arresting cancer in women, or at least detection by using the pap smear? Do we still show the best experience table in that area?

Dr. ENDICOTT. Yes. And of course the disappointing thing about it is that it is far from adequately applied. As I recall the most recent figure, not more than 25 percent of the women who should be getting Pap smears are actually getting them.

Mr. MICHEL. Why is this? Why don't we get better participation. Am I wrong in making the observation that it might be surprising the number of doctors who cannot even take a Pap smear?

Dr. ENDICOTT. That is certainly one of the problems. Historically, this is a long story. Papanicalaou made his original observation of abnormal cells in smear from the vagina first in the thirties. The National Cancer Institute picked up this lead and made a demonstration project in Sheldon County, Tenn., beginning in the late forties and by the early fifties and proved it was feasible to do this, and by doing this you could detect cancer early when it was still in an operable stage.

That program was dropped out of the research area and moved over into the cancer control programs which are defended before you in another part of the budget.

Somewhere in the fifties, and they have been hacking away at this problem now for over 10 years. At first there was resistance on the part of pathologists. I am a pathologist and I can remember that because I was accustomed to a biopsy.

Mr. FLOOD. What is a pathologist?

Dr. ENDICOTT. The man concerned with the anatomy of the sick human. He is the fellow you find in the morgue doing an autopsy or in the operating room looking at a piece of tissue to see if it is malignant. Looking through the microscope.

Mrs. REID. Can you do that right on the spot?

Dr. ENDICOTT. Yes; they prepare frozen sections and examine them in a room next to the operating room. For instance, in breast cancer, when the surgeon makes the original incision, oftentimes if not usually he does not even know if this is cancer or not and so while the patient is under the anesthetic the pathologist makes a frozen section and examines it in terms of whether it is malignant or not, and this helps the surgeon decide whether to use a little incision or a radical operation.

I think I have lost the trend of your question.

At first it was physicians, pathologists really. Then they became convinced and it became necessary then to convince the physician at large. And then the problem began to be how to take care of the work-

load and this led to the development of a special type of paramedical personnel, cyto diagnostic technician or cytologic technician.

So in the cancer control program we have been supporting the training of the ancillary personnel, the training of the pathologists who have to make a final reading, and then an extensive program of going to the practicing physicians in increasingly effective ways, not only to teach them how to do it but to persuade them it is worth doing.

There was quite a long period of time I recall when working with the American Cancer Society, when the society was concerned lest its programs to interest women would succeed so well that the profession would not be able to provide the services. Some of these factors are still operating and probably will continue to operate to some extent for some years to come, but we are making progress, clearly making progress.

I could supply the record a percentage of the eligible population over a period of years.

Mrs. REID. Would you do that?

(The information follows:)

ELIGIBLE POPULATION FOR "PAP" SMEAR

The College of American Pathologists, in cooperation with the cancer control program, has conducted three surveys of cytological testing in the United States. These surveys have shown that about 5 million women had the "Pap" test in 1960, 9.5 million in 1963, and 13.5 million in 1965. A survey of 1968 testing will be conducted this year and is expected to find that more than 18 million women were tested. It is assumed that about 60 million American women should be protected by the test. On this basis, the percentages reached have been:

Year:	*Percent tested*
1960	8.3
1963	15.8
1965	22.5
1968	30.0

Mr. MICHEL. I think next year I would like to ask the question, are we still at 25 or 30 percent. If that holds static for several years, in an area that has proven to be one where real progress has been made but we have not pushed it to the extent that we should, somewhere we have fallen down, have we not?

Dr. ENDICOTT. Of course, as you realize, we are in a period of major reorganization of the health functions of the Department. And there is, I think, a movement in the direction away from categorical support programs to more general support programs to the States.

One of the things that concerns me is if this trend continues—let's suppose we stop earmarking funds for cancer control and provide general funds for the States. I am seriously concerned as to whether service of cytology has sufficiently wide acceptance and sufficiently high local priorities that this program would continue to be pushed. It has obviously taken a lot of time and effort.

Mr. MICHEL. On page 21 of the justifications there is an item here "Other services" showing an increase from $60,085,000 to $63,071,000, just about a $3 million increase. But my first question is what is involved in these other services.

You have all these other little line items of $300,000 or $400,000 and here is a great big one that looks like a miscellaneous $60 million.

Dr. ENDICOTT. Those are contracts and the other big one is grants, subsidies, and contributions, which is $95 million.

GRANTS TO KAROLINSKA INSTITUTE IN SWEDEN

Mr. MICHEL. Did we not at one time have a contract or an arrangement in cancer research with the Karolinska Institute in Stockholm, Sweden?

Dr. ENDICOTT. Yes, sir; we have been making grants to individuals at the Karolinska Institute for many years.

Mr. MICHEL. I was over there several years ago and went through the institute. I remember seeing one of the biggest mice collections over there, 30,000 or 40,000 of them, and being taken through the entire shop. At that time I recall they were getting some assistance from us.

Does that come actually out of your shop in the contract awards?

Dr. ENDICOTT. Yes, sir. Most of our support has gone in the form of grants, although I think we may have one or two contracts there, particularly with Dr. Klein at the present time.

Mr. MICHEL. I believe that I met him while I was there. Can we break that out for the record, what was done there, what was the length of contract and for what amount?

Dr. ENDICOTT. Yes.

(The information follows:)

AWARDS TO KAROLINSKA INSTITUTE, SWEDEN

FOREIGN RESEARCH GRANTS

During the last 5 year period, the National Cancer Institute awarded four grants to three individual investigators at the Karolinska Institute, Stockholm, Sweden.

Two grants have been awarded to Dr. George Klein. One grant, entitled: "Cytogenetics of Variability in Cancer Cell Populations," will terminate in April 1969.

One of the many research accomplishments of this grant is the facilitation of tumor growth by gram negative bacteria (Bacillas pertussis). It has been known that several gram negative bacteria or their components can exert a slight but significant inhibitory effect on the growth of certain tumors. Dr. Klein and his group showed that with certain inoculations of tumor cells they could increase the incidence of tumor growth, but this did not occur in all types of tumors. It was concluded that the same bacterial product might inhibit or promote tumor growth depending upon experimental conditions.

Other accomplishments achieved through support from this grant is further evidence that immunological activity is age-dependent. Since there is an increased incidence of neoplasia with advancing age. Dr. Klein studied the ability of animals of various ages to accept or reject tumor transplants. After completing these investigations, Dr. Klein, concluded that the change he observed in immunological reactivity with age, (as well as the immunodepressive effect of a carcinogen of 3-methycholanthrene), may be relevant to the human situation.

A second grant to Dr. Klein which is being terminated at the end of July 1970 has been supported at a level of somewhat less than $40,000 yearly, over the last 5 years. This study, entitled "Viral Tumorigenesis and Cellular Phenotype," has shown that virus-induced tumors contain tumor specific transplantation antigens, common for whole groups of neoplasms induced by the same virus and capable of inducing rejection reactions against syngeneic (inbred strains) tumor cells of varying strength, depending on the system.

Support from the grant also has permitted Dr. Klein to do further studies on the membrane immunofluorescence reaction of Burkitt lymphoma cells. This reaction is not likely due to blood groups or transplantation antigens, but rather (*a*) a tumor—specific reaction, or (*b*) a nonspecific protein fraction appearing in the serum of Burkitt lymphoma patients. As an outgrowth of these studies, Dr. Klein has been able to establish, in tissue culture, a line of Burkitt lymphoma cells derived from a patient in Kenya, Africa. Through the establishment of this cell line he will be able to further study and characterize Burkitt lymphoma cells.

A third grant, awarded to Dr. Peter Reichard and entitled "Control of Enzymic Synthesis of Deoxyribonucleotides," has been funded at a level of approximately $25,000 per year for each of 5 years. As a result of this research all four protein components of the ribonucleaside diphosphate reductase system were obtained in an essentially pure form. Dr. Reichard's grant terminated at the end of January 1969.

A fourth grant involving studies on the measurement of the sensitivity of neoplastic cells to X-rays in different phases of the cell cycle was awarded to Dr. Laszlo Revesz, for a total amount of $37,000 over a 4-year period. This grant terminated at the end of 1965. Dr. Revesz studied the interclonal variation of radiosensitivity within a genetically heterogeneous tumor cell population. The clones, derived from serially irradiated Ehrlich ascites tumor (ELD) were, also, studied with respect to their chromosomal constitution. He found that there was no correlation between radiosensitivity and chromosomal complement in the 19 lines studied.

FOREIGN RESEARCH CONTRACTS

A contract with Karolinska Institute has just been negotiated to follow up on leads abroad which must be pursued to determine whether a suspected virus (EBV) causes cancer in man.

The work to be performed under the contract with Dr. Klein is designed to help determine whether the Epstein-Barr virus (EBV) causes certain cancers as Burkitt lymphoma, postnasal carcinoma, Hodgkin's disease and other related human tumors. These studies fall into two general areas. One area is to perform serological tests on large numbers of serums collected in Africa, Hong Kong, Singapore, and other areas through existing collaborators, and most importantly through a proposed contract with the International Agency for Research on Cancer in Lyon, France. It is anticipated that serums will be collected from approximately 20,000 individuals each year for 7 years. The usefulness of the Klein immunofluorescent technique has already been established, and it is anticipated that other tests will be developed by Dr. Klein for the detection of the virus or of antibodies to the virus.

Dr. Klein has also developed a unique immunofluorescent test and serological reagents which have shown for the first time that Burkitt lymphoma cells have a new nonvirion but virus mediated antigen on their surfaces. This is an extremely important finding. In order for a virus to cause cancer it must have the capacity to modify the genetic apparatus of the cell. The existence of a new cell antigen in cells exposed to EBV is good evidence that the virus does in fact have this capacity. To the best of our knowledge only tumor viruses are able to program cellular genomes to produce these virus related antigens. It is extremely important that Dr. Klein, with his unique capabilities and facilities, characterize this antigen and search for others with his special materials and techniques.

FOREIGN RESEARCH GRANTS

Mr. MICHEL. How many of these grant awards have we made to either individuals or institutions abroad in the area of cancer research?

Dr. ENDICOTT. Perhaps I could provide you with a 5-year history of our support activities.

Mr. MICHEL. Will you do that?

Dr. ENDICOTT. Very happy to.

(The information follows:)

NATIONAL CANCER INSTITUTE

GRANTS AND CONTRACTS ABROAD—5-YEAR HISTORY, FOREIGN RESEARCH GRANTS

Grant number, title	Principal investigator	Expiration date	Purpose	Amount awarded 1965	1966	1967	1968	1969
Australia:								
CA06851—Chemical, physical, and genetic studies of myxoma virus.	Commonwealth Scientific and Industrial Research Organization, Dr. Sobey.	Aug. 31, 1966	Host-cancer relation	$8,606	$7,216			
CA05360—Continuous microinjection method in cancer and biology.	Melbourne, University of, Dr. Rose	Aug. 31, 1967	Pathogenic mechanisms	48,025	46,160	$31,837		
CA07810—Chemical studies on the flora of Western Australia.	Western Australia, University of, Dr. Jeffries.	Sept. 30, 1967	Therapy operational chemotherapy, Synthesis.	13,580	12,155	13,374	$1,200	
Brazil: CA07464—Chemical investigation of Brazilian plants.	Brazil, University of, Dr. Mors	May 31, 1968	do	29,641	22,240	21,080		
Canada:								
CA06783—Electron microscopy of human introcranial tumors.	Queen's University, Dr. Robertson	Jan. 31, 1966	Cancer morphology and physiology.	6,866	196			
CA05489—Thyroid tumor production by a low iodine diet.	Montreal, University of, Dr. Isler	Mar. 31, 1967	do	14,520				
CA06229—Radiobiological studies on mammalian cells.	Princess Margaret Hospital, Dr. Whitmore.	Apr. 30, 1969	Morphogenesis esternal stimuli.	20,100	20,100	20,100	6,664	$13,137
CA05342—The isolation and identification of polynucleotides.	British Columbia, University of, Dr. Tener.	Aug. 31, 1966	Steady state morphology and physiology.	36,975	33,675			
CA04 64—Relation of virus to various tumors.	Princess Margaret Hospital, Dr. Axelrad.	Aug. 31, 1968	Carcinogenesis, internal stimuli.		40,000	39,748	43,900	
CA08382—Synthesis of potential anticancer agents..	British Columbia, University of, Dr. Rosenthal.	Sept. 30 1968	Therapy operational chemotherapy-synthesis.		11,500	11,500	11,500	
Chile: CA07086—Cell coating and its meaning in malignancy.	Chile, University of, Dr. Gasic	Aug. 31, 1965	Pathogenic mechanisms	34,976				
China-Taiwan: CA06902—Studies on arsenical cancer.	National Taiwan University, Dr. Yeh	May 31, 1968	Epidemiology	9,000	7,000	5,900		
Denmark: CA03087—Danish and international cancer review.	Danish Cancer Registry, Dr. Clemmesen.	Dec. 31, 1968	do	12,800	12,800		12,800	
Finland: CA05347—Inductive agents in normal and malignant tissue.	Helsinki, University of, Dr. Toivonen	Dec. 31, 1965	Pathogenic mechanisms	15,000	3,330			
France:								
CA05703—Treatment of experimental and human leukemia.	Claude Bernard Association, Dr. Mathe	Aug. 31, 1966	Supportive therapy immunology.	8,400	8,400			
CA08900—Fetal-like patterns of enzymes in cancer.	Association de Prevention et d'Etudes des Maladies Moleculaires, Dr. Schapira.	Sept. 30, 1969	Cancer morphology and physiology.			9,500	9,500	9,000
CA06202—The role of viruses in the etiology of cancer.	College de France, Dr. Haguenau	May 31, 1969	Pathogenic mechanisms	17,500	18,375	19,293	16,819	

CA04580—Enzymatic synthesis of polyribonucleotides.	Institut de Biologie Physico-Chimique, Dr. Grunberg-Manago.	Aug. 31, 1969	Steady state morphology and physiology.	21,000	22,000	22,000	20,200	15,050
CA05573—Surface leukocyte antigens and skin grafts.	Paris, University of, Dr. Dausset	Mar. 31, 1969	Integration and immune physiology.	23,800	24,990	24,990	27,550	
CA06604—Action of fatty acids on normal and malignant tissues.	Pasteur Institute, Dr. Ponder	Aug. 31, 1966	Cancer morphology and physiology.	3,600	3,600			
Iceland: CA06188—Stomach cancer in Iceland, relation to diet.	Iceland Cancer Society, Dr. Dungal	June 30, 1967	Epidemiology	32,390	30,500			
Israel:								
CA06867—Polyamines and normal and and malignant tissues.	Hadassah Medical School, Hebrew University, Dr. Bachrach.	Aug. 31, 1966	Cancer morphology and physiology.	12,980	5,980			
CA06582—Surface properties of normal and malignant cells.	Hadassah Medical School, Hebrew University, Dr. Doljanski.	Nov. 30, 1968	Steady state morphology and physiology.	5,490	8,350	8,323	8,350	
CA06996—Protein-bonding purines and pyrimidines.	Israel Institute for Biological Research, Dr. Cohen.	Apr. 30, 1968	Therapy operational	16,400	17,500	19,861	1,513	
CA04344—Effect of carcinogenic agents on oxidative metabolism.	Israel Institute for Biological Research, Dr. Traub.	Nov. 30, 1965	Carcinogenesis, external stimuli.	11,250				
CA05455—A possible 2-stage mechanism in leukemogenesis.	Weizmann Institute of Science, Dr. Berenblum.	Apr. 30, 1969	do	17,300	18,165	20,026	20,026	
CA05263—Biochemical studies on urethan carcinogenesis.	Weizmann Institute of Science, Dr. Berenblum.	Apr. 30, 1968	Pathogenic mechanisms	22,000	22,900	7,632		
CA06165—Immunogenetic studies on tumors and radiation chimeras.	Weizmann Institute of Science, Dr. Feldman.	do	Host-cancer relations	25,610	26,290	24,900		
CA02810—Antitumor compounds from ecballium and related plants.	Weizmann Institute of Science, Dr. Lavie.	Nov. 30, 1964	Therapy operational chemotherapy, synthesis.	2,650				
CA05266—In vitro analysis of mamalian tumor viruses.	Weizmann Institute of Science, Dr. Sachs.	Dec. 31, 1966	Carcinogenesis, internal stimuli.	33,140	34,010	9,000		
Italy:								
CA05544—The role of DNA in malignancy	Milan, University of, Dr. Polli	Aug. 31, 1966	Pathogenic mechanisms	20,000	5,000			
CA05220—Structure of melanins and melanogenesis.	Naples, University of, Dr. Nicolaus	do	Cancer morphology and physiology.	13,700	13,679			
CA07092—Immunological studies on murine leukemia viruses.	Perugia, University of, Dr. Ribacchi	Aug. 31, 1967	Diagnosis	12,000	12,000	12,000		
Japan:								
CA07038—Steroid metabol.sm of experimental testis tumor.	National Institute of Radiological Sciences, Dr. Tamaoki.	Dec. 31, 1966	Cancer morphology and physiology.	7,000	6,500	2,167		
CA09815—Carcinogenesis of the stomach and esophagus.	Kyushu University, Dr. Kuratsune	Aug. 31, 1966	Carcinogenesis, external stimuli.	23,670	23,670			
CA04222—The mechanism and function of oxygenases.	Kyoto University, Dr Hayaishi	May 31, 1969	Cancer morphology and physiology.	12,000	12,600	14,000	12,000	
CA06146—Antitumor activity of unsaturated fatty acids.	Okayama University, Dr Seno	Oct. 31, 1965	Therapy operational chemotherapy.		1,500			
CA08394—Structure determination of natural products.	Tohoku University, Dr. Nakanishi	Sept. 30, 1968	Therapy operational chemotherapy, synthesis.		10,900	10,700	10,500	
CA10322—Studies in carcinogenicity of cycasin.	Gifu Medical College, Dr Hirono, Iwao	May 31, 1970	Carcinogenesis, external stimuli.			5,564	5,078	3,949
CA06035—Experimental studies on the etiology of leukemia.	Kyoto University, Dr. Miyake	Aug. 31, 1966	Carcinogenesis, internal stimuli.	3,800	3,800			

Grant number, title	Principal investigator	Expiration date	Purpose	Amount awarded				
				1965	1966	1967	1968	1969
CA07798—Chromosome alteration and tumor development.	National Institute of Genetics, Dr Yosida.	May 31, 1970	do	7,810	5,660	6,615	5,115	5,115
CA06813—Virological studies of human cancer.	Okayama University Medical School, Dr. Murakami.	Feb. 28, 1966	do	2,460				
CA03481—Hepatoma and cirrhosis of the liver in Japan.	Osaka University, Dr Miyaji	Sept. 30, 1966	Epidemiology	5,000	5,000			
CA05089—Supply of mice and pellets for cancer research.	Central Laboratories for Experimental Animals, Dr. Ando.	Dec. 31, 1966	Miscellaneous	17,624	3,884			
CA05217—Studies on antitumor antibiotics.	Institute of Physical and Chemical Research, Dr. Yusuke, Sumiki.	Aug. 31, 1967	Therapy operational chemotherapy, synthesis.	9,150	9,700	10,250		
CA05085—Isolation and screening of anticancer antibiotics.	Kitasato Institute for Infectious Diseases, Dr. Hata.	Apr. 30, 1969	Therapy operational chemotherapy, biotesting.	18,254	16,968	16,950	17,950	
CA02799—Ascites tumor system for chemotherapy screening.	Medical Institute of Sasaki Foundation, Dr. Yoshida.	May 31, 1966	Therapy operational chemotherapy, testing.	16,026				
CA05082—Studies on antitumor antibiotics	Tokyo, University of, Dr. Umezawa	Apr. 30, 1968	do	27,220	19,915	17,850		
CA04795—Studies on malignolipin, a phospholipid of cancers.	Mie Prefectural University, Dr. Kosaki	Apr. 30, 1966	Diagnosis	5,500				
CA05246—Interaction between carcinogen and celluloar components.	Tokyo, University, Dr. Terayama	Dec. 31, 1968	Pathogenic mechanisms	1,690	1,774	1,862	1,955	
CA08698—Role of viral nucleic acid in mammalian neoplasia.	Aichi Cancer Center, Dr. Ito	Dec. 31, 1967	Carcinogenesis, internal stimuli.		8,608	8,608		
Malaysia: CA05851—Histocompatibility studies in mice.	Malaya, University of Dr. Dhaliwal	Aug. 31, 1968	Host-cancer relation, immunogenetics.		6,344	6,100		
Mexico: CA04639—Biosynthesis of steroid hormones in abnormal tissues.	Instituto Nacional de la Nutrician, Dr. Gual.	Apr. 30, 1966	Cancer morphology and physiology.	9,000	3,000			
Netherlands:								
CA09346—Continuation of the cancer section of Excerpta Medica	Excerpta Medica Foundation, Dr. Woerdeman.	Mar. 31, 1969	Miscellaneous	7,017	18,976	13,230	10,667	
CA03431—Hormonal genesis of mammary cancer.	Netherlands, Cancer Institute, Dr. Muhlbock.	Dec. 31, 1965	Cancer morphology and physiology.	17,000				
New Zealand: CA03707—Etiology of chronic lymphocytic leukemia.	North Canterbury Hospital Board, Dr. Gunz.	Oct. 31, 1966	Epidemiology	2,212	2,212			
Peru:								
CA08264—The effect of high altitude on neoplastic growth.	Universidad Peruana Cayetano Heredia, Dr. Mori-Chavez.	Aug. 31, 1969	Carcinogenesis, external stimuli.		22,900	22,501	25,300	21,804
CA06597—The effect of high altitude on neoplastic growth.	Laboratorio de Investigacion de Cancer, Dr. Mori-Chavez.	Aug. 31, 1965	do	16,169				
Singapore: CA08448—Nasopharyngeal carcinoma.	Singapore, University of Dr. Shanmugaratnam.	Oct. 31, 1969	Epidemiology		16,723	7,140	7,230	

South Africa:								
CA06565—Etiology of esophageal cancer in the Transkeian Bantu.	Rhodes University, Dr. Rose	Aug. 31, 1969	do	19,046	30,372	30,372	35,600	24,324
CO07003—A study of environmental carcinogens in Swaziland.	South African Institute for Medical Research, Dr. Keen.	Apr. 30, 1969	do		18,059	19,852		3,499
Sweden:								
CA06415—Chromosome studies of Rous sarcoma in mammals.	Lund, University of, Dr. Levan	Aug. 31, 1968	Cancer morphology and physiology.	31,124	36,816	43,518	32,520	
CA03700—Cytogenetics of variability in cancer cell populations.	Karolinska Institute, Dr. Klein	Dec. 31, 1968	Host-cancer relations	40,000	40,000	40,000	40,000	
CA04747—Viral tumorigenesis and cellular phenotype.	do	July 31, 1970	Carcinogenesis, internal stimuli.	47,000	47,000	54,800		38,950
CA06633—Sensitivity of neoplastic cells to X-ray.	Karolinska Institute, Dr. Revesz	Dec. 31, 1965	Therapy, supportive radiology	7,500				
CA05278—Protein metabolism and tumor induction.	Stockholm, University of, Dr. Hultin	Aug. 31, 1965	Cancer morphology and physiology.	11,000				
CA07897—Control of enzymic synthesis of deoxyribonucleotides.	Karolinska Institute, Dr. Reichard	Jan. 31, 1969	Steady state morphology and physiology.		26,250	27,562	28,940	
CA06850—Quantum theory of molecules in cancer research.	Uppsala, University of, Dr. Lowdin	Aug. 31, 1966	Pathogenic mechanisms	49,400	11,853			
Switzerland: CA05096—Program of the International Union against cancer.	International Union Against Cancer, Dr. Delefresnaye.	Aug. 31, 1970	Miscellaneous	50,000	50,000	50,000	50,000	50,000
United Kingdom:								
CA06066—The synthesis of oligo- and polyribonucleotides.	Cambridge, University of, Dr. Griffin	Sept. 30, 1969	Steady state morphology and physiology.	10,354	10,518	10,000	11,100	8,986
CA07087—Protein synthesis in normal and malignant cells.	Glasgow, University of, Dr. Munro	Aug. 31, 1966	Cancer morphology and physiology.	19,980	19,400			
CA05855—Biochemical differentiation in cultured mammalian cells.	Glasgow, University of, Dr. Paul	Apr. 30, 1966	Differentiation and growth	20,000	11,439			
CA08522—Sarcoma of the human breast: a study of 100 cases.	Royal College of Surgeons of Edinburgh, Dr. Dawson.	Apr. 30, 1967	Cancer morphology and physiology.	5,040				
CA03188—Cancer chemotherapy and carcinogenesis.	London, University of—Institute of Cancer Research, Dr. Haddow.	Dec. 31, 1967	Cancer morphology and physiology.	100,000	100,000	100,000		
CA06407—Virus etiology of malignant disease.	London, University of—Middlesex Hospital Medical School, Dr. Epstein.	Sept. 30, 1966	Carcinogenesis, internal stimuli.	20,106	20,631			
CA06823—Research on the structure and formation of melanins.	Newcastle-Upon-Tyne, University of, Dr. Swan.	Apr. 30, 1969	Cancer morphology and physiology.	7,190	7,549	11,226	4,112	
CA05392—The survey approach to problems of cancer prevalance.	Oxford University of, Dr. Stewart	Sept. 30, 1970	Epidemiology	13,706	14,009	13,061	14,506	12,350
CA08719—ESR spectra of wet, heterogeneous biological systems.	London, University of—St. Bartholomew's Hospital Medical College, Dr. Herbert.	May 31, 1967	Diagnosis		13,793			
CA08923—Carcinogenesis of skin by monochromatic UV.	London, University of—Institute of Dermatology, Dr. Mangus.	Aug. 31, 1968	Carcinogenesis, external stimuli.			6,063	5,918	
West Germany: CA04601—Function of nucleic acid in virus synthesis.	Max Planck Institute for Virus Research, Dr. Schramm.	Dec. 31, 1967	Pathogenic mechanisms	14,000	14,000	14,000		
Total grants awarded				1,222,347	1,160,434	885,055	498,513	206,614

NATIONAL CANCER INSTITUTE

FOREIGN CONTRACTS—ETIOLOGY

	Contractor	Purpose	Principal investigator	Expiration date	Amount obligated in fiscal year—				
					1965	1966	1967	1968	1969
Canada:									
PH43-65-97	Hospital for Sick Children	Human leukemia and normal tissue collection and preservation.	Dr. J. Darte	May 31, 1969	$8,550	$8,436	$7,895	$7,550	$8,000
PH43-65-1020	Montreal Children's Hospital	Supply of leukemia and normal blood plasma specimens.	Dr. R. Denton	do	9,250	14,814	10,845	8,856	9,000
Columbia: PH43-66-907	Universidad del Valle	Cancer morbidity survey in Cali	Prof. R. Correa	Dec. 28, 1969		20,695		26,540	26,950
France: In process	International Agency for Research on Cancer.	Burkitt tumor studies	Dr. G. Blaudin de Thé						398,000
Israel: In process	Weizmann Institute	Cell surface changes and mechanisms of carcinogenesis.	Prof. L. Sachs						70,000
Italy: PH43-68-1389	University of Padua	Supply of large untreated human tumor specimens.	Prof. G. Dogo	June 6, 1969		8,338	8,338	7,938	8,000
Japan:									
In process	Aichi Cancer Center	Study of human leukemia and lymphoma cells.	Dr. Y. Ito						39,000
PH43-66-61	Hiroshima University	Oncogenic and teratogenic effects of mustard gas in man.	Dr. S. Wada	Feb. 14, 1968		13,750	10,747		
PH43-64-10	Tohoku University	Shifts in cancer risks among Japanese migrants.	Prof. M. Segi	Nov. 30, 1969	39,941	56,933	37,023	67,300	50,315
Nigeria: PH43-67-674	University of Ibadan	Procurement and culture of Burkitt lymphoma clinical materials.	Prof. G. M. Eddington	Apr. 12, 1968			51,395		
Norway: PH43-64-499	Norweigan Public Health Service.	Shifts in cancer risks among Norwegian migrants.	Dr. E. Pedersen	June 25, 1969	49,320	54,737	74,980	55,000	75,000
Sweden: PH43-69-2005	Karolinska Institutet	Studies of the significance of Herpes-type virus in the etiology of some human cancers.	Dr. G. Klein	Apr. 1, 1970					45,000
Uganda: PH43-67-47	Makerere University Medical School.	Collection of Burkitt African lymphoma tissue specimens.	Prof. J. S. W. Lutwama	Sept. 25, 1969			49,325	12,490	46,950
United Kingdom: PH43-65-19 and PH43-66-17.	Wright Fleming Institute	Produce and deliver 200 dozen gradocol membranes for use in sizing viruses.	Prof. K. Dumbell	Sept. 14, 1966	8,100	8,422			
Total etiology contracts					115,161	186,125	250,543	185,674	776,215

NATIONAL CANCER INSTITUTE

FOREIGN CONTRACTS—CHEMOTHERAPY

Country	Contractor	Contract No.	Contract title and purpose	Principal investigator	Expiration date	Obligation level				
						1965	1966	1967	1968	1969
Japan	Japanese Cancer Institute	66-77	Scanning, translating, and abstracting cancer literature.	Dr. T. Yoshida	June 30, 1968	0	$5,000	0	$5,000	0
Australia	Commonwealth Scientific and Industrial Research Organization (CSIRO).	64-522	Fractionation of plant extracts	Dr. C. Culvenor	do	$20,000	23,070	$28,923	14,896	0
Costa Rica	University of Costa Rica	64-31	Supply of plant extracts	Dr. Jose A. Saenz Renauld.	Dec. 17, 1969	10,000	10,300	10,300	12,455	$11,595
Mexico	Syntex, S. A	2357	Steroid preparation laboratory	Dr. Barry Knox	Dec. 15, 1966	160,000	36,100	0	0	0
Uganda	Makerere University College	67-1343	Development of a lymphoma treatment center.	Prof. Sir Ian McAdam	June 27, 1969	0	0	65,260	55,550	90,000
Total chemotherapy contracts						190,000	74,470	104,483	87,901	101,595

RESULTS OF FOREIGN RESEARCH

Mr. MICHEL. Do we get a good read-back from that money spent over there? Hopefully, we get some results from them just as from any award here in our own country. Can we point to anything meaningful dervied from that expenditure of money?

Dr. ENDICOTT. Yes, sir; I would be happy to pull out some highlights for you.

Mr. MICHEL. Give us some facts here that might be helpful.

Dr. ENDICOTT. Yes, sir.

(The information follows:)

GRANTS AND CONTRACTS ABROAD—ACCOMPLISHMENTS

FOREIGN RESEARCH GRANTS

In addition to the outstanding studies performed at the Karolinski Institute as previously discussed, the NCI supports other foreign grants important to the progress of cancer research.

Most of the foreign grants awarded by the NCI involve the study of etiologic or causative factors of cancer in unique populations at high risk due to high exposure to specific implicated carcinogens. Since such studies of populations of people exposed to carcinogens take several years for completion and analysis, data are still being gathered and analyzed in several areas, however the potential benefit to the American people is large since identification and proof that a material is carcinogenic will lead to removal of that carcinogen from the human environment. Foreign awardees are not only outstanding authorities in their particular field, but have unique capabilities, resources, or population groups available for study. Many of these foreign investigators have been involved in carcinogenesis research for many years, and have developed unique testing and other techniques.

One example is the work of Dr. Haddow in England, who discovered that certain raw materials, added in the course of manufacturing rubber products may induce bladder cancer. Also, Dr. Sachs, of Israel, has developed an in vitro (outside the body and in an artificial environment) system to study the transformation of normal cells to tumor cells by carcinogenic hydrocarbons. Because so little is known about the combined effects of viruses and chemicals acting together as carcinogens, Dr. Levan of Sweden performed studies on rats utilizing this combination. He has postulated that the chemical agent acts to enhance or facilitate the entry of the virus into the cell.

Several epidemiological studies being conducted outside the United States are unique. Cancer of the esophagus is a disease found in all areas of the world, but Dr. Rose of South Africa has shown that this disease is prevalent and in excess in Bantu women living in the Transkei area of South Africa. The present investigators have access to this area and are studying the factors in the environment which may have a causal relationship to esophageal carcinoma. This project has many interesting ramifications including environmental variables, as the use of folk medicines, tobacco and alcoholic beverages, pellagra, environmental smoke, and arsenic.

A unique epidemiologic study by Dr. Stewart of the University of Oxford, England, involves collecting data on all children in Great Britain dying of cancer before they are 10 years old. This project started in 1960 as a study of the relationship of X-radiation and leukemia in adults. Later this was expanded to include childhood leukemia and cancer. This study affords a unique opportunity because of the unusual cooperation between the National Health Service and the General Registry Offices, which provide a more complete coverage of the population than would be possible in the United States where cancer is not a reportable disease. For this reason, this type of data could not be collected in so thorough a way in any other country but England.

Dr. Clemmesen, in Copenhagen, Denmark, has collected statistics from the Danish Cancer Registry on testis carcinoma for the period 1943–62. During the period 1943–57, testis carcinoma was unusual in showing higher rates for provincial towns than for the capital. However, analysis of the entire period 1943–62

shows regular trends in good conformity with results reported from other countries although the doubling of morbidity rates in the capital shows a more certain rise, and higher rates than other results on record. Here again we find a study that could only be done so thoroughly in another country.

The several foreign studies cited here are representative of other grants which have been awarded to investigators outside the United States. It must be emphasized that epidemiologic studies should not be restricted to this country alone, but should include comparative analysis of special situations in this country and abroad whenever promising leads of etiological importance seem to exist. Because of the uniqueness of these foreign grants, the National Cancer Institute is better able to carry out its complex and difficult mission.

FOREIGN CONTRACTS—ETIOLOGY

Examples of accomplishments under foreign contracts in the area of etiology are as follows:

(1) Contract No. PH43–66–61—Hiroshima University. The Hiroshima University contract, which terminated in February of 1968, was for a study of an epidemic of respiratory tract cancers among Japanese mustard gas workers. In a report on this contract published in "The Lancet," 49 cancers were observed from the nasal passages and mouth to the main airways of the lungs. Of these, 33 were histologially confirmed. Only one case was expected in this group of workers, as determined from normal cancer rates in Japan. The results show how powerfully carcinogenic a chemical agent can be in man.

(2) Contract No. PH43–64–10—Tohoku University School of Medicine, Japan. The purpose of this contract is to study the reasons for differences in cancer incidence between Japanese in Japan and the Japanese migrant populations in Hawaii and California. The objective is to sort out those aspects of common cancers which may be genetically determined and those which may be related to environmental factors. This contract supports the colletion of baseline data on populations in Japan needed for comparison with observations on Japanese migrants in Hawaii and California.

There are substantial differences in incidence of cancer of certain sites, i.e., stomach cancer, lung cancer, breast cancer between populations in Japan and the Japanese migrants to Hawaii and to California. The information assembled to date suggests that the decline in stomach cancer among the Japanese migrants is most marked among persons who have shifted completely from a Japanese style to Western style diet. Present efforts are directed to identification of those components of the Japanese diet that may be etiologically related to stomach cancer.

(3) Contract No. PH43–67–47—Makerere University Medical School, Uganda. This contract is to study the epidemiologic features of Burkitts tumor and to obtain tissue and sera from patients. This tumor is the first human cancer from which a candidate human oncogenic virus has been obtained. This has been an extremely fruitful project and is providing the background information for a more intensive study of this disease.

An analysis of survival of treated patients shows a 90-percent long-term survival of stage I and II patients; 65-percent stage III, and 30-percent stage IV. Analysis of Ugandian registry data on the Burkitt tumor has revealed a rate of six cases per 100,000 population in one area compared to a rate of two per 100,000 in another area.

FOREIGN CONTRACTS—CHEMOTHERAPY

The chemotherapy program has had a small group of contracts being performed in foreign countries for the years 1965 through 1969. At no time during this period have there been more than four contracts and the dollar value has fluctuated from a high in 1965 of $190,000 to a low in 1966 of $74,470. The present level for 1969 is $101,595.

The contracts were all of a service nature with the exception of a contract developed with Makerere University College in Kampala, Uganda. This contract was established in June 1967 with the primary objective of obtaining quantitative information regarding the therapy and immune competence of patients with Burkitt tumor, Hodgkin's disease, and Kaposi's sarcoma in Africa. In addition, information about the immunologic competence of healthy and ill African patients is obtained to compare it with data from healthy American children and patients

with similar diseases. The African children spend from 3 to 4 months at a time in the 18-bed ward of old Mulago Hospital. All patients on admission are thoroughly evaluated, including hematologic studies, blood chemistries, radiography, bone marrow aspiration, and photography. The treatment protocols have resulted in a large number of complete remissions and provided valuable data in Burkitt's tumor which is an ideal clinical model for the testing of specific chemotherapeutic principles for the control or even chemical cure for cancer. This contract represents $90,000 of the total of $101,595 for chemotherapy foreign contracts in 1969.

The only other active contract is with the University of Costa Rica and involves the supply of native Costa Rican plants for antitumor testing and isolation. This contract has been extremely satisfactory and has resulted in the production of 14 confirmed active species of plant material.

The remaining contracts in being during the 5-year period consisted of a steroid preparation laboratory in Mexico, a contract for fractionation of plant extracts in Australia, and a contract for scanning, translating, and abstracting cancer literature in Japan. These contracts have all been terminated because of budgetary or balance-of-payment restrictions.

AUTHORITY FOR CONSTRUCTION

Mr. MICHEL. There is nothing in your budget for construction, is there?

Dr. ENDICOTT. Not per se. Although the legislative authority under which we contract permits construction of special facilities that are needed for a specific project. This is an authority which we seldom use. I think we have not used it at all this year.

Mr. MICHEL. Is there a maximum or a ceiling on what money could be spent for construction?

Dr. ENDICOTT. Not in the legislation. Obviously one cannot use this authority to build an ordinary laboratory. It has to be something quite special and, for the most part, we have used it to build isolation facilities for experimental animals in which we were doing virus work. I think we built an isolation cowbarn or perhaps two. I better not say cats, but dogs, and so on. We have not other authority than that and make use of it that way.

LABORATORIES FOR THE TASK FORCE ON BREAST CANCER

Mr. MICHEL. Where is this central laboratory for the task force on breast cancer to be located? Is it in being?

Mr. STEINFELD. There are two and I am not sure of their exact locations.

Mr. MICHEL. Supply those two locations for the record.

Dr. STEINFELD. Yes, sir.

(The information follows:)

(1) Worcester Foundation for Experimental Biology, 222 Maple Avenue, Shrewsbury, Mass.

(2) Research Foundation for Mental Hygiene, Inc., Rockland State Hospital, Orangeburg, N.Y.

DEVELOPMENT OF A LESS HAZARDOUS CIGARETTE

Mr. MICHEL. Have you spelled out in the record at all, Dr. Endicott, how much of your budget is going into developing a non- or less-hazardous cigarette?

Dr. ENDICOTT. Yes, Sir. I think we have indicated that there is about $1.4 million. No, sir; that is incorrect. There is $1.4 million for

the lung cancer task force, of which $1 million has been allocated for contracts in the less hazardous cigarette area this year.

Mr. MICHEL. Was there anything in last year's budget for this item?

Dr. ENDICOTT. That is what I was talking about. The current year.

Mr. MICHEL. How about in 1970?

Dr. ENDICOTT. In 1970, it is essentially the same. I think there is a slight increase.

Mr. MICHEL. Has this been going on long enough to give any indication that there is some significant advance in that field?

Dr. ENDICOTT. The work itself really is just getting started. There is not enough time yet to tell

Mrs. REID. Dr. Endicott, you indicated last year that a safe cigarette was technical feasible. You said at that time that the lung cancer task force was not becoming involved. Is this something that has changed?

Dr. ENDICOTT. The lung cancer task force is an advisory committee. It is not a group doing research. It is a committee which is advisory to me. We have a committee called the Tobacco Working Group which is actively planning and certainly will participate themselves in the research. This includes scientists from Government, several different Government agencies, from universities and from the tobacco industry. They are approaching the end of the planning stage on a battery of tests to be set up. We are letting contracts to standardize the tests and now we are in the process of discussing with the Department of Agriculture and with the tobacco industry how to share the work, who should do what; how do we work together—this kind of thing. We will be off and running on a modest scale sometime late this fall.

(The following was subsequently submitted:)

SPECIAL REPORT: TOBACCO AND HEALTH

The lung cancer task force, appointed in July 1967, identified three major approaches to the reduction of lung cancer as a public health problem. Of these three approaches, the task force gave highest priority to the development of a less hazardous cigarette. The remaining two approaches were studies of industrial-atmospheric-occupational factors (chemical carcinogenesis) and efforts to improve early detection and diagnosis.

A year ago, the Less Hazardous Cigarette Working Group, now named the "Tobacco Working Group," was formed as an offshoot of the lung cancer task force and charged with responsibility for devising plans for a program of research and development to produce a less hazardous cigarette. The group was asked to concentrate its attention upon the science involved in identifying the hazardous constituents and means for their removal, leaving the technology of cigarette modification and ultimate marketing of the modified cigarette to the tobacco industry.

The Tobacco Working Group has applied itself diligently to this task, has identified the major problem areas in need of vigorous attack, and has mapped out plans which are believed appropriate to the endeavor. In the course of developing its program plans, the Tobacco Working Group has recognized an inescapable need to avoid any cigarette modification that may result in a decreased risk to one disease being offset by an increased risk to another. This potential dilemma compels employment of a broad approach to the entire problem. In recognition of this need, the Tobacco Working Group has been enlarged to include a cardiovascular pathologist from the National Heart Institute and will be further enlarged to include representatives of other disciplines germane to the relevant major disease categories.

The greatest need at this time is the development of meaningful laboratory assay systems to guide the researcher seeking to identify and modify those constituents of cigarettes and cigarette smoke believed to be responsible for specific

disease conditions in man. A vast experience has been accumulated with respect to certain animal model systems and test tube systems but there remains a need to improve the understanding of the relevance of the individual laboratory systems to the human disease experience. Furthermore, some promising laboratory models need extensive research and development before they can be employed or studied for relevance to human disease experience, and additional models for specific disease entities and abnormal physiology related to cigarette smoking remain to be discovered.

The Tobacco Working Group has had the fullest possible cooperation from a number of sources. The U.S. Department of Agriculture's representatives has brought to it the vast resources of technical information developed by that Department over the years; it is now apparent that numerous varieties of tobacco are available for production of cigarettes varying widely in tar and nicotine content and other constituents. The tobacco industry has provided important, indeed essential, support and cooperation through the participation of several of its scientists in the deliberations of the Tobacco Working Group; volumes of technical information on tobacco composition and industry technology have been provided. The University of Kentucky Tobacco and Health Research Laboratory, in collaboration with the Department of Agriculture and the tobacco industry, is devising a reference cigarette that will be made available to all scientists concerned with tobacco and health research; this cigarette will provide a basis for insuring comparability of results among numerous research laboratories.

The plans of the Tobacco Working Group, at this stage in their development, constitute a realistic and timely initiation of the attempt to deal effectively with one of the most serious public health hazards; namely, lung cancer. Currently, these plans are being broadened to include cardiovascular and pulmonary diseases which, together with lung cancer, constitute an enormous drain on the Nation's manpower resources.

Present plans call for an integrated program of interlocking grants and contracts for goal-oriented research and development related to specific tobacco and health problems. This task-oriented research should be distinguished from the broad base of scientific research supported by grants and continually adding to fundamental or basic scientific information. Initially, within the goal-oriented research, the emphasis will be upon the improvement of laboratory model systems and, through epidemiologic studies, further clarification of smoking and health relationships in man.

Mrs. Reid. Thank you.

PROTOTYPE MACHINE FOR RADIATION THERAPY

Mr. Michel. Doctor, I read somewhere, where under your radiation therapy budget, you are not building a prototype instrument that would encompass all of the advances found the last few years in a single machine because of a lack of founds. Is that right?

Dr. Endicott. We have, and I have here in the budget, $500,000 to build such a prototype in the 1970 budget.

Mr. Michel. Is that what it would take, about half a million dollars?

Dr. Endicott. Approximately. I don't have any bids yet so I cannot be sure. My guesstimate is that it will cost on the order of $500,000 to fabricate the first prototype and install it in the properly shielded place where we can begin to treat patients with it.

We would have tried through reallocation of funds within our existing resources, to go to contract this fiscal year even if it meant moving resources from another area, but the time necessary to develop the specifications and bids, the time elements were such it was obviously not going to be feasible to go to bid within this fiscal year.

Mr. Michel. Are you well enough acquainted with the cost factors

here to make some kind of crystal-ball prediction as to what these might cost in any quantity beyond the prototype?

Dr. ENDICOTT. I think that they will probably run, just for the instrument itself, and after we get the bugs out, probably would run on the order of $300,000 apiece. That is quite a reasonable figure because it is an extremely advanced and versatile instrument. It would replace multiple instruments which in the aggregate might well cost $1 million at the present time.

SURVIVAL RATE OF CANCER VICTIMS

Mr. MICHEL. The chairman made the point about these statistics that run for 5 years. As I recall, 5 years ago we had statistics for 5 years. We must have some figures that would show 10 years; do we not?

Dr. ENDICOTT. We do. It has become kind of a ritual with the medical profession to collect 5-year survival figures but we do have figures on 10 years.

Mr. MICHEL. Frankly, it shows some progress that figures were available. Conceivably you will make it for 20 years or 25. It is one of those optimistic things that you look to and like to talk about rather than the more pessimistic things. I am sorry that you only have 2 years left in being able to point to some and say, "Look, after this they went on and lived for 20, 25, 30 years." It is a psychological lift to give anyone so afflicted.

Dr. ENDICOTT. There are something on the order of one and a half million Americans today living who have had cancer and are now apparently cured. You begin to speak of them as being cured when they survived without recurrence for a period of 5 years. One of the problems is following these patients, because our population is sort of gypsy-like. The best figures that we have come from the Connecticut registry. I would be happy to look through the data that we have from that registry and see what I can give you in terms of followups for periods of 10, 20, or 30 years.

Mr. MICHEL. I would be interested in seeing that.

Dr. STEINFELD. I think the usual reason for this is that it has been assumed that a patient who has been in complete remission for 5 years is cured. This becomes even more interesting when you look at children because a child who has a tumor at age 2 could have had that tumor only as long as 2 years and 9 months. The child was not even conceived before that time. If the tumor is the size of a football and the child lives another 2 years and 9 months, and if a single cell were left behind at the time of the original treatment, that cell should have grown to the same tumor size again, to the size of a football. Therefore, in children you use the age of the child plus 9 months as the magic number after which you assume that the child is cured. Most every series of childhood tumor studied bears this out. The 5-year figure for adults differs. Overall statistical review reveals that most adults with cancer

are cured when they survive 5 years without evidence of disease. In children it is a totally different figure.

(The additional information referred to follows:)

CANCER FOLLOW-UPS—10, 20, OR 30 YEARS

The attached tables contain data on the long-term survival experience of cancer patients in the United States. The data are based on information submitted by more than 100 hospitals participating in the end results evaluation program sponsored by the National Cancer Institute. The participating hospitals include all hospitals in Connecticut, about one-third of the hospitals in California, a cluster of hospitals in Massachusetts (mainly in the Boston area), and eight teaching centers in different parts of the United States.

Survival rates are given for primary sites of cancer with a sufficiently large number of patients and with sufficiently favorable patient survival to yield meaningful 15-year and 25-year survival rates. A comprehensive review for a large number of primary sites of cancer, with 3-year, 5-year, and 10-year survival rates was published this year as End Results, Report No. 3.

To adjust for deaths from intercurrent disease, particularly important in evaluating long-term survival, patient survival is described in terms of the relative survival rate—the ratio of the survival rate observed in the patient population to the rate expected in a comparable group of people in the general population of the United States. This rate is a measure of the percentage of patients who escaped the risk of dying from he specific cancer in question. The 15-year rate may be used as an index of the percentage of patients who were successfully treated. For cancers originating in the selected sites in this illustrative report, the 15-year relative survival rates for patients diagnosed 1950 thru 1954 are:

Primary site	All stages	Localized at diagnosis
Colon	38	61
Rectum	35	57
Larynx	39	55
Female breast	41	67
Uterine cervix	50	66
Uterine corpus	67	80
Bladder	46	58
Thyroid	77	88

On the basis of the trends in 5-year and 10-year survival rates, we anticipate somewhat higher 15-year rates among patients treated in more recent years.

CANCER OF THE COLON—BY PERIOD OF DIAGNOSIS

	Male—				Female—			
	1940–49	1950–54	1955–59	1960–64	1940–49	1950–54	1955–59	1960–64
All stages:								
Number of patients	3,664	3,456	4,493	5,161	4,266	4,224	5,596	6,461
Relative survival rate (percent) at:								
5 years	29	40	43	[1]44	35	43	49	[1]49
10 years	25	38	36	.....	31	40	45	.....
15 years	23	35	.....	.....	29	40	.....	.....
20 years	21	.....	.....	.....	29	.....	.....	.....
25 years	22	.....	.....	.....	26	.....	.....	.....
Localized at diagnosis:								
Number of patients	1,427	1,414	1,812	2,014	1,660	1,717	2,250	2,626
Relative survival rate (percent) at:								
5 years	49	65	71	[1]72	57	69	77	[1]78
10 years	44	64	61	.....	53	65	72	.....
15 years	40	56	.....	.....	50	64	.....	.....
20 years	35	.....	.....	.....	49	.....	.....	.....
25 years	[2]34	.....	.....	.....	[2]44	.....	.....	.....

See footnotes at end of table, p. 251.

CANCER OF THE RECTUM—BY PERIOD OF DIAGNOSIS

	Male—				Female—			
	1940–49	1950–54	1955–59	1960–64	1940–49	1950–54	1955–59	1960–64
All stages:								
Number of patients	4,314	3,109	3,371	3,405	3,013	2,467	2,910	2,823
Relative survival rate (percent) at:								
5 years	25	38	39	[1] 39	33	44	41	[1] 43
10 years	20	33	35	----	28	39	36	----
15 years	20	31	----	----	27	38	----	----
20 years	19	----	----	----	27	----	----	----
25 years	18	----	----	----	29	----	----	----
Localized at diagnosis:								
Number of patients	1,737	1,378	1,530	1,470	1,242	1,108	1,283	1,268
Relative survival rate (percent) at:								
5 years	44	62	63	[1] 64	53	68	66	[1] 70
10 years	36	56	60	----	47	63	59	----
15 years	33	55	----	----	45	60	----	----
20 years	32	----	----	----	46	----	----	----
25 years	34	----	----	----	[2] 50	----	----	----

CANCER OF THE LARYNX—BY PERIOD OF DIAGNOSIS

All stages:								
Number of patients	1,464	1,306	1,766	2,316	114	102	171	268
Relative survival rate (percent) at:								
5 years	39	53	57	([1])	[2] 37	[2] 54	58	[1] 52
10 years	35	45	48	----	[2] 31	[2] 53	([2])	----
15 years	31	39	----	----	([2])	([2])	----	----
20 years	31	----	----	----	([2])	----	----	----
25 years	[2] 32	----	----	----	([2])	----	----	----
Localized at diagnosis:								
Number of patients	741	760	1,052	1,333	61	63	95	147
Relative survival rate (percent) at:								
5 years	58	70	76	[1] 78	[2] 51	[2] 67	[2] 74	[1] [2] 66
10 years	52	60	63	----	[2] 44	[2] 66	([2])	----
15 years	46	54	----	----	([2])	([2])	----	----
20 years	47	----	----	----	([2])	----	----	----
25 years	[2] 52	----	----	----	([2])	----	----	----

CANCER OF THE FEMALE BREAST—BY PERIOD OF DIAGNOSIS

All stages:				
Number of patients	13,274	11,285	13,335	15,558
Relative survival rate (percent) at:				
5 years	52	59	61	[1] 63
10 years	39	47	48	----
15 years	33	41	----	----
20 years	30	----	----	----
25 years	27	----	----	----
Localized at diagonsis:				
Number of patients	4,998	4,700	5,731	7,084
Relative survival rate (percent) at:				
5 years	78	82	83	[1] 85
10 years	66	72	72	----
15 years	58	67	----	----
20 years	53	----	----	----
25 years	47	----	----	----

See footnotes at end of table, p. 251.

CANCER OF THE UTERINE CERVIX—BY PERIOD OF DIAGNOSIS

	Male—				Female—			
	1940–49	1950–54	1955–59	1960–64	1940–49	1950–54	1955–59	1960–64
All stages:								
Number of patients					7,662	5,207	5,846	5,599
Relative survival rate (percent) at:								
5 years					45	57	60	[1] 60
10 years					40	52	55	----
15 years					38	50	----	----
20 years					35	----	----	----
25 years					34	----	----	----
Localized at diagnosis:								
Number of patients					3,495	2,591	3,024	2,845
Relative survival rate (percent) at:								
5 years					63	74	79	[1] 80
10 years					56	68	74	----
15 years					52	66	----	----
20 years					43	----	----	----
25 years					48	----	----	----

CANCER OF THE UTERINE CORPUS—BY PERIOD OF DIAGNOSIS

All stages:								
Number of patients					3,809	3,345	3,981	4,684
Relative survival rate (percent) at:								
5 years					60	71	72	[1] 74
10 years					56	68	69	----
15 years					55	67	----	----
20 years					53	----	----	----
25 years					51	----	----	----
Localized at diagnosis:								
Number of patients					2,428	2,373	2,803	3,467
Relative survival rate (percent) at:								
5 years					76	83	84	[1] 85
10 years					72	80	81	----
15 years					69	80	----	----
20 years					67	----	----	----
25 years					66	----	----	----

CANCER OF THE BLADDER—BY PERIOD OF DIAGNOSIS

All stages:								
Number of patients	3,263	2,809	3,779	4,343	1,201	1,054	1,301	1,630
Relative survival rate (percent) at:								
5 years	41	55	57	[1] 58	43	51	57	[1] 58
10 years	35	50	52	----	39	47	52	----
15 years	33	47	----	----	36	46	----	----
20 years	31	----	----	----	34	----	----	----
25 years	[2] 23	----	----	----	[2] 32	----	----	----
Localized at diagnosis:								
Number of patients	2,179	1,934	2,745	3,335	752	700	882	1,209
Relative survival rate (percent) at:								
5 years	54	68	69	[1] 69	58	68	73	[1] 74
10 years	46	63	63	----	52	61	66	----
15 years	44	57	----	----	49	59	----	----
20 years	42	----	----	----	47	----	----	----
25 years	[2] 30	----	----	----	[3]	----	----	----

See footnotes at end of table, p. 251.

CANCER OF THE THYROID—BY PERIOD OF DIAGNOSIS

	Male—				Female—			
	1940–49	1950–54	1955–59	1960–64	1940–49	1950–54	1955–59	1960–64
All stages:								
Number of patients	203	270	353	453	539	826	1,094	1,114
Relative survival rate (percent) at:								
5 years	50	69	70	[1] 81	68	80	83	[1] 87
10 years	46	71	71	.....	66	80	85	.....
15 years	[2] 45	[2] 71	.....	.....	66	79	.....	.....
20 years	([3])	.....	.....	.....	69	.....	.....	.....
25 years	([3])	.....	.....	.....	([3])	.....	.....	.....
Localized at diagnosis:								
Number of patients	81	97	142	178	293	436	590	612
Relative survival rate (percent) at:								
5 years	[2] 77	85	89	[1] 94	81	95	94	[1] 95
10 years	[1] 75	[2] 89	[2] 89	.....	78	93	96	.....
15 years	[2] 72	([3])	.....	.....	77	88	.....	.....
20 years	([3])	.....	.....	.....	82	.....	.....	.....
25 years	([3])	.....	.....	.....	([3])	.....	.....	.....

[1] Preliminary rate.
[2] Rates have standard errors between 5 and 10 percent.
[3] Number of patients too small to yield reliable rates.

EMPHASIS ON AGE GROUPS

Mr. MICHEL. Doctor, that prompts this one final question. In this whole area of war on cancer is there any age group where emphasis is being placed? Does it run the spectrum? Because of longer life expectancy of young people, babies or children, isn't it more important to put emphasis there than on those in the twilight of life. I am not aware that we have zeroed in on any particular age group in an all-out frontal assault. I am just raising the question as to whether or not there is any emphasis placed on the young cases as against the older age group.

Dr. ENDICOTT. I would like to give an answer which goes something like this: One must take into account the fact that much of the basic research that is going on could apply equally well without regard to age. One can't assign that to one age or another. The emphasis beyond that I think has been determined over the years largely by where the scientists felt that they could make progress without regard to age. Increasingly, childhood cancer is coming in for intensive study because these tumors tend to be very responsive in the first place to treatment and because the time that has elapsed since they were exposed to the cause, whatever it was, from the time the tumor has come up is short and the chances are better for establishing a correlation. So without this being any national policy or anything, I think that there has been quite an emphasis on cancer in the young people.

Mr. MICHEL. Thank you.

STUDY OF PESTICIDES

Mr. HULL. Dr. Endicott, let me ask you about a stand you are quoted as taking in an article 2 weeks ago in a leading medical magazine. The article was entitled "Of Mice and Men, Cancer and Pesticides," and although I'm sure you have seen it, let me describe it briefly for my

colleagues who perhaps did not see it. You said you are holding for reanalysis a 5-year, $2.6 million study of pesticides, which the publication described containing data that is "scientifically moot and politically explosive." You said you were as anxious as anyone to get the information to the public but added "we don't intend to frighten people needlessly."

According to the magazine, the preliminary data indicated that 50 out of 130 widely used pesticides and related chemical compounds studied are capable of causing tumors in mice. The magazine said you agreed that at first glance the available information reveals some new potential health hazards, but that you declined to name the 50 agents because, you said, "some compounds are certain to keep the label of carcinogen, but others will be cleared and it would not be fair to name them now."

Is the article reasonably accurate?

Dr. ENDICOTT. Yes, sir. That is true. I think that that is a quite accurate quote.

Mr. HULL. Are we more or less surrounded by possible carcinogens, doctor, that may or may not be harmful to people?

Dr. ENDICOTT. Yes, sir; I think we are.

Mr. HULL. What are the criteria to be followed generally in animal testing for carcinogens?

One thing I am curious about, doctor. Does any of the research in this 5-year, $2.6 million pesticides study overlap at all with the work done by Dr. Kotin's institute, or with what the University of Kentucky is doing with Agriculture funds?

Dr. ENDICOTT. I don't believe so. As a matter of fact, these studies were planned and the contracts were let when Dr. Kotin and Dr. Falk were on my staff. So they are acutely aware of these contracts and until about 2 years ago they were both project officers on this specific contract. They will be authors on the papers when they appear. I might say that we are giving very top priority to the analysis of the data here.

We will make it public as rapidly as possible and I don't know when your committee report will close but I would be very happy to supply for inclusion in the committee report everything that we have up to that time so that it can be included in the committee report.

Mr. HULL. We would appreciate that.

(The information follows:)

INTERIM REPORT ON STUDIES OF PESTICIDES AND OTHER AGRICULTURAL AND INDUSTRIAL CHEMICALS

BACKGROUND

In May 1963 the President's Science Advisory Committee issued a report on the "use of pesticides," recommending additional studies on "chronic effects on organs of both immature and adult animals, with particular emphasis on tumorigenicity."

In response to this need, the National Cancer Institute, through a contract with Bionetics Research Laboratories,[1] Falls Church, Va., initiated investigations concerned with long-term toxic effects of a number of pesticides and other agricultural and industrial chemicals, some of which are now in rather wide use.

[1] Recently purchased by Litton Industries, Inc.

These complex investigations, underway since 1964, constitute the largest group of such experiments performed in a single effort and involved approximately 20,000 mice and 130 chemical compounds. Evaluation of all the data is not yet complete. It should be emphasized, however, that even with this large number of animals the investigations were designed as probing experiments mainly to provide information suitable for subsequent work rather than to obtain final information for assessing human health hazards.

Also it should be emphasized that the dose levels employed in these probing experiments were purposely administered at the maximally tolerated dose levels and that they are enormously higher than those to which human beings are likely to be exposed.

preliminary analysis of the results in November and December 1968 suggested that some of the compounds administered to mice at these high dose levels might be causing tumor development. A decision was made at that time to submit an abstract for the scientific meeting of the Society of Toxicology to be held on March 10–12, 1969, in Williamsburg, Va. The abstract was accepted by the society for the presentation of a preliminary report at the March meeting. Further study of the data by NCI scientists and consultants, as well as scientists of other Government agencies, led to the conclusion that additional statisical analyses ought to be employed before the data could be interpreted with sufficient certainty as regards determination of tumorigenicity in mice under the experimental conditions employed. Because of these considerations the authors of the preliminary report decided that they should defer presentation of the paper which would have necessarily been incomplete and therefore misleading. It was understood by all that the studies would be reported fully at a later date as soon as all the analyses were completed.

Some of the additional analyses have been completed and an interim report, which is being submitted for publication in the scientific literature follows.

SCIENTIFIC REPORT

A Bioassay of Pesticides and Industrial Compounds for Tumorigenicity in Mice (An Interim Note)

SUMMARY

The tumorigenicity of selected pesticides and industrial compounds was tested by continuous oral administration to both sexes of two hybrid strains of mice, started at the age of 7 days. Maximum tolerated doses were given. It was found that administration of 11 of the 123 test compounds [2] induced a significantly elevated incidence of tumors, mostly hepatomas; such incidence was approximately the same shown by the mean of a group of positive control compounds. The 11 compounds include the insecticides p,p'–DDT, Mirex, bis (2-chloroethyl)-ether, chlorobenzilate, and strobane; the five fungicides PCNB, Avadex, Ethyl selenac, ethylene thiourea, and bis(2-hydroxyethyl) dithiocarbamic acid potassium salt; and the herbicide N-(hydroxethyl) hydrazine. Ninety compounds gave no significant indication of tumorigenicity after oral administration. The possible relevance of these experiments to human exposure is discussed.

The environment of man contains an increasing number of synthetic chemicals which may be hazardous and which require testing for toxicity and tumorigenicity. This statement is an interim report of a large scale study designed to screen selected pesticides and industrial compounds for tumorigenicity in mice. The results were considered to be of sufficient interest to the general public to warrant publication of certain portions of the study at this time. The complete experiment included bioassays on 130 compounds in two hybrid strains of mice by two routes of administration, that is, by single subcutaneous injection and continuous oral administration. Among the compounds were seven carcinogens included as positive controls (1), 104 pesticides and 19 industrial compounds. The compounds were selected for inclusion in the study on the basis of three criteria: (a) chemical structure suggesting possible carcinogenicity, (b) evidence of toxicity described in the literature suggesting potential hazards to man, or (c) widespread use of the chemicals. Even though nearly 20,000 mice were used in these studies, the several investigations were done as preliminary, probing experiments and were not expected to provide final definitive information on every compound.

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[2] Three compounds in the total of 130 were not tested by the oral administration route.

This initial report is motivated by extensive exposure of man to some of the compounds tested and focused on the data of greatest public health significance. Thus, *only the results of oral administration are herein considered.* Evaluation of these data revealed that 11 compounds are clearly tumorigentic for the strains of mice used at the high dose levels which were administered. The results for another group of 19 compounds are still inconclusive and and require further evaluation. Ninety compounds did not give significant indication of tumorigenicity in this study. A full account of the study will be published at a later date.

MATERIALS AND METHODS

Animals and housing:

"Specific pathogen free" mice were obtained from Cumberland View Farms to establish a breeding colony. Females of the C57B1/6 strain were mated with C_3H/Anf or AKR males (herein designated as strains X and Y, respectively) to obtain the two F_1 hybrid strains used in these experiments. The animals were kept in facilities having separate clean and dirty corridors with unidirectional air flow from the clean to the dirty corridor. Animal attendants wore sterile growns, masks, gloves, and shoe covers.

Chemicals, dose determination, and administraition,

Chemicals were obtained from commercial sources. Their composition was confirmed by infra-red spectroscopy, gas chromatography, or thin-layer chromatography. The chemicals were administered to the mice without further purification.

The maximum doses which could be tolerated were given. These levels were selected following a sequence of studies during which the maximum levels resulting in zero mortality were determined for a single dose, then for 6 daily doses and finally for 19 daily doses.

The maximum tolerated dose of each compound in mg/kg of body weight is shown in tables 1–4. For the tumorigenicity testing this dose was given by stomach tube beginning at 7 days of age in a suspension of the vehicle indicated on these tables. The same absolute amount of each compound was given each day until the mice were 4 weeks old; the dose was not readjusted according to weight gain during this period. After weaning at 4 weeks of age, the chemicals were mixed directly with the diet which was provided ad libitum; no vehicle was used. The concentration in the diet, listed as ppm on tables 1–4, was calculated according to the weight and food consumption of the 4 week-old mice so that once again they would receive approximately the maximum tolerated dose that had been calculated according to mg/kg body weight. The same concentration was maintained throughout the entire observation period of approximately 18 months.

Distribution of animals

At weaning, 18 mice of each sex of each strain were retained for study. Thus, 72 animals were given each compound *via* oral administration. One exception to this was the positive control compound ethyl carbamate for which there were 24 mice of each sex of each strain. Six animals were kept in each cage. The animals on test with each compound were placed in one of four rooms. Each room contained an additional group given gelatin suspension during the period when compounds were administered by stomach tube. Each room also housed at least one positive control group.

Autopsy and diagnosis

The experimental design called for autopsy at 18 months of age. The logistics of performing autopsies on a study involving almost 20,000 mice were complex, however, and the actual time of autopsy varied somewhat among the groups. These times are shown as the "weeks at term" on table 5–7. This range of termination times existed among the negative and positive control groups as well as among the experimental groups.

The autopsy procedure included an external examination and a thorough examination of thoracic and abdominal cavities with histological examination of major organs and of any grossly visible lesions. The head was not dissected. Thydroid glands were examined and sectioned in mice treated with Amitrol and one negative control group but not in other groups.

Statistical analysis

Since there were several negative control groups that differed with respect to their location within the four rooms, time of entry into the experiment and length of time until autopsy, the variance among these groups were analyzed with respect to the incidence of hepatomas, pulmonary tumors, lymphomas and total mice with tumors. The first test performed was the "chi-square test for heterogeneity of proportions after adjustment for stratification" as described by Armitage (2). The stratification in this application was the sex-strain combinations. This test was not siginificant at the 5 percent level with any of the four categories of tumors. Similar ordinary chi-square tests were done on each sex-strain category and no significant differences were found. As a final analysis of the negative control groups, the proportions of the various tumors among mice were regressed on the average time until death (3). This was done with each sex-strain combination for each of the types of tumor. In only one of the sixteen such analyses was a significant positive relationship noted: the liver tumors among strain Y males. Here of the 18 mice in one control group, OD, 5 had tumors, 3 of which were hepatomas; this group also had the greatest age at death, 89 weeks (Table 5). However, for liver tumors of strain X, there was a negative correlation between the incidence of hepatomas and the age at term. In both these cases, the figures are based on a very small number of hepatomas. Thus, the conclusion was reached from the several analyses performed that there was no significant evidence of differences among the negative control groups. In subsequent comparisons with positive controls and experimental compounds, the five negative control groups were lumped together.

The individual positive controls and experimental groups were compared with the grouped negative controls. The analysis presents the corrected relative risk (4) for each comparison. The relative risk is a measure of the tumor incidence among the treated mice as compared to the controls. The analysis was performed with four tumor groupings: hepatomas, pulmonary tumors, lymphomas, and total mice with tumors. The significance tests of each sex-strain subgroup and their various combinations are by the Mantel-Haenszel procedure (5), and the combined relative risk uses the weighted geometric mean (6) with the ½ corrections used throughout (7, 8).

As an additional test to compare the tumor incidence of mice treated with experimental compounds with those treated with positive control compounds, the sevent positive controls were lumped together and the corrected relative risk was calculated for each experimental group compared to this baseline.

RESULTS

The tumors seen in this study were principally those of the liver, lung, and lymphoid organs. Tumors of other organs were rare except in the case of two positive control compounds: Amitrol which induced thyroid carcinomas in practically all the animals; and ethyl carbamate which induced a substantial number of adenomas of the Harderian gland. Because of the rarity of other types of tumors, only tumors of the three principal organs affected are considered here. Other tumors are counted, however, in the column "Total Mice with Tumors" of the tables.

The diagnostic criteria for liver tumors were those described by Lemon (9). According to her criteria, liver tumors are diagnosed as "hepatomas" unless metastases are found; then they are designated as carcinomas. This distinction is not made to indicate that those which do not metastasize are benign, but rather because the histologic appearance of tumors of the liver of the mouse is not a good guide to their behavior. Mestastasizing hepatic-cell tumors were rare in the present study. Thus, the tables in this manuscript and the statistical calculations include the two subclassifications grouped together as "hepatomas."

Pulmonary tumors consisted principally of adenomas according to the criteria of Stewart (10). A few adenocarcinomas of the lung were noted, but because of their relative scarcity both types are considered together as "pulmonary tumors."

Tumors of the lymphoid organs were originally classified by the criteria of Dunn (11). Most of the tumors were type B reticulum-cell sarcomas. A smaller number of animals had malignant lymphomas associated with leukemia while other types of lymphoma were rare. In a study designed to investigate the tumorigenicity of chemicals rather than the pathogenesis of tumor types, it was

felt to be more meaningful to combine all of these tumors into a single category, "lymphomas."

As indicated in tables 6 and 8, the tumorigenicity of the positive control compounds was manifest primarily through the induction of hepatomas. Insosafrole was only weakly tumorigenic, but all other positive controls had an elevation of hepatomas significant at the 0.01 level. Only three of the seven positive controls had a significant increase in pulmonary tumors, and only ethyl carbamate induced a significant yield of lymphomas.

The pattern of tumor types among experimental compounds was similar to that with positive control compounds. Thus, the major evidence for tumorigenicity by experimental compounds lies in the increased incidence of hepatomas (tables 7 and 9). For each of the 11 experimental compounds listed in table 9, the increased incidence of hepatomas was significant at the 0.01 level for the sum of both sexes and both strains, the sum of males of both strains and for the males of at least one of the strains considered separately. Females were generally less affected than males, but several compounds induced hepatomas in them as well. When the relative risk for hepatoma development among these 11 experimental compounds was compared with the overall risk in the positive controls (table 10) it was found that in 16 of them, at least one sex-strain subgroup had a greater risk than the corresponding sex-strain subgroup of the combined positive controls. The remaining compound, chlorobenzilate, had a relative risk approaching that of positive controls for males of both strains.

The incidence of tumors of the lung and lymphoid organs showed a less striking elevation than hepatomas. The incidence of lymphomas in some subgroups of mice treated with p,p'-DDT, ethyl selenac, ETU, and Strobane and the incidence of pulmonary tumors among mice treated with Avadex were significantly increased over the negative controls.

Mice treated with compounds listed in table 3 did not have a significant elevation of tumor incidence at the 0.01 level of any type of tumor in any sex-strain subgroup or combination of groups after oral administration. Mice treated with compounds listed in table 4 had an elevation of tumor incidence in an uncertain range; with these compounds, additional statistical evaluation and/or experimentation will be required before an interpretation can be made.

DISCUSSION

The interpretation of these data require consideration of two questions: "What is the biologic behavior of mouse hepatomas?" and, "What relevance do studies with a single, high-dose level in one species have for evaluating the hazard of other dose levels in other species?"

Confusion arises from the fact that classical terminology of neoplastic disease would suggest that the term "hepatoma" refers to benign tumors, whereas a malignant tumor of the liver should be referred to as a "carcinoma." The opinion of Lemon (9) has already been quoted on the impossibility of making this distinction between benign and malignant liver tumors in the mouse. Andervont and Dunn (12) reported the transplantability of mouse liver tumors. They found no correlation between transplantability and morphologic characteristics. Many transplantable tumors had cytologic characteristics which were so similar to normal liver that the distinction was difficult to make upon microscopic observation. Gross observation appeared to be a more reliable criterion. Thus, the term "hepatoma" as used in this manuscript should not be considered as implying that these tumors are benign. Indeed, it seems more reasonable to conclude that the great majority had malignant potentiality.

The problem of species specificity for chemical carcinogens has been discussed by several authors (13, 14, 15) and will not be discussed in detail here. There are differences among species; some may be susceptible to tumorigenesis by a given chemical and others may show relative or absolute resistance. At the present time, there is no way to predict whether man may be more or less susceptible than the mouse to the induction of tumors by the compounds reported here. It should be stressed that the dose received by the mice was far in excess of that likely to be consumed by humans.

Another problem in interpretation lies in the fact that laboratory experiments are designed to test a single chemical and to prevent exposures to other chemicals as much as possible. The environment of man, on the other hand, contains a complex mixture of chemicals. The way in which these interact to either enhance or inhibit carcinogenicity is a complex, difficult problem which has received insufficient investigation.

ADDITIONAL COMMENT

In the report it is clear that 11 of the compounds chosen for study at very high doses are capable of producing an increased incidence of tumors in mice. Also, 90 compounds clearly did not produce an increased tumor incidence in these studies. An additional 19 compounds could not be assigned with certainty to either of these two groups. Additional studies employing larger groups of animals will be required to determine the tumorigenicity of these 19 latter compounds in mice.

These probing experiments again point out the complexity and difficulties inherent in the use of animal model systems for assessing health hazards, including tumor development. In general, animal experiments have proved their usefulness in many fields of biomedical research as aids in making judgments about man. Nevertheless, it is well-known that considerable differences in responsiveness of different animal species to a given chemical substance occur. This is generally the reason studies conducted under a variety of conditions and experimental data from more than one species of animal are needed before extrapolation to the human situation is appropriate. Moreover, it is often important to have extensive information on dose response relationships and also insight into how the administered compounds are metabolized. Therefore, caution must be exercised in interpreting the data from a single species. Thus, the data reported in this study must be examined along with all other pertinent information before conclusions as to their significance for man can be made.

An additional complexity with certain kinds of tumors is the great difficulty in determining whether they are malignant. Experts differ as to the appropriate classification, definition, and criteria of malignancy.

Although it is difficult occasionally to determine whether tumors should be classified as malignant on the basis of their microscopic morphology, most human tumors diagnosed by biopsy are deemed malignant on this basis. Some pathologists believe that malignancy cannot be definitely determined, however, unless it has been demonstrated that the tumor has spread to other sites (metastases) ; others believe transplantability of a tumor to a different animal is an important criterion for malignancy.

Mouse hepatomas clearly illustrate this difficulty. They demonstrate varying degrees of alteration from the normal structure of the liver. There is not a good correlation between structure and transplantability, though a number of hepatomas with very little change from the normal structure are known to transplant under conditions where normal liver tissue is not transplantable. Some hepatomas metastasize and others apparently do not. The longer the animal lives after the tumor is initiated, the greater the chances are that metastases will be found if the tumor does metastasize. Though available data are not extensive, it is likely that few mouse hepatomas do metastasize. Nevertheless, many mice with hepatomas will die with shortened lifespan before metastases appear.

In these studies, because of the difficulties outlined above, the tumors have been listed as hepatomas without attempts to separate them into benign or malignant categories. This has been done on the advice of leading experts, including those especially knowledgeable regarding mouse liver tumors. Since the available data do not provide a distinction between benign and malignant tumors, it is not possible at this time to categorize the positive compounds as carcinogenic.

A group of experts will, therefore, be constituted in the near future to review all pertinent information and make recommendations on whether any of the compounds should be labeled as "carcinogenic."

Further animal experiments already are underway. In addition to the 19 compounds for which tumorigenicity results were uncertain, additional chemicals in wide use will be studied as further capacity for screening becomes available. As indicated above, testing is needed in multiple species, at different dose levels, by different routes of administration, etc., under carefully controlled and standardized conditions. Thus, a sizable apparatus will be required if society's needs are to be met. Such an apparatus does not now exist, although the National Cancer Institute has initiated beginning efforts in this direction. Moreover, because of difficulties in interpreting animal data in reference to man, epidemiologic studies on human carcinogenicity must be expanded in order that the data from man can be related meaningfully to data from animal studies.

The scientific staff of the National Cancer Institute will continue to work closely with both Federal and non-Federal scientists and concerned members of society in order to resolve these problems.

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TABLE 1.—POSITIVE CONTROL COMPOUNDS

Compound No.	Common name	Chemical name	Dosage, mg./kg.	Vehicle [1]	P.p.m.
034	Urethan	Ethyl carbamate	158	0.5 percent gelatin	600
078	———	Ethylene Imine	4.64	do	13
089	Amitrol	3-Amino-1,2,4-triazole	1,000	Dis. H_2O	2,192
122	Aramite	2-(p-Tert. butyl phenoxy)-isopropyl 2'-chloroethylsulfite.	464	.5 percent gelatin	1,112
160	Dihydrosafrole	4-Propyl-1,2-methylenedioxybenzene	464	Dis. H_2O	1,400
161	Isosafrole	4-Propenyl-1,2-methylenedioxybenzene	215	do	517
162	Safrole	4-Allyl-1,2-methylenedioxybenzene	464	do	1,112

[1] Used during stomach tubing period only.

TABLE 2.—EXPERIMENTAL COMPOUNDS WHICH RESULTED IN AN ELEVATED TUMOR INCIDENCE

Compound No.	Common name	Use	Chemical name	Dosage mg./kg.	Vehicle [1]	P.p.m
060	PCNB	F	Pentachloronitrobenzene	464	0.5 percent gelatin	1,206
065	p,p'-DDT	I	2,2-Bis(p-chlorophenyl)-1,1,1-trichloroethane.	46.4	do	140
096	Mirex	I	Dodecachlorooctahydro-1,3,4-metheno-2H-cyclobuta[cd]-pentalene.	10	do	26
098	Avadex	F	2,3-Dichloroallyl diisopropyl thiolcarbamate.	215	do	560
190	———	I	Bis(2-Chloroethyl)-ether	100	Dis. H_2O	300
129	Ethyl Selenac	F	Selenium diethyl dithiocarbamate	10	0.5 percent gelatin	26
153	ETU	F	Ethylene thiourea	215	do	646
154	———	H	N-(2-Hydroxyethyl) hydrazine	2.15	Dis. H_2O	5
168	Chlorobenzilate	I	Ethyl-4,4'-Dichlorobenzilate	215	0.5 percent gelatin	603
170	———	F	Bis(2-Hydroxyethyl) dithiocarbamic acid potassium salt.	464	do	1,112
171	Strobane	I	Terpene Polychlorinates	4.64	do	11

[1] Used during stomach tubing period only.

Note: I—Insecticide; F—Fungicide; H—Herbicide; R—Rodenticide; IC—Industrial compound.

TABLE 3.—EXPERIMENTAL COMPOUNDS WHICH DID NOT CAUSE A SIGNIFICANT INCREASE IN TUMORS AFTER ORAL ADMINISTRATION

Compound No.	Common name	Use [1]	Chemical name	Dosage mg/kg	Vehicle [2]	Parts per million
024	Simazine	H	2-Chloro-4,6-bis-(ethylamino)-1,3,5-triazine	215	0.5 percent gelatin.	603
025	Propazine	H	2-Chloro-4,6-bis(isopropylamino)-1,3,5-triazine	46.4	do	102
026	Captan	F	N-Trichlorometny.thio-4-cyc.ohexene-1,2-dicarboximide	215	do	560
029	N-Propyl isome	I	Di-n-Propy.-3-methyl-6,7-methy.enedioxy-1,2,3,4-tetrahydronaphthalene 1,2-dicarboxy.ate.	2,000	do	6,000
030	2,4-D Isopropyl ester	H	2,4-Dichlorophenoxy acetic acid, isopropyl ester	46.4	do	111
031	2,4-D Buty. ester	H	2,4-Dichlorophenoxy acetic acid, n-butyl ester	46.4	do	149
032	2,4-D Isoocty lester	H	2,4-Dichlorophenoxy acetic acid, isooctyl ester	46.4	do	130
047	Sevin	I	1-Naphthyl-N-methyl carbamate	4.64	do	14
048	IPC	I	Isopropyl-N-phenyl carbamate	215	do	560
050	Dowcide-7	F	2,3,4,5,6-Pentachlorophenol	46.4	do	130
051	Zineb	F	Zinc ethylene bis thiocarbamate	464	do	1,298
053	Diuron	H	3-(3,4-Dichlorophenyl)-1,1-dimethylurea	464	do	1,400
054	Dodine	F	n-Dodecylguanidine acetate	21.5	do	82
056	Maneb	F	Manganese ethylene bis thiocarbamate	46.4	do	158
057	Maleic Hydrazide	H	1,2-Dihydrophyridazine-3,6-dione	1,000	do	3,000
058	Thiram	F	Tetramethylthiuram disulfide or bis (dimethylthiocarbamyl) disulfide	10	do	26
061	2,4,5-F	H	2,4,5-Trichlorophenoxy acetic acid	21.5	do	60
062	Ferbam	F	Ferric dimethyl dithiocarbamate	10	do	32
063	2,4-D	H	2,4-Dichlorophenoxy acetic acid	100	do	323
	2,4-D		do	46.4	do	149
066	Atrazine	H	2-Chloro-4-ethylamino-6-isopropylamino-s-triazine	21.5	do	82
069	Captax	IC	2-Mercaptobenzothiazole	100	do	323
070	Ethyl zimate	F	Zinc-diethyldithiocarbamate	100	do	260
071		IC	Phenyl isothiocyanate	46.4	do	158
074	Altax	IC	Benzothiazyl disulfide	464	do	1,577
075	Unads	F	Tetramethyl thiuram monosulfide	100	do	377
076	Dichlone	F	2,3-Dichloro-1, 4-naphthoquinone	10	do	30
077	Dicryl	H	3,4'-Dichloro-2-methyl acrylanilide	21.5	do	73
079	Nabam	F	Disodium ethylenebisdithiocarbamate	21.5	Dis. H_2O	73
080	Agerite DPPD	IC	Diphenyl-p-phenylenediamine	1,000	DMSO	3,385
082	Bismate	F	Bismuth dimethyldithiocarbamate	10	0.5 percent gelatin.	34

TABLE 3.—EXPERIMENTAL COMPOUNDS WHICH DID NOT CAUSE A SIGNIFICANT INCREASE IN TUMORS AFTER ORAL ADMINISTRATION—Continued

Compound No.	Common name	Use[1]	Chemical name	Dosage mg/kg	Vehicle[2]	Parts per million
085	Hercules-7531	H	3-(Hexahydro-4,7-methano-indan-5-yl)-1,1-dimethylurea	464	do	1,492
086	Folpet	F	N-Trichloromethylthiophthalimide	215	do	603
087	Tillam-6-E	F	Propyl ethyl-n-butyl thiocarbamate	100	Corn oil	323
090	Zetax	IC	Zinc salt of 2-mercaptobenzothiazole	1,000	0.5 percent gelatin.	3,385
091	Sulfads	F	Dipentamethylene thiuram hexasulfide	100	do	300
092	Butacide	I	Piperonyl butoxide in solvent vehicle	464	do	1,112
093	Botran	F	2,6-Dichloro-4-nitroaniline	215	do	603
094	Karathane	F	Dinitro(1-methylheptyl)-phenyl crotonate	1.0	do	3
095		H	2-(2,4,5-Trichlorophenoxy)-propionic acid	46.4	do	121
099	Cumate	F	Copper dimethyl dithiocarbamate	46.4	do	168
100	Mucochloric acid	F	α,β-Dichloro-δ-formyl acrylic acid	21.5	do	56
101		F	2-Sec.-butyl-4,6-dinitro phenol	2.15	do	7
102	Agerite Powder	IC	Phenyl-β-naphthylamine	464	do	1,206
103	Rotenone	I	Tubatoxin	1.0	do	3
104		IC	Biphenyl	215	do	517
105	Anthraquinone	F	9,10-Anthraquinone	464	do	1,206
106	ANTU	R	1-(1-Naphthyl)-2-thiourea	2.15	do	6
107		IC	Diphenylacetonitrile	215	do	560
108	Planofix; NAA	H	1-Naphthalene acetic acid	215	do	517
111	Dehydroacetic Acid	F	3-Acetyl-6-methyl-2,4-pyrandione	100	do	240
112		H	1-Naphthalene acetamide	464	do	1,298
113		IC	Diphenylcarbonate	100	do	260
114		H	Monochloroacetic acid	46.4	Dis. H_2O	149
115	Cacodylic acid	H	Dimethyl arsinic acid	46.4	Dis. H_2O	121
116	Paraxenol	IC	p-Phenyl phenol	464	0.5 percent gelatin.	1,400
117	Dowicide 1; orthoxenol	IC	o-Phenyl phenol	100	do	280
118		F	Copper-8-hydroxy quinoline	1,000	do	2,800
119	α-Chloralose	R	Anhydroglucochloral	10	do	28
120	Pma; Pmal; Pmas; Scutl; nylmerate	H	Phenyl mercuric acetate	10	do	24
121		IC	p-Methoxyphenylacetic acid	215	do	560

123	Vanguard GF	F	Ferric nitrosodimethyl dithiocarbamate and tetramethyl thiuram disulfide	100	do	240
125	Butyl zimate	F	Zinc dibutyl dithiocarbamate	1,000	do	2,600
128		F	2, 6-Dichloro-4-nitro aniline	215	do	731
130	Agerite white	IC	Sym. dibeta-naphthyl-p-phenylene diamine	100	do	280
131	Durax	IC	N-Cyclohexyl-2-benzothiazole sulfenamide	215	do	692
132	Methyl zimate	F	Zinc dimethyl dithiocarbamate	4.6	do	15
133	Methyl Selenac	F	Selenium dimethyl dithiocarbamate	10	do	34
135	Amax	IC	N-oxydiethylenebenzothiazole-2-sulfenamide	464	do	1,492
136	Ethyl cadmate	F	Cadmium diethyl ditniocarbamate	21.5	do	65
137	Agerite 150	IC	p-Isopropoxydiphenylamine	1,000	do	3,000
138	Agerite Alba	IC	Hydroquinone monobenzyl ether	464	do	1,492
139	Phenothiazine	I	(Thiodiphenylamine) dibenzo-1,4-thiazine	215	do	560
140	Vanguard N	F	Nickel dibutyl dithiocarbamate	46.4	do	158
	do	do	do	.1	do	.20
141	Vancide BN	F	Sodium bithonolate disodium 2,2′-thio bis(4,6-dichlorophenoxide)	2.15	do	7
142	Gibberellic acid	H	2,4a,7-Trihydroxy-1-methyl-8-methylenegibb-3-ene-1,10-carboxylic acid 1-4 lactone.	464	do	1,298
143		F	Dimethyl dithiocarbamic acid dimethyl amm. salt	100	do	260
145		H	α-(2,4-Dichlorophenoxy) propionic acid	100	do	260
146		H	α-(2,5-dichlorophenoxy) propionic acid	46.4	do	93
147	Ovex	F	p-Chlorophenyl-p-chlorobenzene sulfonate	464	do	1,019
148		R	Triphenyl Tin Acetate	.464	do	1,206
150	CIPC	I	Isopropyl-N(3-chlorophenyl)-carbamate	464	do	1,112
151	2-(2,4-DP)	H	2-(2,4-Dichlorophenoxy)-propionic acid	10	do	28
152	Isolan	I	1-Isopropyl-3-methyl-5-pyrazolyl-dimethyl carbamate	.0215	Dis. H_2O	.0603
157	Ethylene urea	H	2-Imidazolidinone	215	0.5 percent gelatin.	646
158	Tetrafidon	F	2,4,5,4′-Tetrachlorodiphenyl sulfone	100	do	260
159	Telodrin	I	1,3,4,5,6,7,8,8-Octachloro-3a,4,7,7a-Hexahydro-4,7-methano phthalen	.215	do	.646
165	Genite-R99	F	2,4-Dichlorophenyl benzene sulfonate	1,000	do	2,400
166	Heteroauxin	H	Indole-3-acetic acid	215	do	646
167		I	4-Dimethylamino-3,5-xylenol	100	do	300
169	Thiodan (Endosulfan)	I	6,7,8,9,10,10-Hexachloro-1,5,5a,6,9,9a-hexhydro-6,9-methano-2,3,4-benzo dioxathiepin-3-oxide.	2.15	do	6
				1.0	do	3

[1] Key: I—Insecticide; F—Fungicide; H—Herbicide; R—Rodenticide; IC—Industrial compound.

[2] Used during stomach tubing period only.

TABLE 4.—EXPERIMENTAL COMPOUNDS WHICH REQUIRE ADDITIONAL EVALUATION

Compound No.	Common name	Use [1]	Chemical name	Dosage mg/kg	Vehicle [2]	Parts per million
027	Piperonyl butoxide	I	α-[2-(2-n-Butoxyethoxy)-ethoxy]-4,5-methylenedioxy-2-propyl tuolene	100	0.5 percent gelatin.	300
028	Piperonyl sulfoxide	I	1,2-Methylenedioxy-2[2-octyl sulfinyl propyl]-benzene	46.4	do	111
049	SDDC	F	Sodium diethyldithiocarbamate	215	Dis. H_2O	692
052	o,p'-DDD	I	2-(o-Chlorophenyl)-2-(p-chlorophenyl)-1,1-dichloroethane	215	0.5 percent gelatin.	560
059	Monuron	H	3-(p-Chlorophenyl)-1,1-dimethyl urea	215	do	517
067	p,p'-DDD	I	2-2-Bis(p-chlorophenyl)-1,1-dichloroethane	100	do	300
068	Ethyl tellurac	F	Tellurium diethyldithiocarbamate	46.4	do	149
072	Perthane	I	1,1-Bis(p-ethylphenyl)-2,2-dichloroethane	215	do	815
073	Chloranil	F	Tetrachloro-p-benzoquinone	215	do	646
081	Vancide PB	F	1,2,3-Trichloro-4,6-dinitrobenzene	46.4	DMSO	121
083	Redax	IC	N-Nitrosodiphenylamine	1,000	DMSO	3,769
088	Ledate	F	Lead Dimethyldithiocarbamate	46.4	0.5 percent gelatin.	130
097	Omal; dowicide 2S	F	2,4,6-Trichlorophenol	100	do	260
110	Azobenzene	H	Diphenyldimide	21.5	do	56
124	Cyanamide	H	Calcium cyanamide	100	do	240
127	Vancide	F	2,2-Thio bis(4,6-dichlorophenol)	46.4	do	111
134	Ethyl tuads	F	Tetraethyl thiuram disulfide	100	do	323
149	Zectran	I	4-Dimethylamino-3,5-xylyl-methyl carbamate	4.64	do	11
156	CCC	H	2-Chloroethyl trimethyl-ammonium chloride	21.5	do	65

[1] Key: I—Insecticide; F—Fungicide; H—Herbicide; R—Rodenticide; IC—Industrial compound.

[2] Used during stomach tubing period only.

TABLE 5.—TUMORS AMONG NEGATIVE CONTROL MICE

Compound	Compound No.	Strain [1]	Mice at term		Total mice Necropsied		Weeks at term		Hepatomas		Pulmonary tumors		Lymphomas		Total mice with tumors	
			Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Untreated control—OD		X	14	16	17	18	88	88	1	0	2	1	1	2	6	3
		Y	18	16	18	17	89	89	3	0	2	0	1	2	5	2
Untreated control—OE		X	15	17	15	18	78	78	3	0	2	1	0	1	5	2
		Y	18	13	18	15	78	78	0	0	3	0	0	1	3	1
Untreated control—OF		X	12	18	14	18	80	80	3	0	0	1	2	1	4	2
		Y	18	17	18	18	80	80	1	0	0	0	0	0	2	0
Untreated control—O		X	16	16	17	17	81	81	1	0	1	0	2	0	7	1
		Y	17	14	18	15	81	81	0	1	3	2	0	0	3	2
Gelatin control		X	16	16	16	16	82	82	0	0	0	0	0	0	0	0
		Y	18	15	18	17	83	83	1	0	2	1	0	1	3	2
Total, negative control		X	73	83	79	87	----	----	8	0	5	3	5	4	22	8
		Y	89	75	90	82	----	----	5	1	10	3	1	4	16	7

[1] Strain X equals (C57B1/6 x C_3H/Anf)F_1; strain Y equals (C57B1/6 x AKR)F_1.

TABLE 6.—TUMORS AMONG POSITIVE CONTROL MICE

Compound	Compound No.	Strain[1]	Mice at term		Total mice Necropsied		Weeks at term		Hepatomas		Pulmonary tumors		Lymphomas		Total mice with tumors	
			Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Ethyl carbamate[2]	34	X	9	13	20	23	71	69	8	12	6	6	1	3	13	19
		Y	15	18	22	19	73	74	14	5	15	17	6	1	20	18
Ethylene imine	78	X	4	14	17	15	78	77	15	11	15	15	0	0	16	15
		Y	1	3	16	11	77	77	9	2	12	10	0	2	16	11
Amitrol	89	X	0	0	18	18	54	58	16	18	0	0	0	0	16	18
		Y	0	0	18	18	53	60	16	17	0	0	1	0	16	17
Aramite	122	X	16	16	16	17	81	78	6	1	0	1	1	1	7	8
		Y	17	16	17	16	78	81	1	0	0	3	0	0	2	4
Dihydrosafrole	160	X	16	16	17	17	82	82	10	0	4	5	1	1	12	7
		Y	15	15	17	18	82	82	8	1	5	4	0	1	11	6
Isosafrole	161	X	18	16	18	16	82	82	5	1	3	1	1	0	8	2
		Y	17	16	17	16	82	82	2	0	0	0	1	0	4	0
Safrole	162	X	14	14	17	16	82	82	11	16	0	0	0	0	11	16
		Y	17	16	17	17	82	82	3	16	0	0	0	0	3	16

[1] Strain X=(C57B1/6×C_3H/Anf)F_1; strain Y=(C57B1/6×AKR)F_1.
[2] Adenomas of the harderian gland were found in 24 mice.
[3] Carcinomas of the thryoid were found in 64 mice.

TABLE 7.—TUMORS AMONG MICE RECEIVING EXPERIMENTAL COMPOUNDS WHICH RESULTED IN A HIGH TUMOR YIELD

Compound	Compound No.	Strain[1]	Mice at term		Total mice Necropsied		Weeks at term		Hepatomas		Pulmonary tumors		Lymphomas		Total mice with tumors	
			Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
PCNB	60	X	14	18	18	18	78	78	2	4	2	1	2	0	5	5
		Y	16	17	17	17	78	78	10	1	1	0	1	1	11	2
p, p'-DDT	65	X	17	11	18	18	81	81	11	4	2	0	0	1	11	5
		Y	18	13	18	18	81	81	7	1	2	0	1	6	8	7
Mirex	96	X	0	0	18	16	59	70	6	8	0	0	0	0	7	8
		Y	0	0	15	16	59	69	5	10	0	0	0	0	5	10
Avadex	98	X	15	16	16	16	85	84	13	3	4	2	0	1	14	5
		Y	16	14	18	15	85	86	10	1	4	1	0	0	12	2
Bis(2-chloroethyl)ether	109	X	11	18	16	18	80	80	14	4	0	0	2	0	16	4
		Y	15	17	17	18	80	80	9	0	2	0	0	1	10	1
Ethyl Selenac	129	X	16	14	18	17	82	82	12	3	0	0	3	2	16	6
		Y	17	14	17	17	82	82	3	0	3	1	1	3	5	4
ETU	153	X	14	18	16	18	83	82	14	18	1	3	0	1	14	18
		Y	18	13	18	16	82	82	18	9	2	0	3	4	18	12
N-(2-Hydroxyethyl) hydrazine	154	X	17	17	17	18	79	79	8	1	1	1	1	0	10	2
		Y	18	16	18	17	79	79	10	0	1	2	0	1	10	3
Chlorobenzilate	168	X	12	17	17	18	83	83	9	0	0	1	3	1	11	2
		Y	16	18	17	18	83	83	7	0	0	2	1	1	8	3
Bis(2-Hydroxyeth-71) dithiocarbamic Stacid potassium salt robane	170	X	14	17	16	18	80	80	13	12	0	1	1	0	14	13
		Y	15	16	17	17	80	80	13	3	1	2	0	2	13	7
	171	X	10	17	15	18	80	80	2	0	1	1	5	2	8	3
		Y	18	18	18	18	80	80	11	0	0	0	0	0	11	0

[1] Strain X=(C57Bl/6 x C_3H/Anf)F_1. Strain Y=(C57Bl/6 x AKR)F_1.

TABLE 8.—RELATIVE RISK FOR DEVELOPMENT OF TUMORS AMONG MICE TREATED WITH POSITIVE CONTROL COMPOUNDS WHEN COMPARED TO NEGATIVE CONTROLS

Compound	Compound No.	Strain	Hepatomas			Pulmonary tumors			Lymphomas			Total mice with tumors		
			Male	Female	Sum	Male	Female	Sum	Male	Female	Sum	Male	Female	Sum
Ethyl carbamate	34	X	[1] 5.72	([2])	[1] 9.06	[1] 6.07	[1] 8.97	[1] 7.24	1.04	3.17	2.07	[1] 4.60	[1] 40.53	[1] 10.99
		Y	[1] 26.52	[1] 20.61	[1] 24.65	[1] 15.84	[1] 159.00	[1] 30.78	[1] 23.51	1.41	[1] 6.05	[1] 37.02	[1] 124.16	[1] 58.36
		Sum	[1] 11.66	[1] 40.07	[1] 15.17	[1] 10.57	[1] 23.52	[1] 15.22	[1] 5.04	2.35	[1] 3.29	[1] 9.35	[1] 57.84	[1] 19.10
Ethylene imine	78	X	[1] 52.15	([2])	[1] 80.91	[1] 83.982	[1] 748.43	[1] 135.39	0	0	0	[1] 28.11	([2])	[1] 52.11
		Y	[1] 19.69	14.30	[1] 18.08	[1] 21.296	[1] 159.00	[1] 37.30	0	4.59	3.77	([2])	([2])	[1] 84.81
		Sum	[1] 29.65	[1] 45.76	[1] 32.94	[1] 36.028	[1] 256.93	[1] 59.66	0	2.79	1.87	[1] 44.09	[1] 259.35	[1] 80.87
Amitrol	89	X	[1] 55.52	([2])	[1] 101.68	0	0	0	0	0	0	[1] 16.87	([2])	[1] 30.22
		Y	[1] 102.60	[1] 633.89	[1] 183.09	0	0	0	5.11	0	2.07	[1] 29.80	[1] 117.44	[1] 50.22
		Sum	[1] 74.33	[1] 1,150.55	[1] 139.42	0	0	0	1.86	0	1.04	[1] 2.35	[1] 159.79	[1] 40.16
Aramite	122	X	[1] 5.21	([2])	[1] 5.97	0	2.19	1.30	1.31	1.69	1.48	2.02	[1] 8.37	[1] 3.88
		Y	1.41	0	1.47	0	5.89	2.73	0	0	0	.73	3.63	1.75
		Sum	[3] 3.56	5.12	[3] 3.78	0	4.00	2.00	1.40	1.20	1.29	1.40	[1] 5.79	[1] 2.82
Dihydrosafrole	160	X	[1] 11.78	0	[1] 11.78	[3] 4.52	[1] 10.62	[1] 6.74	1.23	1.69	1.44	[1] 5.81	[1] 6.68	[1] 6.21
		Y	[1] 13.91	4.66	[1] 10.83	3.37	[3] 7.05	[1] 4.48	0	1.50	1.55	[1] 7.99	[1] 5.23	[1] 6.6
		Sum	[1] 12.72	4.66	[1] 11.26	[1] 3.82	[1] 8.70	[1] 5.42	1.34	1.59	1.48	[1] 6.83	[1] 5.93	[1] 6.4
Isosafrole	161	X	3.43	([2])	[3] 4.18	3.06	2.34	2.79	1.16	0	.94	2.07	1.67	1.91
		Y	2.51		2.31	0	0	0	5.42	0	2.24	1.51	0	1.20
		Sum	[3] 3.05	5.28	[3] 3.32	1.8	1.61	1.73	2.14	0	1.37	1.81	1.13	1.61
Safrole	162	X	[1] 14.88	([2])	[1] 24.53	0	0	0	0	0	0	[1] 4.52	([2])	[1] 7.55
		Y	3.75	[1] 597.67	[1] 15.56	0	0	0	0	0	0	1.09	[1] 110.73	[1] 4.99
		Sum	[1] 8.52	[1] 1,069.85	[1] 19.86	0	0	0	0	0	0	[3] 2.51	([2])	[1] 6.19

[1] Increased tumor yield significant at 0.01 level.
[2] Relative risk calculated as infinite. This figure may result from the absence of tumors in the control group and is not necessarily significant.
[3] Increased tumor yield significant at 0.05 level.

TABLE 9.—RELATIVE RISK FOR DEVELOPMENT OF TUMORS AMONG MICE TREATED WITH EXPERIMENTAL COMPOUNDS WHEN COMPARED WITH NEGATIVE CONTROLS

Compound	Compound No.	Strain	Hepatomas			Pulmonary tumors			Lymphomas			Total mice with tumors		
			Male	Female	Sum	Male	Female	Sum	Male	Female	Sum	Male	Female	Sum
PCNB	60	X	1.27	(1)	[2] 2.75	2.05	2.07	2.06	2.05	0	1.50	1.04	[2] 3.81	1.87
		Y	[3] 21.76	4.94	[3] 15.45	.70	0	.68	5.42	1.59	2.61	[3] 7.99	1.62	[3] 4.65
		Sum	[3] 6.68	[3] 12.26	[3] 7.64	1.28	1.46	1.34	2.80	1.13	1.95	[3] 2.90	2.74	[3] 2.83
p,p'-DDT	65	X	[3] 12.90	(1,3)	[3] 15.61	2.05	0	1.60	0	1.59	1.03	[3] 3.92	[3] 3.81	[3] 3.87
		Y	[3] 10.14	4.66	[3] 8.49	1.16	0	1.03	5.11	[3] 9.07	[3] 7.86	[2] 3.66	[3] 6.57	[3] 4.73
		Sum	[3] 11.55	[3] 11.80	[3] 11.59	1.51	0	1.26	1.86	[3] 5.12	[2] 3.91	[3] 3.79	[3] 5.04	[3] 4.28
Mirex	96	X	[2] 4.37	(1,3)	[2] 7.33	0	0	0	0	0	0	1.67	[3] 19.35	[3] 3.53
		Y	[3] 8.14	[3] 87.78	[3] 18.12	0	0	0	0	0	0	2.37	[3] 16.26	[3] 5.85
		Sum	[3] 5.74	[3] 107.39	[3] 11.54	0	0	0	0	0	0	1.95	[3] 12.20	[3] 4.46
Avadex	98	X	[3] 32.45	(1,3)	[3] 34.37	[2] 4.88	4.16	[3] 4.58	0	1.80	1.15	[3] 14.82	[2] 4.47	[3] 7.48
		Y	[3] 19.20	5.62	[3] 14.60	2.38	2.35	2.37	0	0	0	[3] 8.68	1.86	[3] 5.21
		Sum	[3] 24.35	12.27	[3] 21.22	[3] 3.27	3.26	[3] 3.27	0	1.27	1.06	[3] 10.57	[2] 3.18	[3] 6.19
Bis(2-Chloroethyl)-ether	109	X	[3] 48.79	(1,3)	[3] 49.88	0	0	0	2.34	0	1.65	(1,3)	2.90	[3] 5.07
		Y	[3] 17.37	0	[3] 12.53	1.24	0	1.08	0	1.50	1.55	[3] 6.32	.86	[3] 3.78
		Sum	[3] 26.52	10.42	[3] 22.74	.99	0	.87	2.20	1.08	1.61	[3] 8.73	1.95	[3] 4.24
Ethyl Selenac	129	X	[3] 16.18	(1,3)	[3] 18.39	0	0	0	3.06	2.99	3.03	[3] 16.87	[3] 5.29	[3] 8.56
		Y	3.75	0	3.24	1.85	2.06	1.91	5.42	4.21	[2] 4.54	1.99	3.36	[2] 2.49
		Sum	[3] 9.02	9.13	[3] 9.03	1.40	1.48	1.43	3.59	[2] 3.60	[3] 3.60	[3] 4.59	[3] 4.30	[3] 4.44
ETU	153	X	[3] 48.79	(1,3)	[3] 91.53	1.31	5.45	3.03	0	1.59	1.06	[3] 14.82	(1,3)	[3] 27.44
		Y	(1,3)	[3] 68.82	[3] 127.36	1.16	0	1.05	13.47	[2] 6.28	[3] 8.16	(1,3)	[3] 27.96	[3] 38.18
		Sum	[3] 82.08	[3] 158.90	[3] 106.04	1.22	3.49	1.87	4.52	[2] 3.83	[2] 4.04	[3] 24.04	[3] 42.93	[3] 32.75
N-(2-Hydroxyethyl) hydrazine	154	X	[3] 7.53	(1)	[3] 8.15	1.23	2.07	1.58	1.23	0	.95	[2] 3.58	1.42	[2] 2.64
		Y	[3] 19.20	0	[3] 1.387	.66	3.66	1.61	0	1.59	1.59	[3] 5.58	2.43	[3] 4.12
		Sum	[3] 11.64	4.83	[3] 10.46	.89	2.87	1.59	1.32	1.13	1.22	[3] 4.47	1.90	[3] 3.32
Chlorobenzilate	168	X	[3] 9.40	0	[3] 9.40	0	2.07	1.23	3.27	1.59	2.51	[3] 4.52	1.42	[3] 3.05
		Y	[3] 11.10	0	[3] 8.47	0	3.44	1.68	5.42	1.50	2.52	[3] 4.04	2.27	[3] 3.26
		Sum	[3] 10.14	0	[3] 8.93	0	2.77	1.46	3.77	1.54	2.52	[3] 4.27	1.83	[3] 3.16
Bis(2-Hydroxyethyl) dithiocarbamic acid potassium salt		X	[3] 32.45	(1,3)	[3] 49.38	0	2.07	1.25	1.31	0	.99	[3] 14.82	[3] 22.96	[3] 19.09
		Y	[3] 46.64	13.11	[3] 31.02	.70	3.66	1.66	0	2.81	2.54	[3] 13.55	[3] 7.19	[3] 9.89
		Sum	[3] 38.91	[3]36.48	[3] 38.27	.60	2.87	1.50	1.40	1.88	1.65	[3] 14.06	[3] 12.74	[3] 13.35
Strobane	171	X	1.56	0	1.56	1.40	2.07	1.69	[3] 7.10	2.81	[3] 4.88	2.90	2.11	[2] 2.56
		Y	[3] 23.84	0	[3] 16.52	0	0	0	0	0	0	[3] 6.92	0	[3] 4.73
		Sum	[3] 7.88	0	[3] 6.86	.79	1.43	1.05	[3] 5.70	1.86	[3] 3.52	[3] 4.54	1.46	[3] 3.31

[1] Relative risk calculated as infinite. This figure may result from the absence of tumors in the control group and is not necessarily significant.

[2] Increased tumor yield significant at 0.05 level.
[3] Increased tumor yield significant at 0.01 level.

TABLE 10.—RELATIVE RISK FOR DEVELOPMENT OF TUMORS AMONG MICE TREATED WITH EXPERIMENTAL COMPOUNDS WHEN COMPARED WITH TOTAL POSITIVE CONTROLS

Compound	Compound No.	Strain	Hepatomas			Total mice with tumors		
			Male	Female	Sum	Male	Female	Sum
PCNB	60	X	0.111	0.331	0.215	0.198	0.179	0.188
		Y	1.871	.163	1.005	1.281	.097	.515
		Sum	.705	.268	.466	.519	.142	.297
p,p'-DDT	65	X	1.126	.331	.658	.744	.179	.383
		Y	.872	.154	.566	.586	.391	.481
		Sum	.991	.264	.617	.658	.272	.431
Mirex	96	X	.382	1.067	.638	.316	.439	.371
		Y	.700	2.900	1.465	.379	.969	.618
		Sum	.506	1.730	.945	.344	.646	.472
Aradex	98	X	2.832	.277	.885	2.813	.210	.560
		Y	1.651	.186	.975	1.393	.111	.585
		Sum	2.032	.242	.930	1.775	.165	.573
Bis (2-Chloroethyl)-ether	109	X	4.259	.331	.902	(1)	.136	.260
		Y	1.494	0	1.029	1.014	.051	.473
		Sum	2.127	.256	.958	1.376	.101	.371
Ethyl Selenac	129	X	1.412	.258	.705	3.201	.248	.622
		Y	.323	0	.242	.319	.200	.256
		Sum	.773	.200	.498	.752	.225	.387
ETU	153	X	4.259	(1)	6.559	2.813	(1)	3.957
		Y	(1)	2.274	3.259	(1)	1.667	2.457
		Sum	6.851	3.174	4.239	4.366	2.289	2.997
N-(2-Hydroxyethyl) hydrazine	154	X	.657	.092	.399	.679	.067	.303
		Y	1.651	0	1.147	.895	.145	.443
		Sum	1.051	.079	.652	.784	.103	.371
Chlorobenzilate	168	X	.821	0	.569	.858	.067	.344
		Y	.955	0	.686	.648	.136	.348
		Sum	.884	0	.624	.741	.099	.346
Bis (2-Hydroxyethyl) dithiocarbamic acid potassium salt	170	X	2.832	2.052	2.338	2.813	1.077	1.533
		Y	4.009	.433	1.453	2.172	.429	.884
		Sum	3.422	1.094	1.869	2.406	.663	1.127
Strobane	171	X	.136	0	.100	.550	.099	.265
		Y	2.049	0	1.368	1.110	0	.704
		Sum	.831	0	.540	.799	.075	.401

[1] Infinite.

CHEMICAL CURE FOR CANCER

Mr. HULL. Dr. Endicott, I have here a report from the Washington Post of not too long ago, headlined "Chemical Cancer Cure Expected in 5 Years." It concerns a news conference held by the chief of the National Cancer Institute's drug therapy program. And it says that NCI scientists expect to find a chemical cure for several different cancers, including cancer of the lung, within 5 years.

Is this true, Doctor?

Dr. ENDICOTT. I was not at the conference but the man they are attributing this to, Dr. Zubrod, assures me he didn't say any such thing, rather, that he said it would be at least 5 years before he would know whether they were curing cancer in patients now.

Mr. HULL. Next question. Can we really expect a chemical cure for cancer within 5 years?

Dr. ENDICOTT. I'd better stick my neck out. I think it is quite clear, especially in choriocarcinoma in women, that we have chemical cures for cancer. If you want to be a real stickler and wait until these women in childbearing age, most of them even now, until they are 70 years old, then we have about 30 years to go before you can say for sure.

Mr. HULL. I am curious. I wonder how one can pinpoint in time so clearly the discovery of a cure for a disease science knows so little about. I am even more curious to know why, if NCI is so sure this can be done, you can not put more money in the project and hasten the cancer cure. Would it hasten the cure, do you think, if you had more money for basic research or for drug therapy?

Dr. ENDICOTT. Yes, sir, it would.

Mr. HULL. Would it hasten the cure, do you think, for instance, if the more than $3 million being spent by the National Clearinghouse for Smoking and Health were to be spent on this cancer-cure program?

Dr. ENDICOTT. That is a hard one for me to answer. I am not trying to evade the question.

Mr. HULL. I understand that.

Dr. ENDICOTT. Because it is hard to evaluate what they are accomplishing in terms of disease prevention. I honestly don't know. That program I think has to be looked upon largely in terms of the extent to which through education and studies of motivation, and so on, they reduce the consumption of cigarettes and, as a followup, reduce human morbidity and mortality. It is very hard to get a quantitative measure on that. It is even harder to get a quantitative measure on what you get out of spending money in cancer research. I don't really know how to answer that.

Mr. HULL. Do you have the feeling, Dr. Endicott, that overemphasis on the positive association between smoking and cancer is inhibiting the flow of any public or private moneys into basic cancer research?

Dr. ENDICOTT. Not that I am aware of, sir.

VIRAL CAUSATION OF CANCER

Mr. HULL. Another story in the Washington Post—one of less than 2 weeks ago—tells about seven cases of bone cancer in one small town in northern Minnesota. The implication of such a high incidence of such a relatively rare disease seems to be that a virus may be involved. What can you tell us, Doctor, about virus and cancer, especially now that you have Dr. Huebner as chief of your viral carcinogenesis branch?

Dr. ENDICOTT. I can tell you one thing. As a result of having Dr. Huebner with us, things are getting lively. He is a very, very busy fellow. In connection with the cluster of sarcoma cases, I think on the basis of recent progress in the study of sarcoma in animals and viruses, that we may at a fairly early date establish a casual relationship between viruses and sarcoma. In the laboratory animals there is a curious interrelationship of leukemia viruses and sarcoma viruses. They can be made to interact and in different ways to result in the production of either one disease or other diseases through laboratory manipulations. They can even be hybridized in a centrifuge by pressing them together with great centrifugal force.

There have been several such clusters reported in the case of sarcoma and other clusters in the case of leukemia. The statisticians around the country and epidemiologists are still having intensely hot debates as to what the significance of it is. I don't really know.

Mr. HULL. Thank you very much, Doctor.

Dr. ENDICOTT. Thank you, sir.

Mr. HULL. Mr. Shriver?

EFFECTS OF ANTICANCER PROGRAMS

Mr. SHRIVER. Dr. Endicott, on the first page of your statement you mention the continuing unfavorable balance of the occurrence of cancer

over the cure. Was this just a figure of speech, or does such a numerical index exist with which the committee could approximately judge the effects of anticancer programs over the years?

Dr. ENDICOTT. Mr. Shriver, there are three indexes one must consider in judging the effects of anticancer programs over the years. One index is that of incidence or the rate of occurrence of cancer per 100,000 individuals. This is a measure of the effectiveness of cancer prevention. If incidence rises, then clearly the prevention of cancer is losing ground. Another index is the cure rate, that is what percentage of patients who get cancer are cured through the forms of therapy in use at the time. The third figure is mortality rate, and this is in effect an index which is influenced by both of the others. If the rate of incidence increases more rapidly than the cure rate, then the mortality rate will rise. Actually, that is what has been happening for a good many years.

Mr. SHRIVER. Could you estimate now when the drug PolyI : C which has had promising effects on animals might be used on human patients?

Dr. ENDICOTT. We are having difficulty in formulating this drug. The solutions tend to become cloudy and coagulate. We are also encountering serious toxicity in experimental animals. When I discussed this with Dr. Zubrod a few days ago, his estimate was that he might be ready to proceed with the first human trials in about 2 months, but of course, this is only an estimate.

LUNG CANCER TASK FORCE

Mr. SHRIVER. Would you be more explicit as to what actions have been taken in response to the committee's expression of concern that the lung cancer task force use all sources and look into all aspects of this disease.

Dr. ENDICOTT. The Lung Cancer Task Force recommended five major approaches to the solution of the lung cancer problem. One was to develop new and improved techniques for early diagnosis when the chance for surgical cure is improved. We are in the process of negotiating a contract in this area and hope to have the studies underway before the end of this fiscal year.

A second recommended approach was experimentation with combination therapy in the treatment of more advanced cancers. Protocols have been developed and studies are under way using combinations of surgery and radiation, surgery and drugs and combinations using all three.

A third approach recommended was that we explore factors which predispose individuals to lung cancer, that is factors which make them more susceptible. Knowledge in this area might help us in two ways, first to be able to watch more closely those who are at greater risk and perhaps even to discover means by which susceptibility could be reduced. There are no clear-cut leads at this time, and our policy has been to encourage fundamental research in this area.

The fourth approach was to identify environmental and especially industrial environmental factors which produce lung cancer and to develop means to eliminate these factors from the environment. Increased efforts in this area are being made both in the National Cancer Institute and in the National Institute of Environmental Health Sciences through a combination of in-house research and contract research.

The fifth approach, and this is the one which the task force felt

was the most promising and should be given the highest priority, was to develop through collaboration with the tobacco industry, the Department of Agriculture and the growers of tobacco a less hazardous cigarette. We have established a tobacco working group to draw up detailed and specific plans for such a program. The working group has representatives from interested Government agencies, the Department of Agriculture and the tobacco industry as well as scientific experts drawn from nonfederal institutions. The working group is at different stages of planning in different aspects of the work. Perhaps the most rapid progress has been in developing protocols for a battery of chemical and biological tests, which can be used to assess whether modifications of the tobacco or the filter and so on represent progress in the right direction. A number of protocols have been agreed upon, and we are in the process of negotiating contracts where these tests will be standardized and put to work.

REGIONAL CANCER INSTITUTES

Mr. SHRIVER. On page 25 of the justifications it is stated that the Institute has initiated just two regional cancer centers in response to the committee's wishes that up-to-date cancer control information be widely dispersed geographically. Are more of these regional centers planned in the near future? Will more of this information become available through the regional medical program?

Dr. ENDICOTT. There has been a most heartening response to the concept of increasing the number of cancer centers or institutes not only in those areas of the country where there are none but also in densely populated areas where a cancer institute or two may already exist. In some instances the interest has been created through efforts on the part of the National Cancer Institute staff, but in many other cases the interest was spontaneous and at least preliminary planning has been carried out without our knowledge.

We have established a joint planning group with the staff of regional medical programs so as to coordinate our efforts and arrive at a plan which will take into account geographic distribution, populations to be served, the number of centers or institutes which are feasible in the light of resources and where they should be located. Shortage of funds and lack of ability to construct physical facilities will of course delay the activation of a number of them now in the planning stage.

Mr. SHRIVER. On page 32 it is stated: "The role which man's environment plays, as related to his susceptibilty to malignant disease from nonviral carcinogenesis agents, will continue to be studied with particular emphasis on prevention." Does the word, "prevention" here mean the shielding of man from these environmental carcinogens? Since there seem to be so many of these cancer-causing agents in our environment, wouldn't it be a sounder approach to emphasize studies on combating carcinogenesis within the human body?

Dr. ENDICOTT. I think it is essential that we pursue both approaches with the utmost vigor. It has already been demonstrated repeatedly that occupational cancers can be prevented by identifying the causative chemical and shielding the worker from exposure to that chemical. This is a proven method of prevention which I think we cannot afford to abandon until we know how to combat the carcinogenesis within the human body. In this area I cannot think of a single example of success except in the laboratory. In the laboratory it has been possible to coun-

teract chemical carcinogenesis with the use of protective chemicals, and it has been possible to prevent viral cancer through vaccination. Insofar as resources permit, we are intensifying our efforts in both of these areas.

Mr. SHRIVER. On page 32 you say that all leukemic children should have platelet transfusion resources available. Are these resources easily available?

Dr. ENDICOTT. Platelet transfusion resources are presently available in a mere handful of institutions in the entire country.

Mr. SHRIVER. Regarding the reductions in the fellowships and the training grants programs, the justifications state that this reflects the past administration's emphasis to the development of health services personnel rather than research personnel. Does the new administration agree with this emphasis? Are any changes being recommended?

Dr. ENDICOTT. I am sure the new administration has this matter under study, but it is my impression that a final decision has not yet been reached.

Mr. SHRIVER. Can you estimate the total amount being spent this year from all sources on cancer research? How much of this represents Federal money?

Dr. ENDICOTT. It is almost impossible to arrive at an accurate estimate of the total amount being spent this year from all sources, but I think it is safe to assume that it is in excess of $300 million and somewhere between 50 to 75 percent represents Federal money.

Mr. SHRIVER. Why is it necessary to request separate funding for the new research development and radiation therapy program—$500,000—rather than including it with the ongoing cancer therapy program?

Dr. ENDICOTT. It was not necessary to request separate funding for this program, but I felt that it would be appropriate to identify this new activity in order to have clear-cut approval of the activity by the Congress. In future requests we would be happy to consolidate it with the cancer therapy program if the committee so wishes.

Mr. SHRIVER. On page 47 it is stated that it is now certain that drugs used appropriately in major cancer treatment centers can completely control several different kinds of cancer in man. Are you speaking of leukemia and Hodgkin's disease here? How soon will these drugs be used on a wide scale? What are the problems involved, aside from final approval of the drugs?

Dr. ENDICOTT. I was referring to choriocarcinoma and Evilm's tumor as well as the diseases you mentioned. The drugs are being used on a wide scale and final approval of the drugs is not the limiting factor. The secret of success has been the intensive interrupted treatment with combinations of drugs in institutions staffed and equipped to provide special supportive care such as platelet transfusion and life islands. It is difficult to estimate how long it will take to provide enough such centers to research the total population.

Mr. SHRIVER. On page 50 you say that in addition to the two formal task forces on breast cancer and lung cancer, there are several informal task forces within the Institute. What are these?

Dr. ENDICOTT. We have task forces on the lymphomas, chronic leukemia and multiple myeloma, clinical trials, colon-rectum, and prostate-bladder.

Mr. SHRIVER. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Amounts Available for Obligation

	1969	1970
Appropriation	$185,149,500	$184,402,000
Transfer to "National Institute of Environmental Health Sciences"	- 197,000	---
Comparative transfer to "Salaries and Expenses, Office of the Director"	- 1,467,000	---
Cutback required by P.L. 90-364	- 2,067,000	---
Total obligations	181,418,500	184,402,000
Disposition of cutback:		
To be returned to the Treasury	2,067,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
31	Research		$80,052,000		$80,488,000		+$436,000
	General research support grants		(6,838,000)		(6,831,000)		(-7,000)
	Scientific evaluation grants		(151,000)		(151,000)		-----
	Specialized research centers		(12,950,000)		(12,950,000)		-----
	Leukemia research support centers		(1,500,000)		(1,500,000)		-----
36	Fellowships		4,374,000		4,201,000		-173,000
38	Training		11,641,000		11,186,000		-455,000
	Direct operations:						
40	Laboratory and clinical research	473	16,113,500	478	17,178,000	+5	+1,064,500
42	Collaborative research and development	729	64,380,000	749	66,102,000	+20	+1,722,000
54	Biometry, epidemiology, and field studies	89	1,380,000	97	1,565,000	+8	+185,000
56	Review and approval of grants	116	2,459,000	119	2,598,000	+3	+139,000
57	Program direction	57	1,019,000	58	1,084,000	+1	+65,000
	Total obligations	1464	181,418,500	1501	184,402,000	+37	+2,983,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
NATIONAL INSTITUTES OF HEALTH			
Total number of permanent positions.....	1,390	1,427	+37
Full-time equivalent of all other positions.....	35	35	---
Average number of all employees.....	1,417	1,409	-8
Personnel compensation:			
Permanent positions.....	$14,511,000	$14,650,000	+$139,000
Positions other than permanent.....	278,000	278,000	---
Other personnel compensation.....	149,000	149,000	---
Total personnel compensation.....	14,938,000	15,077,000	+ 139,000
Personnel benefits.....	1,651,000	1,667,000	+ 16,000
Travel and transportation of persons..	661,000	690,000	+ 29,000
Transportation of things.....	128,000	128,000	---
Rent, communications, and utilities...	501,000	501,000	---
Printing and reproduction.....	467,000	467,000	---
Other services.....	60,085,000	63,071,000	+2,986,000
Supplies and materials.....	3,480,500	3,486,000	+ 5,500
Equipment.....	2,550,000	2,550,000	---
Grants, subsidies and contributions...	96,067,000	95,875,000	- 192,000
Subtotal.....	180,528,500	183,512,000	+2,983,500
Deduct quarters and subsistence charges.	-10,000	-10,000	---
Total, National Institutes of Health.....	180,518,500	183,502,000	+2,983,500

Obligations by Object--continued

	1969 Estimate	1970 Estimate	Increase or Decrease
ALLOCATION TO VETERANS ADMINISTRATION			
Total number of permanent positions.....	74	74	---
Full-time equivalent of all other positions.....	10	10	---
Average number of all employees.....	82	82	---
Personnel compensation:			
Permanent positions.....	$563,000	$574,000	+$11,000
Positions other than permanent.....	137,000	137,000	---
Other personnel compensation.....	1,000	1,000	---
Total personnel compensation.....	701,000	712,000	+ 11,000
Personnel benefits.....	52,000	52,000	---
Travel and transportation of persons....	65,000	60,000	- 5,000
Transportation of things.....	1,000	1,000	---
Rent, communication, and utilities.....	2,000	2,000	---
Printing and reproduction.....	1,000	1,000	---
Supplies and materials.....	30,000	30,000	---
Equipment.....	48,000	42,000	- 6,000
Total, Veterans Administration.....	900,000	900,000	---
Total obligations by object.....	181,418,500	184,402,000	+2,983,500

Summary of Changes

1969 estimated obligations	$181,418,500
1970 estimated obligations	184,402,000
Net change	+ 2,983,500

A. Increases:	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
1. Built-in				
(a) Annualization of 1969 pay raise costs	---	---	---	+$ 36,000
2. Program:				
(a) Research grants	---	$80,052,000	---	+ 436,000
(b) Laboratory and clinical research	473	9,389,500	+ 5	+ 65,500
(c) Collaborative research and development	729	63,893,000	+20	+1,779,000
(d) Biometry, epidemiology, and field studies	89	1,289,000	+ 8	+ 185,000
(e) Review and approval of grants	116	1,541,000	+ 3	+ 35,000
(f) Program direction	57	1,019,000	+ 1	+ 15,000
Subtotal, program increases	---	---	+37	+2,515,500
3. Payment to "National Institutes of Health Management Fund" for centrally furnished services:	---	8,220,000	---	+1,060,000
Total increases	---	---	+37	+3,611,500

B. Decreases:	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
1. Program:				
(a) Fellowships.....	---	$4,374,000	---	-$ 173,000
(b) Training.....	---	11,641,000	---	- 455,000
Total decreases..	---	---	---	- 628,000
Net change.....	---	---	+37	+2,983,500

Explanation of Changes

Research grants--The program increase of $436,000 will provide an additional $443,000 for regular program grants, offset by a decrease of $7,000 in general research support grants.

Fellowships--The program decrease of $173,000 will provide for support of 192 postdoctoral and special fellowships and 93 career award and career development fellowships.

Training--The program decrease of $455,000 will provide for support of 79 graduate training and 103 cancer clinical training grants.

Laboratory and clinical research--A program increase of $65,500 is requested for five new positions and related research costs in the areas of biology and biochemistry, and of cancer immunology.

Collaborative research and development--The program increase of $1,779,000 and 20 new positions is requested for expansion of the Special Virus Cancer Research, Cancer Therapy and Lung Cancer Task Force programs; and larger increases for expansion and initiation of contract efforts in the Third National Cancer Survey and Radiation Therapy programs.

Biometry, epidemiology and field studies--The program increase of $185,000 is requested for eight new positions necessary for conduct of the Third National Cancer Survey to be carried out in conjunction with the nationwide 1970 census.

Review and approval--The program increase of $35,000 and three positions will provide scientific and administrative staff for review and approval activities specifically related to extramural programs of cancer centers and clinical investigations of anti-cancer drugs.

Program direction--The program increase of $15,000 and one position will support the operations research and systems communication aspects of the program planning activity in the Office of the Director.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action Taken or to be Taken
1969 House Report	
(1) The committee hopes that the newly established Lung Cancer Task Force will marshall the best advice from all sources and stimulate research on all the aspects of the disease (pages 18 and 19 of House Report).	(1) Plans for a major program have been developed and specific projects are being initiated.
(2) The committee indicated that one of the most hopeful, long-term prospects in cancer research is the possibility of a vaccine approach to leukemia and other forms of cancer, should they prove to be caused by viruses (page 19 of the House Report).	(2) Viruses are known to many kinds of cancers in many different animals; research is continuing in an attempt to identify viruses as causes of cancer in man.
(3) The continuation of encouraging progress in the drug treatment of leukemia and other forms of cancer classified as fast-growing tumors offers hope that effective drug treatment can also be developed for solid or slow-growing tumors. The committee indicated that the search for effective drug treatment of solid tumors warrants high priority at this time (page 19 of the House Report).	(3) Special report requested on this subject by the committee has been furnished.
(4) The committee was concerned that modern cancer centers need to be established within the Regional Medical Programs, or under other geographically dispersed arrangements, if attention given the cancer patient is to keep pace with the continued expansion and improvement of medical services in this country (page 19 of the House Report).	(4) New cancer centers have recently been initiated in Seattle, Washington and San Francisco, California, areas without major comprehensive cancer care and cancer research centers.

Item	Action Taken or to be Taken
1969 Senate Report	
(1) The committee indicated that particular emphasis should be given to the task force approach to stimulate large-scale investigations in areas that offer the greatest promise of definitive results. It is believed that concerted attacks on lung cancer, breast cancer, cancer of the colon and rectum, and cancer of the prostate and bladder can result, in the very near future, in a significant reduction in the number of lives lost to cancer each year (pages 39 and 40 of the Senate Report).	(1) The task force approach in promising areas of cancer research is being pursued. The most recent group established is the Lung Cancer Task Force.
(2) The committee was interested in the establishment of additional comprehensive cancer centers where research, training and patient care can be combined in proper balance to increase fundamental understanding and improve medical management of cancer in man. Noting the demonstrated effectiveness of the existing comprehensive centers, the committee emphasized that a start must at least be made in establishing additional, urgently needed centers (page 40 of the Senate Report).	(2) New cancer centers have recently been initiated in Seattle, Washington and San Francisco, California.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act Section 301-Research and Investigation, in general.....	Indefinite
Title IV, Part A--National Cancer Institute.....	Indefinite

PUBLIC HEALTH SERVICE ACT

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in Section 301 of the Public Health Service Act.

The Public Health Service Act, Title IV, National Research Institutes, Part A, National Cancer Institute--

"Sec. 401. The National Cancer Institute shall be a division in the National Institutes of Health."

"Sec. 402. In carrying out the purposes of section 301 with respect to cancer, the Surgeon General, through the National Cancer Institute and in cooperation with the National Cancer Advisory Council, shall--

(a) Conduct, assist, and foster researches, investigations, experiments, and studies relating to the cause, prevention, and methods of diagnosis and treatment of cancer;

(c) Provide training and instruction in technical matters relating to the diagnosis and treatment of cancer;

(d) Provide fellowships in the Institute from funds appropriated or donated for such purpose;"

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Transfer to: "National Institute of Environmental Health Sciences".....	$197,000	--------	To transfer funds covering expenses of research contracts pertaining to carcinogenesis of occupational environments.
Comparative transfer to: "Salaries and expenses, Office of the Director"....	1,467,000	--------	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH Management Fund.

National Cancer Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$75,218,000	$83,308,000	$110,203,000	$91,257,000
1961	88,869,000	102,469,000	126,375,000	111,000,000
1962	117,167,000	125,672,000	160,000,000	142,836,000
1963	139,109,000	150,409,000	158,409,000	155,742,000
1964	145,114,000	144,340,000	145,114,000	144,340,000
1965	139,714,000	138,970,000	148,970,000	148,970,000
1966	153,968,000	157,618,000	163,768,000	163,768,000
1967	163,957,000	170,656,000	175,656,000	175,656,000
1968	183,356,000	183,356,000	192,356,000	183,356,000
1969	187,707,000	182,592,000	191,592,000	185,149,500
1970	184,402,000			

Justification

National Cancer Institute

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	1,464	$17,332,000	1,501	$17,498,000	+37	+$166,000
Other expenses.....	---	164,086,500	---	166,904,000	---	+2,817,500
Total	1,464	181,418,500	1,501	184,402,000	+37	+2,983,500

General Statement

The National Cancer Institute conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling cancer in man. These objectives are pursued directly through universities, non-profit research organizations and commercial concerns supported with grants and contracts and include both laboratory and clinical studies.

The overall 1970 increase requested totals $2,983,500. This amount includes a net increase of $1,887,500 for the Institute's program; $36,000 for annualization of 1969 pay raise costs; and an increase of $1,060,000 for payment to the National Institutes of Health Management Fund for centrally furnished services.

The program increase of $436,000 for Research Grants will allow for cost-of-living increases throughout the grant program, e.g. research in cancer causation, tumor growth, host-tumor relationship, epidemiology, diagnosis, and therapy. The cancer center program will continue at the same level in 1970 as funded in 1969.

There are program decreases in Fellowship and Training Grants of $173,000 and $455,000, respectively. Within the Fellowship program, the reductions will be effected in the postdoctoral and research career development areas. In Training Grants, the reductions will be effected in the graduate portion of the program.

The direct operations portion of the budget allows for modest program increases in the following activities: $65,500, Laboratory and Clinical Research; $185,000, Biometry, Epidemiology, and Field Studies; $35,000, Review and Approval of Grants; and $15,000, Program Direction. The largest program increase within direct operations totals $1,779,000 in the area of Collaborative Research and Development. This provides small increases for Cancer Therapy ($87,000), Etiology ($87,000), and the Lung Cancer Task Force ($65,000), and larger increases are requested for development of radiation therapy equipment ($500,000), and to conduct the Third National Cancer Survey in conjunction with the 1970 Census ($1,040,000).

Research Grants

	1969 estimate	1970 estimate	Increase or Decrease
Research Projects.....	$58,613,000	$59,056,000	+$443,000
Special Programs.....	21,439,000	21,432,000	-7,000
Total Research Grants.....	80,052,000	80,488,000	+436,000

Introduction

The National Cancer Institute, through its research grant program, stimulates and supports research activities on the causation, diagnosis, treatment, prevention and control of cancer. Research projects are conducted by investigators or groups of investigators at colleges, universities, hospitals, research institutions, and various other non-profit institutions. These programs cover a broad spectrum of activity ranging from projects having single objectives to those which are broadly-based and cover multi-disciplinary areas, involving the coordination and efforts of many investigators.

Program Plans in 1969 and 1970

In basic research emphasis is placed on projects of known or potential relevance to cancer including radiation, chemical carcinogenesis, immunology, drug development, and epidemiology. There will be continued study of a variety of cancers in laboratory animals, in human patients, and in selected populations. Projects to be supported include the identification of cancer-producing agents in air, water, food, tobacco, drugs, and other related aspects of mankind's total environment.

Continuing will be studies in the techniques of therapy, and the combined use of drugs and radiation in controlling the growth and spread of cancerous cells in living organisms.

The clinical investigation of new and complex anticancer therapies will continue to be carried out in approximately 250 institutions across the nation. The investigators at these institutions are presently organized in 22 cooperating groups on the basis of the therapy under study, e.g. chemotherapy, radiation therapy, or their specialty interest, e.g. pediatrics, urology. It is estimated that these physicians, in addition to their research efforts, actively participate in the care of over 130,000 cancer patients each year and contribute significantly to the training of almost all medical students in their clinical years and one-half of the medical interns in the United States.

In conjunction with the cooperative therapeutic research program, the Institute will continue to support investigations into the control and treatment of the two major causes of death in cancer -- hemorrhage and infection. These two complications frequently occur in leukemic patients before standard therapy can be administered and prevent or compromise the administration of the new, intensive, complex and more effective therapies under investigation.

The control of hemorrhage is being investigated by approximately 30 investigators supported by Leukemia Research Support Center funds. These 30 investigators have already demonstrated that a 65% reduction in deaths due to hemorrhage in leukemic children treated at their centers can be achieved with massive transfusions of blood platelets. The success of this research indicates that all leukemic children should have platelet transfusion resources available.

Research on the control of infection is being actively pursued at four institutions where the complicated "life island" and even more complex "laminar flow" techniques are under study. These procedures attempt, by physical and chemical means, to produce a germ-free environment for the patient during the periods of greatest susceptibility to infection, and require specially trained dietetic, nursing, and microbiological supporting services. Although this "Protected Environment" program is beginning to demonstrate the beneficial effects of these procedures, further confirmation of these benefits will be sought during the coming year before plans are made to alter the scope of this program.

Funding priorities will be based on scientific merit, progress to date and program relevance. It is expected that those projects most likely to receive high priority and therefore continue to be supported involve the following: (1) factors relating to man's susceptibility to neoplastic disease, (2) research in experimental radiobiology and radiation therapy, (3) the roles played in causation of malignancies by viruses, (4) development and procurement of anticancer drugs and (5) studies in the provision of germ-free environment for the patient and the requisite dietary and nursing services.

The NCI currently supports 31 Specialized Research Centers which are performing intensive, highly specialized clinical research or laboratory research relating to prevention, diagnosis and treatment of cancer in man. These centers are organized on a single or multi-disciplinary basis which enables investigators in key disciplines to assist each other in developing and testing new principles and methods essential to the effective diagnosis and treatment of cancer. The programs at these centers are continually changing as new developments take place in cancer research and therapy. Early investigations related primarily to chemotherapeutic trials, but more recently have expanded to include host-defense mechanisms, the effect of cytotoxic drugs on immune responses, and attempts to define more precisely the mechanism of the action of other anticancer agents. The role which man's environment plays, as related to his susceptibility to malignant disease from non-viral carcinogenesis agents, will continue to be studied with particular emphasis on prevention. Studies of radiation biology, physics, and nuclear medicine are being intensified. Emphasis will continue to be given to determining the optimum methods of employing chemotherapeutic drugs and other forms of therapy and to the use of radiation as an adjuvant to surgery and chemotherapy. Grants are also used to aid institutions in the development of long-range plans for cancer research, training, and clinical services, the development of specialized equipment and resources, the evaluation of the status and progress of cancer activities, and the establishment of new centers.

Leukemia research support centers are utilized to make platelet transfusions and domiciliary care available to children under treatment for leukemia. Platelet transfusions are an essential factor in the modern treatment of childhood leukemia. Marked improvement in the results of anti-leukemic therapy have followed upon the

use of this technique. The massive platelet transfusions required have not been widely available and this program provides for the preparation, administration and evaluation of platelet transfusions in institutions across the country responsible for the care of leukemic children.

Many children with leukemia must travel long distances with their parents to the medical centers capable of providing adequate treatment. Accommodations near the hospital for short term use by these families permit more children to be treated on an out-patient basis and therefore expand the available medical facilities for these children.

Research Grants Program Analysis

	1969 estimate	1970 estimate	Increase or Decrease
Fields			
Cancer causation	$13,012,000	$13,111,000	+$99,000
Tumor growth	12,661,000	12,756,000	+95,000
Host-tumor relationship	3,107,000	3,130,000	+23,000
Epidemiology	291,000	295,000	+4,000
Diagnosis	938,000	945,000	+7,000
Therapy	16,881,000	17,008,000	+127,000
Basic research and other*	11,723,000	11,811,000	+88,000
Subtotal regular program	58,613,000	59,056,000	+443,000
General research support grants	6,838,000	6,831,000	-7,000
Scientific evaluation grants	151,000	151,000	---
Specialized research centers	12,950,000	12,950,000	---
Leukemia research support centers	1,500,000	1,500,000	---
Total research grants	80,052,000	80,488,000	+436,000

*Includes Sloan-Kettering single instrument grant

Distribution of Research Grants

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Noncompeting continuations.....	803	$41,430,000	790	$41,873,000	-13	+$443,000
Competing projects....	310	15,544,000	318	15,663,000	+8	+119,000
Supplementals.....	(117)	1,639,000	(108)	1,520,000	(-9)	-119,000
Subtotal Regular program.....	1,113	58,613,000	1,108	59,056,000	-5	+443,000
General research support.....		6,838,000		6,831,000		-7,000
Scientific evaluation.		151,000		151,000		---
Specialized research centers.....		12,950,000		12,950,000		---
Leukemia research support centers.....		1,500,000		1,500,000		---
Total research grants.....		80,052,000		80,488,000		+436,000

Fellowships

	1969 estimate	1970 estimate	Increase or Decrease
Total fellowships.....	$4,374,000	$4,201,000	-$173,000

Introduction

Several kinds of awards designed to meet particular objectives are granted under this program. The program provides research training to individuals whose career development extends from the immediate postdoctoral period through the advanced stages of scientific attainment. Postdoctoral awards are made to qualified individuals with doctoral degrees and up to three years of relevant research experience. Special fellowships are for those who have had at least three years of postdoctoral research or professional experience, or who have completed at least three years of residency training in a clinical specialty. Special fellowships may also be awarded to senior investigators who wish to undertake additional training during sabbatical leave periods.

This budget activity also supports two other types of awards made to institutions for the purpose of increasing the number of stable, full-time research career opportunities for scientists of high potential and capability in disciplines important to cancer research. Research career development awards support investigators who require five to eight years experience in order to improve their research skills and to develop a capability for independent investigation. Research career awards have been made to established investigators of high quality for a protracted period of their research careers.

Program Plans in 1969 and 1970

The fellowship program will continue in 1969 to support research training for young scientists with outstanding research potential for careers of independent research in disciplines related to cancer research. A primary goal of this program is to produce researchers who can also train others to conduct research in cancer-related fields. Continued emphasis will be given to the shortage areas of radiation therapy, surgery, hematology, and clinical pharmacology.

Funds requested for 1970 will provide for 285 awards, compared to 299 in 1969, a decrease of 14. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Fellowships

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Continuations:						
Noncompeting.....	152	$2,618,000	156	$2,834,000	+4	+$216,000
Competing.....	34	480,000	32	450,000	-2	-30,000
Supplementals.....	(6)	20,000	(8)	30,000	(+2)	+10,000
New awards.....	113	1,256,000	97	887,000	-16	-369,000
Total fellowships..	299	4,374,000	285	4,201,000	-14	-173,000

Fellowships (By type of program)

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Postdoctoral.....	131	$1,120,000	124	$1,062,000	-7	-$58,000
Special.....	69	876,000	68	876,000	-1	---
Development awards...	87	2,013,000	81	1,898,000	-6	-115,000
Career awards.....	12	365,000	12	365,000	---	---
Total fellowships..	299	4,374,000	285	4,201,000	-14	-173,000

Training Grants

	1969 estimate	1970 estimate	Increase or Decrease
Total training grants.....	$11,641,000	$11,186,000	-$455,000

Introduction

The National Cancer Institute provides grants to institutions for graduate research training for the purpose of strengthening the cancer manpower pool by establishing and maintaining stable research programs able to provide quality training in a variety of disciplines and specialties. These grants may provide stipends for those in training in the various fields related to cancer research and underwrite expenses for equipment, supplies, and training staff. Through the clinical cancer training grants program, the National Cancer Institute aims to: (1) upgrade the quality of cancer instruction offered to graduate and undergraduate medical and dental students, and to interns, residents, clinical fellows, practitioners, and scientists; (2) broaden the scope and content of current cancer teaching; and (3) undertake innovations in methodology for teaching the clinical and public health aspects of comprehensive cancer management. These grants are provided to qualified institutions to expand and advance training in the prevention, diagnosis, treatment, rehabilitation, and public health aspects of cancer.

Program Plans in 1969 and 1970

In Graduate Training, emphasis will continue to be placed in disciplines where cancer researchers are in short supply, such as radiation therapy, clinical pharmacology, and chemical carcinogenesis. The Cancer Clinical Training Program will continue to make awards to raise the quality of clinical cancer instruction, to broaden the scope and content of the cancer training in the prevention, diagnosis, treatment, rehabilitation, and public health aspects of cancer, and to coordinate and cooperate with regional medical program activities in cancer.

Of the $11,186,000 designated for training grants, $8,169,000 is required to allow for the continuation of 136 on-going non-competing projects. Approximately $2,719,000 will be needed to continue the support of 41 selected renewal projects which will be funded on a constricted basis. In view of the decrease fund availability, it will be necessary to reduce or curtail support on some on-going projects and to decrease the number of full-time equivalent trainees by 45 in fiscal year 1970.

Funds requested for 1970 will provide for 182 awards, compared to 191 in 1969, a decrease of 9. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Training Grants

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Continuations:						
Noncompeting.....	130	$7,782,000	136	$8,169,000	+6	+$387,000
Competing.....	57	3,601,000	41	2,719,000	-16	-882,000
Supplementals.....	(4)	100,000	(4)	100,000	---	---
New programs.....	4	158,000	5	198,000	+1	+40,000
Total training grants.....	191	11,641,000	182	11,186,000	-9	-455,000

Training Grants (By Program)

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Graduate.....	86	$5,978,000	79	$5,523,000	-7	-$455,000
Cancer clinical training.....	105	5,663,000	103	5,663,000	-2	---
Total training grants.....	191	11,641,000	182	11,186,000	-9	-455,000

Laboratory and Clinical Research

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	473	$5,645,000	478	$5,672,000	+5	+$27,000
Other expenses.....	---	10,468,500	---	11,506,000	---	+1,037,500
Total.....	473	16,113,500	478	17,178,000	+5	+1,064,500

Introduction

The research within the General Laboratories and Clinics area of the National Cancer Institute is designed to add to our knowledge about the basic processes of cancer and to improve methods of therapy. At the present time, while experimental biologists and physicians can describe cancer in anatomical terms and can describe structural changes in cancer cells, there is relatively little knowledge to permit us to explain how these cells grow independently, how they invade normal tissue and why they spread from one part of the body to another.

Program Plans in 1969 and 1970

Planned studies range from determining the nutrient requirements and biochemical changes in normal and malignant cells grown in tissue culture to studies of the surgical treatment of large tumors, particularly tumors that had not been previously amenable to surgery. Included are biochemical studies of the regulatory processes of protein synthesis by nucleic acids, of determination of the nutrient requirements of tumors and effects of the tumor on normal body functions. These studies result from the cooperation of a broad spectrum of biomedical specialists including biochemists, physiologists, geneticists, and a number of physician specialists.

As an example, research in immunology in both causation and control of cancer is receiving increasing attention. Evidence of immunity to tumors caused by viruses has been demonstrated in certain animals and is being sought in man. The identification of tumor-producing viruses, or immunologic specificity of tumors in man, could result in new forms of therapy. Proteins produced by an unusual tumor (multiple myeloma) have recently been discovered to have antibody activity. Such basic biologic information enhances our understanding of the cancer problem and forms the foundation for new diagnostic and therapeutic approaches to cancer.

From this research, in our own laboratories and from research in universities and cancer institutes there will continue to emerge, as there has emerged in the past, national programs in the therapy and causation of cancer.

Program plans for 1969 and 1970 envision no major changes in research emphasis. NCI laboratory and branch personnel will continue to modify their own research

programs based upon assessment of their present work and a continuing assessment of the research carried out by others within the NCI and other institutes and universities.

In 1970, increased efforts in the laboratory will be undertaken in tumor immunotherapy, research on the cell membrane (cell wall), mathematical models of physiological processes, studies of hormonally dependent tumors, the role of hormones in treatment of breast cancer, and immunological diseases related to cancer.

The program increase of $65,500 and five positions for 1970 will permit continuation and modest increases in the efforts noted above. An increase of $11,000 is requested for annualization of 1969 pay raise; there is also an increase of $988,000 for centrally furnished services for the National Institutes of Health Management Fund.

Collaborative Research and Development

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	729	$8,554,000	749	$8,648,000	+20	+$94,000
Other expenses.....	---	55,826,000	---	57,454,000	---	+1,628,000
Total.....	729	64,380,000	749	66,102,000	+20	+1,722,000

Introduction

The programs under Collaborative Research and Development include national efforts utilizing the contract research mechanism as well as investigations carried on directly in institute laboratories, to concentrate on major problems relevant to cancer. The research projects within the programs under this activity are interrelated, and are continually critically assessed and modified as research findings accumulate in these targeted programs conducted by NCI.

The National Cancer Institute established the Etiology and Cancer Therapy areas under this activity to provide strong central leadership and responsibility for carefully planned research activities. The etiology programs are focused on causes of cancer, the patterns of cancer occurrence, and their prevention. The therapy programs are concerned with finding the best methods of treating cancer through the screening, testing and clinical evaluation of drugs, as well as radiation. The Breast Cancer and Lung Cancer Task Forces comprise the Cancer Task Forces area. Programs initiated from these activities will tend to cut across organizational lines and are dependent on a variety of ongoing activities within the Institute. Research Development and Radiation Therapy is new to the budget in FY 1970 and is requested to take advantage of recent, promising leads in new, more efficient and versatile radiation therapy equipment.

The following table indicates level of support by these major program areas:

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Etiology.....	283	$30,603,000	290	$31,738,000	+7	+$1,135,000
Cancer Therapy.....	376	27,171,000	383	27,266,000	+7	+95,000
Task Forces.....	16	4,513,000	20	4,579,000	+4	+66,000
Research Development and Radiation Therapy.....	---	---	2	500,000	+2	+500,000
Supporting Services.....	54	1,606,000	54	1,608,000	---	+2,000
National Institutes of Health Management Fund	---	487,000	---	411,000	---	-76,000
Total Collaborative Research and Development.....	729	64,380,000	749	66,102,000	+20	+1,722,000

Etiology

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Total	283	$30,603,000	290	$31,738,000	+7	+$1,135,000
Office of the Scientific Director	21	818,000	21	819,000	---	+1,000
Special Virus Cancer	157	2,415,000	164	2,506,000	+7	+91,000
Contracts	---	17,882,000	---	17,882,000	---	---
Carcinogenesis	105	1,638,000	105	1,641,000	---	+3,000
Contracts	---	6,196,000	---	6,196,000	---	---
Demography Contracts	---	1,654,000	---	2,694,000	---	+1,040,000

Introduction

The Etiology area is charged with responsibility for the major share of the Institute's programmed research on cancer causation and prevention. Its investigations extend from the studies of cancer induction in defined human and animal populations to studies under laboratory conditions of the fundamental aspects of the metabolism in living systems. Scientists are responsible not only for their individual research, but also for provision of strong central leadership in and management of the conceptualization, design, and implementation of a broad, multidisciplinary integrated programmatic attack upon these problems, in collaboration with other investigators in this country and abroad.

Central to the Etiology area's approach is the concept of an interaction of multiple causative factors contributed by man as a host and by his environment. The Demography programs (further described under "Biometry, epidemiology and field studies"), in addition to providing a continuous monitoring of cancer incidence, prevalence, and mortality rates and trends, are designed to analyze defined populations having unusual risks to specific cancers or known exposure to high risk environments and to reveal statistically significant cause-and-effect associations and disassociations leading to the discovery of etiologic factors and agents. The experimentally oriented units of the Etiology area select and combine, under carefully controlled conditions, those host and environmental factors which appear to be significant in cancer etiology. From this point, they proceed to verify or deny such significance by success or failure in producing cancer in animals. It may then be seen that the synthetic approach on one hand and the analytic approach on the other are purposely united in the Etiology area to complement one another.

Program Plans in 1969 and 1970

Special Virus Cancer

The Viral Oncology area has responsibility for planning, implementing, and managing all programmed research of the National Cancer Institute on viruses in relation to cancer. This constitutes the National Cancer Institute's Special Virus Cancer Program. Scientists within this program represent all of the scientific disciplines necessary for broad operational management, as well as for studying in depth specific problems within special disciplines that are essential to the attainment of program objectives.

Principal activities are: (1) Human Leukemia Etiology and Prevention, (2) Special Animal Leukemia Ecology Studies, and (3) Solid-Tumor Virus. Two other activities--Program Resources and Logistics; and Biohazards Control and Containment--provide necessary relevant support.

In 1968, six important new animal tumor viruses were discovered. This means there are now over 60 viruses which are known to cause virtually all kinds of cancer in every major group of animals, including subhuman primates. The direct application of this laboratory information to human disease has revealed that two classes of virus-like particles can be detected and in some cases isolated from patients in different geographic regions who are afflicted with different types of cancer. Particles of one kind appear to be identical with those known to cause leukemia in laboratory animals. Particles of another type are similar in size, shape, and chemical make-up to, but different immunologically from herpes viruses known to cause fever sores or shingles in man, and cancers in some animals. The repeated detection and isolation of human viruses similar to those known to cause cancer in animals is in itself indirect suggestive evidence of virus involvement of human cancer.

We have also firmly established the growth of tumor cells in the laboratory from 180 different patients with leukemia, lymphoma and other cancers. We can now grow these living human cancer cells in the laboratory as well as produce significant quantities of purified and concentrated virus. This virus material is needed to determine its ability to induce cancer in animals and for the development of diagnostic antigens and potential test vaccines.

Largely during the past year five new highly sensitive methods have been developed for the detection and recovery of tumor viruses from animal cancers. (Helper viruses; co-cultivation of cancer cells with normal cells; DNA-RNA homology; T-antigen and other serological techniques; and centrifugal concentration.) These techniques are directly and immediately applicable to the detection and rescue of viruses in human cancers and, because of their high sensitivities, should dramatically enhance our ability to detect and recover very small amounts of complete or incomplete forms of the virus in human cancer materials.

The same virus which appears to cause infectious mononucleosis in the United States has been isolated from the tissue of 25 of 26 African children afflicted with a malignant lymphoma. In addition, 100% of African children with this disease

have high titers of antibody to this virus, as compared with less than 50% of normal children living in the same area. Moreover in the 50% of normal children, the titers are generally much lower. Studies are underway this year to attempt to determine whether these herpes-type viruses are causatively related to this lymphoma and perhaps to other human neoplasms, such as carcinoma of the nasopharynx, as well.

An improvement in the specificity of a technique for determining the presence or absence of the herpes-type associated with Burkitt lymphoma tissue culture isolates has been made. With this improved immunofluorescent technique a consistent correlation has been found between positive staining and the presence of virus particles as determined by electron microscopic examination. This means we can now conduct immunological studies in a defined system and it should help to further characterize the agent or agents.

To fully explore all new leads and approaches in investigating the role of viruses in human cancer, it is necessary to develop a capability of making field studies in populations of the natural histories of human cancers and the associated viruses in their natural ecology, plus expansion of related laboratory capabilities. The program increase of seven positions and $87,000 in 1970 will permit us to begin to develop this capability.

Carcinogenesis

The Carcinogenesis area is responsible for planning and implementing a coordinated program on the chemical induction of cancer and its prevention. The program includes research on: identification of population groups with different risks to cancers; chemical definition of the human environment; selection of chemical agents for carcinogenesis bioassays and experimental studies; development and definition of biological models for carcinogenic action of selected agents; and development and evaluation of corrective measures based on modification of the environment or on modifications of the host.

A plan for a broad program to meet responsibilities of the Chemical Carcinogenesis area was developed during the first half of the fiscal year. Implementation this year of high priority activities in this plan within available resources will be achieved through an integrated intramural and contract-supported program. Emphasis is given to the identification of cancer hazards for the human population, including studies on the roles of tobacco smoke, food additives, air pollutants, industrial chemicals, and other agents of known or suspected potential for cancer causation.

On-going investigations continue to seek the development of reliable test systems for identifying carcinogens, elucidating their modes of action, and the development of techniques for contolling these hazards in man's environment. New collaborative studies for the screening of potential carcinogens and for selection of the most effective biological test systems are being initiated, and progress continues to be made in studies on transformation of normal cells into cancer cells, immunology, and other processes involved in host reactions to

carcinogenesis. Urgent demands for the dissemination of information about suspected chemical agents have led to the reactivation of Carcinogenesis Abstracts in 1969, and plans for the establishment of a data collection and retrieval system for chemical carcinogenesis will be implemented this year.

Several new research projects will also be initiated in 1969 concerned with tobacco. These are funded in part by the Lung Cancer Task Force and are further described under the heading "Cancer Task Forces".

The Carcinogenesis programs will be continued at approximately the same level in 1970. Reallocating available funds will permit an expanded effort in the area of respiratory carcinogenesis, and a modest increase in the program of bioassay research on substances judged likely to constitute a carcinogenic hazard in man.

Demography Contracts

The Demography area is responsible for analyzing defined populations having unusual risks to specific cancers or known exposure to high risk environments, in order to reveal statistically significant cause-and-effect associations and dis-associations leading to the discovery of etiologic factors and agents.

The program increase of $1,040,000 represents funds for contracts to conduct the Third National Cancer Survey in ten large metropolitan areas and two states. The Survey is to gain information on the incidence of cancer occurrence and must be conducted in relationship to the 1970 census. The information is vital to secure knowledge not otherwise available since cancer is not a reportable disease. This program is administered by the Biometry Branch and is discussed in detail under the budget activity "Biometry, Epidemiology, and Field Studies".

Cancer Therapy

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Total	376	$27,171,000	383	$27,266,000	+7	+$95,000
Office of the Scientific Director	74	1,241,000	74	1,243,000	---	+2,000
Clinical Trials	81	1,368,000	81	1,370,000	---	+2,000
Experimental Therapeutics	46	625,000	46	626,000	---	+1,000
Cancer Chemotherapy National Service Center	56	873,000	56	875,000	---	+2,000
Therapy Contracts	---	21,241,000	---	21,241,000	---	---
Baltimore Cancer Research Center	45	923,000	52	1,011,000	+7	+88,000
Allocation to VA	74	900,000	74	900,000	---	---

Introduction

It is now certain that drugs used appropriately in major cancer treatment centers can completely control several different kinds of cancer in man. The percentage of these patients, now without evidence of disease, treated in these centers, who will be completely cured, can be assessed only some years hence. It is safe to assume that the program to find drugs to control cancer has been successful for these patients, and that the road is clearly demarcated for exploitation of these successes and for understanding the reasons for failures. As indicated under "Research Grants" in this budget, all patients with these diseases should have access to modern treatment technology. One key to this success was the development of a group of scientists and physicians within the federal establishment with the competencies and resources to pursue rapidly each important clue to drug control of cancer. The effort in chemotherapy is an example of cooperation between universities, industry, and the team within government providing the essential elements for the developmental aspects of the cancer chemotherapy program. The chemotherapy effort is far more than a "screen" for new drugs set up with contracts. It includes an intramural component where drug research goes on in laboratories and clinics and close operating relationships with industry and with universities primarily through contracts and grants, respectively. The rapid development of L-asparaginase, an enzyme used as a drug for treatment of certain tumors, is an example of this coordination. The focalizing of drug development within the National Cancer Institute permits nationwide and worldwide surveillance of every new lead, and the quick capacity to check out its importance.

The successful controls have occurred among the fast growing tumors, and the failures have been among the slowly growing tumors. These empirically established facts have directed the attention of the scientists in explaining why. It has been shown that both fast growth and drug susceptibility are related to the growth fraction of the tumor, i.e. the percent of cells in the tumor undergoing division. When the cells are not dividing, they are not a target for most drugs currently available. In the last year and at present, chemotherapy resources are being redirected in order to extend the successes among the fast growers to the more common slow growers.

Program Plans in 1969 and 1970

The target for cancer chemotherapy is the dividing tumor cell, and in order to choose the right drug and dose schedule to destroy the target, an estimate is needed of the fraction of cells in the tumor undergoing cell division. This is not possible for lack of adequate techniques. Considerable effort is underway for the development of techniques in tissue cultures, animals and patients to determine the fraction of cancer cells undergoing division. The present techniques require the uptake of radioactive labelled materials. The processing of these is slow so that efforts are underway to automate scanning under the microscope, and the counting of radioactivity by a computer. To understand growth rates, knowledge of the molecular events for the division cycle is needed, especially of the signals that switch on or off the procession of the cycle. A new branch has been established in the National Cancer Institute to concentrate on identifying the molecular target. At the same time studies are proceeding to find out about the delivery of drugs to the target, and to develop data on the concentration and time that the drug must be at the target site to kill tumor cells. Similar studies are being done in normal cells, for in order to avoid toxicity to the patient, drugs must not be kept at the same target sites in normal cells in destructive quantities. A laboratory of molecular pharmacology has just been established and a laboratory of toxicology will shortly be established to speed these studies. In addition, the Baltimore Cancer Research Center has grown so that many of these studies can be extended to patients.

Since there is considerable knowledge about different chemicals that can kill tumor cells, it is now possible to study the relations between chemical structure and tumor killing capacity, and toxicity. In this way it is hoped that one can predict the best chemical structures for activity and safety. It is planned to develop a program with the outstanding workers in this field so that computer searches and analyses will permit design predictions for superior drug structures.

The strategy for the therapy program of fast growing tumors will be to follow up on the known successes, so that as new drugs emerge, they will be added on to the present combinations, and also to encourage physicians to make use of the new knowledge. That this is happening can be seen from the sharp increase in drug utilization across the country for use in acute leukemias, Hodgkin's disease and other fast growing tumors. While these drugs have an Investigational New Drug (IND) status, the Chemotherapy program provides them to authorized clinical investigators. When their use is established industry is being encouraged to make them commercially available. New drugs such as BCNU and dimethyl triazeno imidazole

carboxamide have successfully been used in the clinic and a number of other new agents are about to go into trial, but proof of their usefulness requires four to five years of clinical assessment.

The strategy for control of the slowly growing tumors is twofold: -- control will be accomplished either by unique drugs or else by unique ways of administering the drugs already known to be effective in the fast growing tumors. The animal model tumor systems now available for predicting for the latter have been considerably improved and by further changes in these systems, it will be possible to investigate the best ways of administering the known agents. For unique drugs it is of course necessary to continue random searching through natural products, antibiotics and synthetic chemicals. It is also necessary to develop in animals an analogue or analogues of the slow growing tumors of man. Studies are under way in both spontaneous and transplanted tumors of animals and several of these are candidates for additions to the screen.

In the clinic several unique materials such as camptothecin and Poly-IC will be put into trial in slow growing tumors. Also in the clinic there will be extensive studies in three slow growing tumors -- cancers of lung, breast and colon, utilizing a surgical adjuvant design and the latest information from animal systems on the best way to improve cure rate.

There is a need, because of the more rapid development of new drugs to expand the clinical apparatus for the early studies in patients -- Phase I, early Phase II and clinical pharmacology. Internal re-arrangements within the direct operation (Bethesda, Baltimore and VA-Washington, D. C. hospitals) have filled part of this need, but in addition a new clinical contract will be undertaken this fiscal year.

Morbidity and mortality from various infections continues to be a problem in cancer patients. Work is going forward for the more adequate prevention and treatment of such infections. The "Life Island" protective concept has certainly shown that infection can be prevented. However the "Life Island" is psychologically unacceptable to many patients and requires large numbers of personnel. The Laminar Flow Room has been shown to remove both objections but requires vast renovation of existing hospitals. A contract will deliver later this year a portable laminar unit that can be inserted into existing hospital rooms. A dozen such units will be field tested under a variety of conditions to see if these can be used widely.

Treatment of established infections in patients deficient in white blood cells requires a technique for administration of white blood cells. The blood cell separator developed thru the NCI Chemotherapy program is now harvesting enough white cells to test effectiveness. Additional separators will be field tested this year.

The entire chemotherapy staff except for the clinical operation will move into Building 37 on the NIH grounds this year. This will bring together widely scattered elements of the direct operation that have operated in geographic separation at considerable disadvantages. Additional laboratory renovation and staff will be required as the program evolves.

The program increases of seven new positions and $87,000 will be utilized at the Baltimore Cancer Research Center. All other programs outlined herein for FY 1970 will be accomplished within the 1969 level of funding.

Cancer Task Forces

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Total.....	16	$4,513,000	20	$4,579,000	+4	+$66,000
Breast Cancer.....	13	413,000	13	414,000	---	+1,000
Contracts.....	---	2,700,000	---	2,700,000	---	---
Lung Cancer.....	3	300,000	7	365,000	+4	+65,000
Contracts.....	---	1,100,000	---	1,100,000	---	---

Introduction

Breast Cancer is the most common "single" type of cancer in women in the United States. Because of its variable course, it presents a unique challenge to medical practice and biological theory. The program of the Breast Cancer Task Force, established in 1966 with funds specifically earmarked by Congress in the NCI appropriation, represents an attempt to meet this challenge. The scope of the program includes basic, applied and developmental research on the cause, diagnosis and treatment of breast cancers. The Task Force approach implies an integrated multi-discipline endeavor including endocrinology, chemotherapy, surgery, radiology, virology and epidemiology.

In his Health Message for 1968, President Johnson called for the establishment of a Lung Cancer Task Force. The primary areas of research encompassed by this activity include: (1) Smoking and tobacco; (2) lung cancer causation other than smoking, including air pollution and host modification aspects; (3) diagnosis; and (4) treatment. Research efforts are in large measure based upon leads provided by biometric and epidemiological studies.

The Cancer Institute has established several other task forces or study groups. Generally, there are no specific funds allocated for their use. They exist and work through the established organizational set-up, evaluating the present state of knowledge and planning future research efforts without regard to cost figures. They identify major problem areas, formulate general research objectives, and as the state of the art permits, plan and recommend specific programs and projects for implementation.

Program Plans in 1969 and 1970

Breast Cancer Task Force

The Breast Cancer Task Force during 1969 will continue comprehensive studies of women who develop breast cancer. These include detailed pathology and measurement of steroid excretion and plasma hormones. Virus-like particles have

been identified by electron microscopy in animal and human breast cancer and in milk from women with breast cancer. These findings will be the subject of expanded studies. A central laboratory will soon become available enabling physicians throughout the country who are utilizing surgery of the pituitary or adrenal glands for the treatment of women with metastatic breast cancer to obtain estimates of urinary steroids. This may help the physician in deciding whether surgery will be successful.

Program plans for 1970 envision continued research on hormonal and non-hormonal environmental factors relating to pre-cancerous and cancerous lesions of the breast.

Lung Cancer Task Force

Plans for a major program using an integrated approach to the lung cancer problem have been developed in 1969. The program is designed to seek a balance between fundamental research on the mechanism of lung cancer causation and more applied efforts which endeavor to identify potential causative agents. Since the program embraces issues broader than cancer causation, research on heart disease, chronic degenerative lung diseases, and other biological effects will also be studied and supported jointly with other organizational components of NIH.

A subcommittee of the Lung Cancer Task Force is currently planning the investigation of techniques for developing a less hazardous cigarette. This endeavor involves the development of means for evaluating modified cigarettes and/or tobacco, the selection of biological and chemical assay systems, and the development of systems for monitoring populations and assaying cigarettes actually smoked.

A beginning toward implementing the program this year is being made by initiation of specific projects designed to evaluate the carcinogenic potential of cigarette smoke and cigarette smoke condensate, skin painting, and intra-tracheal techniques, plus epidemiologic studies of filter versus non-filter cigarette smoking.

During 1970 a program increase of four positions and $65,000 for the Lung Cancer Task Force will support the continued efforts of this program, to establish test systems for evaluating tobacco and smoke constituents, including the development of more extensive capabilities in the fields of pathology, pharmacology, and toxicology. Co-carcinogenic and promoting effects of various chemical and viral agents will also be studied.

Research Development and Radiation Therapy

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Total	---	---	2	$500,000	+2	+$500,000
In-house	---	---	2	50,000	+2	+50,000
Contracts	---	---	---	450,000	---	+450,000

Introduction

This item is new to the NCI Collaborative Research and Development budget in 1970. The establishment of this program is necessary in order to pursue promising leads which have recently been developed in the area of radiation therapy of cancer patients.

The development of megavoltage therapy units about fifteen years ago has led to improvement of radiation therapy. With the availability of super voltage radiation sources such as cobalt units, linear accelerators, and betatrons, marked improvement in the cure rate of certain malignancies has been noted. At the same time electron beam therapy was found to produce cures in superficial tumors such as may be found in the head and neck. During this period engineering and radiation physics advances indicate that an optimal dual purpose linear accelerator can be developed encompassing all of the advances found over the last few years in a single machine. This will provide the best and most advanced source of ionizing radiations to treat human cancer. The building of a prototype instrument with subsequent clinical testing has been postponed because of a lack of funds.

Program Plans in 1969 and 1970

During the past year specifications have been developed for an advanced linear accelerator designed for radiation therapy.

In 1970, it is planned to award a contract for the development of one new radiation therapy machine which will provide better radiation therapy to the cancer patient with radio-curative tumors.

Supporting Services

Supporting Services is primarily a service oriented unit of the National Cancer Institute which provides the whole Institute with selected administrative, office, and laboratory support services. Also included in this item is the editorial review and publication of the Journal of the National Cancer Institute.

In 1970, the amount of funds requested will enable the National Cancer Institute to continue this type of support to the Institute as well as the continued support of the NCI Journal. Also, in 1970 a portion of the total funds will be used to cover moving and occupancy costs related to the new cancer building.

The Collaborative Research and Development area includes a request of $19,000 for annualization of the 1969 pay raise in 1970. There is also a decrease of $76,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Biometry, Epidemiology, and Field Studies

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	89	$1,118,000	97	$1,146,000	+8	+$28,000
Other expenses.....	---	262,000	---	419,000	---	+157,000
Total.....	89	1,380,000	97	1,565,000	+8	+185,000

Introduction

Of major concern to the organizational groups funded under this budget activity are: characterization of the occurrence and behavior of cancers by specific organ sites in human populations, both in the United States and abroad; continuous monitoring of populations for cancer incidence, prevalence, mortality rates and trends, and associated demographic features such as age, sex, residence, occupation, etc.; the effects of migration on these cancer patterns; the search for environmental and other factors, including genetic features and other disease states, associated with different types of cancers; and application of advanced mathematical and statistical techniques to cancer problems.

A description of how the National Cancer Institute's Demography programs relate to other activities with which they are associated organizationally may be found in the Introduction to the Etiology Area under "Collaborative Research and Development."

Program Plans in 1969 and 1970

During 1969, studies will continue on the concurrence between congenital defects and cancers designed to provide insight into the factors responsible for childhood malignancy. Such studies are now possible from last year's activities permitting data retrieval on 22,000 death certificates in the National Registry of Childhood Cancer Deaths. A recently developed laboratory test (transformation of human skin fibroblasts in culture by cancer-producing viruses) is being applied to skin specimens obtained from persons at very high risk of cancer--to determine if the test predicts predisposition to cancer and to clarify its genesis. Human cells from certain high risk groups are transformed more easily than other cells. In the area of adult carcinoma, studies are in progress on the effects of radiation, the risks of smoking, the role of certain diseases in relation to subsequent cancer experience, and unique factors of specific occupations. These epidemiological studies of human cancer are augmented by similar studies of domestic animals. Analysis of animal-disease data will continue in expectation that the more than 50,000 case records (all diseases) now reviewed annually will yield new information on the origin of cancer in animals and thereby provide enlightenment on the genesis of human cancer.

Following publication in the fall of calendar 1968 of End Results in Cancer, Report No. 3, the most comprehensive information on major trends in the results of cancer treatment in the United States, a series of more detailed separate reports will be published in the medical journals, both general and specialized.

The Third National Cancer Survey, which must coincide with a Census year (1970), was subject to a detailed field test in 1968. Data collection is beginning this year and will continue through 1971 in ten metropolitan areas across the United States, two States, and Puerto Rico. The combined population of these areas is 25 million. The Survey will provide detailed information on cancer incidence and prevalence and several associated factors on approximately one-quarter million cancer cases, and will provide measures of the economic and societal impact of cancer on a smaller selected sample of cases which the NCI's ongoing End Results program and other studies cannot provide. The most recent survey of this type was done around the 1950 Census year, and the twenty-year-old data are now obsolete.

The Epidemiologic Pathology Unit plans to continue its close collaboration with other components of the Etiology Area. The bringing together of data and concepts from pathology, biometry, and epidemiology in an integrated fashion permits detections of additional associations of factors with cancers and affords added insights into causation and prevention. One effort exemplifying the value of this intermingling is the biometric migrant population investigations which, when coupled with pathologic observations, detected differences in cancer of the lower colon among Japanese in Hawaii from their cohorts in Japan. Studies will continue on possible environmental influences suggested by this observation.

With the exception of the Third National Cancer Survey, the functions described above will be conducted at the same level in 1970. Activities of the Survey during 1970 will include: interviewing; collecting, editing, and coding of data obtained from doctors, hospital records, death certificates, and other sources; writing and testing of computer programs; tabulating and editing data; and supervising and providing guidance to field staff. The Survey will collect detailed information, including age, sex, medical history, treatment, etc., as well as certain kinds of socio-economic information, such as cost of treatment and time lost from productive activity, on every known cancer case in the Survey area during the three-year period 1969-71. The main purpose of the Survey is to determine cancer incidence rates. Other products to be derived from the Survey are up-to-date figures on special problems, as suspected cancer hazards; and, to determine more explicitly the extent of the burden of cancer on the national economy.

The program increase of eight positions and $185,000 are requested for the management of the Third National Cancer Survey during 1970. In addition, $2,000 is requested for annualization of the 1969 pay raise. There is also a decrease of $2,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Review and Approval of Grants

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	116	$1,258,000	119	$1,270,000	+3	+$12,000
Other expenses.....	---	1,201,000	---	1,328,000	---	+127,000
Total.....	116	2,459,000	119	2,598,000	+3	+139,000

This activity under the Associate Director for Extramural Activities supports the administrative staff for all contract activities of the National Cancer Institute and both the scientific and administrative staff responsible for the review of all cancer grants. The staff obtains the necessary information regarding all grant applications and in cooperation with study groups makes recommendations for the consideration of the National Advisory Cancer Council which recommends approval or disapproval of grant applications.

The program increase of $35,000 and three positions will provide two scientists and one secretary in support of the Clinical Center Program of the NCI which is concerned with the application of the most recent developments in basic and clinical research to the care and treatment of patients with cancer. The increase is also for management of the program concerned with clinical investigation of new anti-cancer drugs in institutions throughout the country.

An increase of $2,000 is requested for annualization of the 1969 pay raise. There is an increase of $102,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Program Direction

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	57	$757,000	58	$762,000	+1	+$5,000
Other expenses.....	---	262,000	---	322,000	---	+60,000
Total.....	57	1,019,000	58	1,084,000	+1	+65,000

This activity provides for the overall administration and direction of the programs of the Institute. The Director and his staff give professional leadership and technical guidance to the varied activities of the Institute.

The program increase of $15,000 and one position will increase the operations research and systems communication aspects of the program planning activity for application in such selected areas as increased automation and computer technological utilization in laboratory operation.

An increase of $2,000 is requested for annualization of the 1969 pay raise. There is also an increase of $48,000 for centrally furnished services from the "National Institutes of Health Management Fund."

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Laboratory and Clinical Research			
Scientist	GS-14		$16,946
Chemist	GS-13		14,409
Biologist	GS-9		8,462
Biologist	GS-7		6,981
Chemist	GS-7		6,981
		(5)	53,779
Collaborative Research and Development			
(2) Medical Officer	GS-15		39,560
Scientist	GS-15		19,780
Biologist	GS-14		16,946
Scientist	GS-14		16,946
Scientist	GS-13		14,409
Medical Officer	GS-12		12,174
Biologist	GS-11		10,203
Biologist	GS-9		8,462
Chemist	GS-9		8,462
Contract Specialist	GS-9		8,462
Statistical Assistant	GS-9		8,462
(3) Biologist	GS-7		20,943
(3) Chemist	GS-7		20,943
Biologist	GS-5		5,732
Secretary	GS-5		5,732
		(20)	217,216
Biometry, Epidemiology, and Field Studies			
Mathematician	GS-15		19,780
Medical Officer	GS-14		16,946
(2) Medical Officer	GS-13		28,818
Mathematician	GS-11		10,203
Statistician	GS-11		10,203
Statistician	GS-9		8,462
Clerk-Stenographer	GS-5		5,732
		(8)	100,144
Review and Approval of Grants			
Scientist	GS-15		19,780
Scientist	GS-13		14,409
Secretary	GS-7		6,981
		(3)	41,170
Program Direction			
Public Health Program Specialist	GS-13		14,409
		(1)	14,409
Total new positions, all activities		(37)	426,718

THURSDAY, MARCH 27, 1969.

NATIONAL HEART INSTITUTE

WITNESSES

DR. THEODORE COOPER, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
R. H. HENSCHEL, EXECUTIVE OFFICER, NATIONAL HEART INSTITUTE
JOHN REEDER, FINANCIAL MANAGEMENT OFFICER, NATIONAL HEART INSTITUTE
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	6,160	6,309	6,481
Positions other than permanent	215	223	242
Other personnel compensation	50	52	52
Total personnel compensation	6,425	6,584	6,775
Personnel benefits: Civilian employees	696	703	715
Travel and transportation of persons	277	281	285
Transportation of things	98	100	109
Rent, communications, and utilities	225	242	242
Printing and reproduction	124	118	118
Other services	22,308	24,925	26,169
Supplies and materials	1,398	1,691	1,706
Equipment	910	946	964
Grants, subsidies, and contributions	128,861	125,420	126,058
Total obligations	161,322	161,010	161,141

PERSONNEL SUMMARY

Total number of permanent positions	682	600	620
Full-time equivalent of other positions	28	28	30
Average number of all employees	641	610	626
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

Program by activities:			
1. Grants:			
(a) Research	104,825	99,666	101,307
(b) Fellowships	6,769	7,604	7,309
(c) Training	17,267	18,150	17,442
2. Direct operations:			
(a) Laboratory and clinical research	12,017	13,168	13,641
(b) Collaborative research and development	10,500	17,354	18,148
(c) Biometry, epidemiology, and field studies	1,199	1,692	1,724
(d) Training activities	142	225	204
(e) Review and approval of grants	2,253	2,561	2,723
(f) Program direction	652	590	643
Total program costs, funded [1]	155,624	161,010	163,141
Change in selected resources [2]	5,698		
Total obligations	161,322	161,010	163,141

See footnote at end of table.

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)—Continued

Financing:			
Comparative transfers to other accounts	812	919	
Unobligated balance lapsing	3,813	4,999	
Budget authority	165,947	166,928	163,141
Budget authority:			
Appropriation	167,954	166,928	163,141
Transferred to other accounts	−2,007		
Appropriation (adjusted)	165,947	166,928	163,141
Relation of obligations to outlays:			
Obligations incurred, net	162,134	161,929	163,141
Obligated balance, start of year	113,458	107,853	127,072
Obligated balance, end of year	−107,853	−127,072	−134,248
Adjustments in expired accounts	−3,413		
Outlays	164,326	142,710	155,965

[1] Includes capital outlay as follows: 1968, $663,000; 1969, $946,000; 1970, $967,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $17,275,000; 1968, $22,973,000; 1969, $22,973,000; 1970, $22,973,000.

Mr. NATCHER. The committee will come to order.

We have before the committee this morning Dr. Theodore Cooper, the Director of the National Heart Institute.

Dr. Cooper, I believe this is your first appearance before our committee in the capacity of Director?

Dr. COOPER. Yes, sir.

Mr. NATCHER. With your statement you have a biographical sketch which we will insert in the record at this point.

(The biographical sketch follows:)

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name: Theodore Cooper, M.D.

Position: Director, National Heart Institute.

Birthplace and date: Trenton, N.J., December 28, 1928.

Education: June 1946, graduated from high school; June 1949, B.S., Georgetown University; June 54, M.D., St. Louis University; 1956, Ph. D., St. Louis University.

Experience: 1968–present: Director, National Heart Institute: 1967–68: Associate Director for artificial heart-myocardial infarction program. National Heart Institute; 1966–68: Professor and chairman, Department of Pharmacology and professor of surgery, University of New Mexico School of Medicine; 1964–66; Professor of surgery, St. Louis University; 1962–64: Associate professor of surgery, St. Louis University; 1961–65: Director, Center for Cardiovascular Research, St. Louis University; 1960–62: Assistant professor of surgery, director section of surgical physiology, St. Louis University; 1959–60: Surgeon, U.S. Public Health Service, National Heart Institute; 1958–59: Assistant Resident in Surgery, St. Mary's Group of Hospitals, St. Louis University; 1956–58: S.A. Surgeon, U.S. Public Health Service, National Heart Institute; 1954–55: Intern, St. Mary's Group of Hospitals, St. Louis University.

Association memberships: American Society for Clinical Investigation, American Physiological Society, Society for Experimental Biology and Medicine, American Society for Pharmacology and Experimental Therapeutics, Society of Sigma XI, International Cardiovascular Society, American College of Chest Physicians, American Society of Artificial Organs, American Federation for

Clinical Research, American Association of University Professors, American Association for Advancement of Science, American College of Cardiology.

Special awards, citations, or publications: Borden Award—St. Louis University, 1954; Who's Who in American Colleges and Universities, 1956; Research Development Award, USPHS, 1962–1966; Author or coauthor of approximately 125 publications. Editorial board, circulation, American Journal of Physiology, Journal of Applied Physiology, editorial board, Journal of Pharmocolgy and Experimental Therapeutics.

Mr. NATCHER. We will be pleased to hear from you, Dr. Cooper.

GENERAL STATEMENT

Dr. COOPER. Mr. Chairman and members of the committee, the year 1968 marked the 20th year of the National Heart Institute. The National Heart Act, passed in 1948, provided for the establishment of the Heart Institute for the purpose of conducting research into the causes, prevention, diagnosis, and treatment of cardiovascular diseases; fostering, supporting, and coordinating cardiovascular research and related activities by public and private agencies; and providing training in matters relating to the cardiovascular system.

During this 20-year period, there has been a dramatic reduction in the mortality rates from several heart diseases. For example, the mortality rate from hypertension—high blood pressure—has decreased by 46 percent; that from rheumatic heart disease by 38 percent; and that from stroke by 11 percent. Particularly heartening have been the decreases in mortality rates among persons under 65: down 46 percent for hypertension, nearly 20 percent for stroke, and 53 percent for rheumatic heart disease.

While the Institute is extremely proud of its accomplishments, I would be less than candid if I did not also call to your attention some of our failures. For example, during the past 10 years the mortality rate from arteriosclerosis has increased by 11 percent, currently accounting for approximately three-fourths of all deaths from heart diseases. The number of deaths from cardiopulmonary diseases, chiefly emphysema and chronic bronchitis, has tripled.

In the aggregate, heart diseases still account for over 1 million deaths each year, and probably cost the Nation more than $28 billion annually. I would like to very briefly describe the Institute's program in some of the major cardiovascular disease areas.

ARTERIOSCLEROSIS

Arteriosclerosis, hardening of the arteries, continues to be the leading cause of heart disease mortality, accounting for approximately 800,000 deaths per year. The disease may involve the arteries of the heart itself, those of the brain, as well as those of other parts of the circulatory system.

Our primary goal is prevention; however, we are also concerned with the reality that approximately 15 million people and possibly as many as 29 million already have some form of heart disease. Hence we attempt to balance the allocation of available resources among three activities: prevention, diagnosis, and treatment. In the case of arteriosclerosis, about 59 percent of the available $57 million which we

allocated for this general problem is used to support research on the prevention of the disease, about 32 percent for research on treatment, and the remaining 9 percent for research on improved diagnosis.

In addition to its regular systematic study of this disease, the Institute also supports within this figure a coronary drug project, the myocardial infarction program, the artificial heart program, and the national blood resource program.

The coronary drug project is designed to test the efficacy of four drugs in the prevention of a second heart attack in men between the ages of 30–64. When the study becomes fully operational next July, it will involve some 7,000 patients at approximately 53 participating clinics. The current level of funding for the study is $4.6 million. The request for 1970 is for an additional $1 million to support full operation during the new fiscal year.

The myocardial infarction program, currently funded at about $5 million per year, is aimed at reducing deaths and disability from acute heart attacks. The program currently supports nine myocardial infarction research units of a national network which is planned eventually to be increased to 12. The myocardial infarction research program places a high priority on the solution of the problem of sudden cardiac death, which accounts for nearly one-half of all deaths following a heart attack.

ARTIFICIAL HEART PROGRAM

The artificial heart program, which has been funded at about $8 million per year for the past 3 years, is concerned with the development and evaluation of devices for providing pumping assistance to a failing heart and, eventually, the development of a totally implantable artificial heart. Our major needs at the present time are accelerated progress in materials development and establishment of a critical test and evaluation program so that these circulatory assist devices can be thoroughly evaluated before being made available for clinical application.

Total replacement of the heart by transplantation was first achieved, as you know, a little over a year ago. Since then more than 121 heart transplants have been performed. The Institute currently supports programs totaling approximately $1.7 million in this area. However, this great advance must be kept in proper perspective. Even if the major problems of transplantation are solved, there will probably never be sufficient donor hearts available to meet the total need. Thus we must continue to prevent irreversible disease and to develop circulatory assist devices and, eventually, a totally implantable artificial heart.

BLOOD RESOURCE PROGRAM

The national blood resource program is related to arteriosclerosis because disorders of the blood-clotting mechanism appear to be important factors both in the development of the disease and in such consequences as heart attacks and strokes. A principal goal of the program is improved methods of acquisition, storage, distribution, and utilization of blood and blood components, for example, antihemophilic factor for the treatment of individuals afflicted with the disease hemo-

philia. The program also supports a clinical trial on the effectiveness of the drug urokinase for dissolving blood clots obstructing blood flow to the lungs. This clinical trial is an essential prelude to further evaluation of clot-dissolving agents in the treatment of heart attacks and other clotting complications of heart and blood vessel diseases. We hope to allocate about $2.8 million for this program during 1970.

CARDIORESPIRATORY DISEASES

Cardiorespiratory diseases, especially emphysema and bronchitis, cause about 25,000 deaths each year and completely disable perhaps 20,000 more individuals. As many as 14 million Americans may suffer from these diseases, and the number both of affected individuals and of deaths appear to be increasing at a most alarming rate.

Research related to the respiratory diseases is planned at the level of about $9 million during 1970. Because we place a high priority on this disease problem and because problems of the lungs are so inextricably related to the function of the heart and circulatory system, the Institute established during 1968 a special advisory committee to evaluate the current status of research in this area, to identify obstacles to continued progress, and to assess research and clinical manpower needs.

HYPERTENSION

Hypertension, or high blood pressure, continues to account for approximately 30,000 to 50,000 deaths each year and afflicts perhaps 10 to 20 million Americans. Though mortality rates have decreased some 46 percent since 1950, it remains a serious health problem both in its own right and because it contributes to illness and mortality from other cardiovascular diseases, most notably stroke. Substantial progress has been made toward controlling the disease with new drugs. However, the cause of the most common form of the disease is still unknown. Accordingly, the program is planned at the level of approximately $14 million during 1970. This will include support for three nationally organized cooperative studies on high blood pressure and kidney disease which are designed to evaluate suppressive antibacterial therapy in the treatment of certain forms of the disease, as well as to further characterize other causes and natural history of the disease.

HEART DISEASES AND HEART FAILURE

Congenital heart disease causes about 10,000 deaths each year, one-third of them during the first month of life, and most of these during the first week. The Institute's research program in this area places heavy emphasis on improvement of methods for the diagnosis and evaluation of congenital heart defects and on improvement of methods of corrective surgery. The program also includes a study of the natural history of the disease which will provide information on which the prognosis for patients with these anomalies may be predicted.

Rheumatic and infectious heart diseases have declined markedly during recent decades. Although in theory one might think that full application of existing knowledge and techniques could prevent almost

all recurrent attacks of rheumatic fever and a large proportion of initial attacks, rheumatic fever and rhemautic heart disease continue to occur and the yearly deaths from these causes number about 15,000. It is estimated that the disease affects about 1.3 million Americans. Infectious heart diseases have also declined; however, there is some evidence that some of these may be related to viral infections and there is some additional evidence that these may be increasing. The total program for congenital and infectious heart disease is planned at approximately $3 million during 1970.

Heart failure may represent a weakness of the heart muscle itself or some defect in the energy production or energy utilization mechanisms of the heart. We do not yet know; but the answer may be found in intensive studies on the ultrastructure of the heart muscle fibers or in research on the complex mechanisms by which the heart generates the chemical energy that drives the contractile process.

Cardiogenic shock and acute circulatory failure may occur with many forms of cardiac disease, and usually carry mortality rates of 70 to 90 percent. New techniques for mechanically assisting the heart and new drug therapies plus aggressive management during the period of acute crisis seem to be improving survival; however, a great deal of additional research is still needed. Approximately $18 million will be allocated for heart failure and shock research during 1970. In addition, many of the activities supported by the myocardial infarction program and the artificial heart program bear directly on the solution of these problems.

TRAINING

Since 1948 the Institute has provided training grant or fellowship support for approximately 15,000 trainees. Others have been trained in our own laboratories at the NIH. Many of these investigators have gone on to highly responsible positions in the research, medical, and academic community. The training of adequate numbers of physicians and scientists and ancillary personnel for the heart field is of vital concern to us. The 1970 request for the support of training grants and fellowships total $24,751,000.

SPECIALIZED RESEARCH CENTERS

Since 1966 the Institute has provided support for planning for specialized research centers at 14 medical schools and other institutions. Complex cardiovascular problems can often be attacked most efficiently in a special center established for this purpose. Further, the centers will shorten the time span from laboratory investigation to clinical application and will provide an important resource for training additional research and clinical manpower. The 1970 request of $925,000 may be adequate to continue the planning effort and to provide minimal operational support for perhaps one such center.

In conclusion, Mr. Chairman, the request for the National Heart Institute is $163,141,000 for 1970 as compared with an operating level of $161,009,500 in 1969, an increase of $2,131,500. Of the requested increase, $638,000 will be allocated to that portion of these disease programs supported through the grants mechanism. The remaining

$1,493,500 will be allocated among programs supported as direct operations. This will hopefully permit us to maintain our current levels of activity and productivity.

I shall be happy to answer any questions the committee may have.

CORONARY DRUG PROJECT—ATROMID-S

Mr. NATCHER. Thank you, Dr. Cooper.

Dr. Cooper, as you know, this committee has indicated its interest in the coronary drug project ever since it was started. It was largely because of this committee's interest it was started. In your statement you brought us up to date concerning the funding level and other matters pertaining to the coronary drug project. I would like to know if those people who were very much interested, and are interested in Atromid-S, are reasonably well satisfied with the way this project is going?

Dr. COOPER. As you know, Atromid-S is one of the four drugs I mentioned in the coronary drug project. There has been some suggestion by various members of the scientific community that the promise of Atromid-S warrants extension of the study to what is called the primary study of prevention; that is, the prevention of heart attacks in people who have not yet had their first one, as opposed to the plan which exists in the coronary drug project, the prevention of a recurrent heart attack.

In this respect, I believe that the information which we could gain from the coronary drug project, as it currently exists, would be most beneficial if the results are positive for Atromid-S, for the planning of a large-scale primary study which would involve many more thousands of patients.

EARMARKING OF FUNDS FOR PARTICULAR DRUGS

Mr. NATCHER. Dr. Cooper, what do you think about earmarking funds for a particular drug, such as Atromid-S. There were people who tried to get this committee to do that last year.

Generally how do you feel about earmarking funds for a particular drug such as this?

Dr. COOPER. I think if the scientific evidence warrants a study that would only use one drug because its principle of action is really known and its basic mechanism of action is unique and known, then I think a study for one drug would be justified.

Mr. NATCHER. You think the committee would be justified in taking action and earmarking a particular amount and pointing it out in the committee report or earmarking it in the bill for a particular drug?

What I have in mind, does this shut out other people, other companies, other research? Is it a bad procedure? We didn't do it last year.

Dr. COOPER. I would feel as you have said, Mr. Chairman, that until we could pinpoint the mechanism of action of the drug, there would be not even a scientific basis for restricting the suggestion to the use of one drug. Atromid-S may prove to be effective as a drug in the coronary drug project but we are not sure that its mechanism of action, if it were effective, is due to its lipid-lowering effect in the blood. There may be other mechanisms of action which could be involved.

If we are testing the principle of lipid lowering we should, as was designed, use a broad spectrum of drugs which will test the principle, give additional evidence on the mechanism of action of all the drugs. There are different chemical entities, and therefore I think it would be scientifically inappropriate to earmark for one drug at our current state of knowledge.

Mr. NATCHER. I remember last year, Dr. Marston, that Dr. Shannon was very much opposed to the earmarking of funds for this particular drug. I guess that was his theory about any drug as far as earmarking of funds. He was opposed to the practice, not opposed to this particular drug, necessarily. Would you like to say something to the committee?

How do you feel about that?

Dr. MARSTON. Yes.

I would like to support very strongly the view that Dr. Shannon expressed last year and which Dr. Cooper is also supporting here. The basic goal of this committee and of the National Heart Institute is the same, that is, to get the information that is necessary to prevent heart disease in patients.

To make the assumption, before the evidence is in, that you know that one drug has an advantage over another, puts a limit on the flexibility that is needed to get the information which all of us want and which will allow us to do something about patients with heart disease. It makes a prior judgment before you have the information that you are seeking to achieve by the test. It puts a limitation on research activities by not allowing one to modify the research plan in the light of new information that may come up during the year.

There is never going to be any holding back of the investigation of a promising therapeutic agent by the Heart Institute or by the scientific community because that is what they exist for. I would speak very strongly, as a general principle, against the earmarking of dollars for a specific drug made by a specific company to be used for a specific purpose. I think this tends to be bad science. On the other hand, as Dr. Cooper has indicated in his statement, when we find areas of promising leads it is the responsibility of the Heart Institute to call this to your attention so that you have the option of making funds available to follow up these leads. And, of course, we take very seriously—as we must—the opinions expressed in the committee report in following up these leads, much as you have already indicated.

The interest of the committee in the drug study was one of the stimuli for launching and carrying out that study.

Mr. NATCHER. Thank you.

REDUCTION IN RESEARCH PROJECTS

Dr. Cooper, in total you have an increase of $641,000 for the regular research grants programs. You indicate on page 81 of the justifications that you will be able to fund 329 fewer projects. What is the explanation for that?

Dr. COOPER. The explanation, Mr. Chairman, lies in the fact that the cost of research is increasing. The average value of the research project

individually is increasing and concomitant indirect costs are increasing. Therefore, along with our continuing commitments, it is our estimate by projection and extrapolation that this would be the net effect.

Mr. NATCHER. Dr. Cooper, how serious is this cutback in the number of projects to your Institute? Is it a serious matter?

Dr. COOPER. Yes, sir, I think it is. The program of the National Heart Institute has been oriented and focused to seek solutions to a broad spectrum of cardiovascular disease through the grants mechanism as the prime method of support. We have a relatively small collaborative line. When we lose grant support we are restricting our programs, as we have been for the last 2 or 3 years, with a constant reduction in the number of investigators that we can involve in the solution of these problems, total problems. I think the net effect in grants programs, since our basic large element of programing is grant supported, will be seriously affected.

OBSTRUCTIVE RESPIRATORY DISEASE

Mr. NATCHER. On page 75 you refer to an alarming upsurge of the obstructive respiratory diseases demonstrated by a six-fold increase in mortality in the last 25 years. What do you include, Dr. Cooper, as obstructive respiratory diseases?

Dr. COOPER. The main ones that are usually referred to are emphysema, chronic bronchitis, but there are other disease entities that are involved in the concept of obstructive pulmonary diseases, certain asthmatic conditions. Certain vascular obstructive diseases may also be included in this concept. It is not clear at all what the etiology of this spectrum of pulmonary disease is and what their basic mechanisms might be. Some of them may be related to chemical irritations, some of them may be related to immunological problems, some of them to allergic problems, but some related to primary vascular phenomena of the small vessels that supply the very fragile tissues of the lung, one of the more common being pulmonary embolism.

Mr. FLOOD. As we all know, there has been an alarming upsurge in these problems. Is there a cause, or are there causes, for this alarming upsurge? One cause or a group of causes?

Dr. COOPER. There are a group of causes, in my opinion, Mr. Chairman, all of which have not yet been defined. As I just mentioned, some of these may be related to chemical irritants that are taken into the lung through the ventilatory process. Others may be related to vascular phenomena that reach the lung and do damage through the circulatory route.

Mr. FLOOD. What are we doing about it now and what should we be doing?

Dr. COOPER. I feel that we need to expand the number of people that are involved in investigating this problem, people that are trained comprehensively in diseases of the chest so that they can deal adequately both with the circulatory aspects and the ventilatory aspects as a primary initial requirement. We need new ideas in the ways to attack this problem.

ANTHRACOSILICOSIS

Mr. FLOOD. I come from the hard coal fields in Pennsylvania. We have been born and raised in the midst of this terrible scourage in the hard coal mining industry. We call it miner's asthma, anthracosilicosis. Are you acquainted with this problem? Have you ever seen this thing?

Dr. COOPER. I have seen patients, yes, sir, with anthracosilicosis.

Mr. FLOOD. We know it to be a progressive condition. We know there is no cure but we certainly would like to be sure that you people know what a wasting disease this is and how it strikes men down. I have seen men who were in high school with me—I didn't work in the mines but I worked on the outside—but boys who were in my class in high school worked so many years in the mines and they would look 20, 25 years older than me, just because of what this horrible thing had been doing to them after they acquired this lung condition.

It can only get progressively worse, as I suppose you know. Any attention you can give to it will be welcomed. There is great publicity in the soft coal areas as a result of some of these tragedies. They call it black lung. We never used that term. Of course, it is pretty much the same condition, isn't it, as miner's asthma?

Dr. COOPER. In its end effects, yes, sir. Again, there are two ways to approach it. As a preventive public health problem, one can do all one can to prevent exposure to environmental conditions which one feels might be able to reduce the incidence of the disease.

Mr. FLOOD. Do you examine in your business, or your people, ways and means to prevent the inhalation of these dusts which produce these conditions?

Dr. COOPER. No, sir.

The programs of the heart institute have not been directed in this area. This has been largely the responsibility of the Chronic Disease Bureau.

Mr. FLOOD. Is it not in your shop?

Dr. COOPER. No, sir.

Mr. FLOOD. Would you like to get into it? Is there any reason why you should?

Dr. COOPER. I think the area that we should get into is expanded activity in understanding at the level of the lung tissue, why the inhalation of these products causes both vascular damage and damage to the alveolar structures, the basic structures of the breathing apparatus.

Mr. FLOOD. Have you seen these lungs?

Dr. COOPER. Yes, sir.

HEART TRANSPLANTS

Mr. FLOOD. I notice that you testified in your statement about this very exciting business of heart transplants. I saw a recent newspaper article saying that apparently we have gone too far too fast. The original dramatic impact of the heart transplant is wearing off and the great dangers are now coming to the fore.

I understand that it is not as great a panacea as we thought it was a year or two ago. Are you engaged in this area?

Dr. COOPER. Yes, sir. The Institute, as I mentioned in my opening statement, supports research amounting to about $1.7 million. There have been 121 cases of heart transplants performed as of this week with about 34 survivors.

Mr. MICHEL. In this country or all around the globe?

Dr. COOPER. Sixty-seven of the cases were performed in the United States by 19 surgical teams, and 54 in foreign countries. There are only seven patients who have survived 6 months or more.

Mr. FLOOD. What is the problem?

Dr. COOPER. The problem is basically one of what is called rejection by the body of the foreign tissue.

Mr. FLOOD. The actual physical transplant as a piece of surgery is no great trick; many competent teams of surgeons can do the actual physical transplant. That is not the problem, is it; it is the fallout after that?

Dr. COOPER. It is not the limiting factor. I would not say any team of surgeons could do it. It takes a skillful surgeon able to accomplish the transfer in a reasonable period of time with a great deal of technical skill.

Mr. FLOOD. That is not the real problem?

Dr. COOPER. It is not the limiting problem. The limiting problem is the ability of the body to tolerate the implanted heart; yes, sir.

Mr. FLOOD. What are you doing about that? There is the problem. Now you have at least identified the problem and you know what it is. What do you propose to do, what have you done, and what are you doing?

Dr. COOPER. What we are doing and what we propose that should be done is that we must——

Mr. FLOOD. You are not surprised that this is the problem?

Dr. COOPER. No. sir. I am not. What we are doing is trying to find better ways of detecting early rejection, body reaction to the transplant, so that aggressive therapy could be applied in a more effective way.

Mr. FLOOD. What about drugs?

Dr. COOPER. By the use of immunosuppressive drugs; yes, sir. More important is the—and this has been the real fallout that you mentioned—the fact that the scientists now recognize that the heart is also an immunologically active organ.

There was some consideration many years ago that because of its size and basic structure, that the heart might not be as potent an immunogenic stimulus as other organs or other tissues might be.

Mr. FLOOD. The heart is simply a pump. It has no other particular purpose like some organs. It is a mere pump, is it not?

Dr. COOPER. Its primary function is a pump. It has some other minor functions related to control mechanisms of the entire circulation. Its primary purpose is a pump and it is a striated muscle but it has built into it a large energy apparatus and there are many cellular constituents than can act as primary stimuli for rejection. It is now the hope that the scientists working in this field will be able to isolate specific soluble antigens from the heart which can be identified and then improve the ability to match the donor and the recipient

on a more effective basis. Therefore, the need for strong drugs would be reduced. That is why those that have survived longest are the best so-called matches.

Mr. FLOOD. Shouldn't those procedures be followed before the operation? Can you do your screening and matching then in preparing for the operation?

Dr. COOPER. Yes. The current technology for that is a rather prolonged one. It takes several hours to properly match a prospective recipient and donor. It is our hope that this can be shortened in its time and it is our hope also that there can be a mechanism made available that every doner that is a useful donor could be utilized in an efficient manner so that people who may not match well, the donor heart could then be available to others.

Mr. FLOOD. What about Dr. Hufnagel's project concerning the possibility of a calf's heart being placed into the human body rather than a transplant of another human heart?

Dr. COOPER. The experience thus far with transplanting between species——

Mr. FLOOD. There never has been such a transplant attempted thus far?

Dr. COOPER. Not between the calf in the United States but between the chimpanzee and man there has. Several years ago there was one such an attempt in extremis in which the heart beat for about 1 hour and then stopped. This is the usual experience that one sees when one transplants a heart from one animal to another animal species. It is a very serious immunological problem. It is more severe than working in the same species. The calf would not be too promising at this point in time with the current state of our immunological knowledge.

ARTIFICIAL HEART

Mr. FLOOD. What about the programs we heard about last year for the development of an artificial heart, miniaturization of it, and the actual creation of the artificial heart?

Dr. COOPER. The totally implanted artificial heart?

Mr. FLOOD. Yes

Dr. COOPER. This program directs its activities at basically five major areas of scientific activity. Some of these have shown substantial progress in pump design, miniaturization, in understanding ways to drive it and control it, but there is one area that remains a very important barrier to continued accelerated progress in this field. This is the problem of basic biomaterials, the development of a suitable synthetic material that will be compatible for a long time with the blood and with other body tissues and fluids. We have not made a great deal of headway in this area.

Mr. FLOOD. Is a serious effort being made to do this?

Dr. COOPER. Yes, sir. We intend to now that we have in the rest of our systems demonstrated that the other principles can in fact be developed and assembled as a suitable device. I feel that we must now direct our major scientific attention to the solution of the very difficult problem of finding and developing a suitable material out of which these pumps can be made.

ARTIFICIAL PACEMAKER

Mr. FLOOD. What is an artificial pacemaker?

Dr. COOPER. An artificial pacemaker is a device which has the capability of electrically driving the heart and setting its rate at a selected rate that will take over that function of that portion of the heart which determines how fast the heart beats.

Mr. FLOOD. I talked to an old friend of mine, old colleague of mine yesterday, a Member of the House, who told me that he was walking around now with an artificial pacemaker. Just what does that do?

Dr. COOPER. There are two things that determine the effectiveness of the heart to do its job, which is basically to deliver enough blood to all the body tissues. That is like any pump, how much is put out per stroke and how many strokes it makes per minute. What the pacemaker does is insure that the heart will beat enough times per minute so that it can pump enough blood to get it to all the tissues in the body.

Mr. NATCHER. Would you yield to me at that point?

How is it hooked up—I have never seen that—from the standpoint of the body?

Dr. COOPER. There are several ways of hooking it up. The most common way, if it is going to be permanently implanted, is that you have two fine wires of special design so that they won't break in there while the heart continues to beat. These wires are sewn to the surface of the heart and then at a small distance away, a power source, and as small electrical circuit is placed that is battery powered at the present time for the most part. This can be implanted wholly under the skin and this battery and electrical circuit fires at, say, 70 times per minute.

It sends its signals to the wires and it stimulates the heart regularly and the heart responds to each stimulus and contracts with each beat.

Mr. NATCHER. Thank you.

Mr. FLOOD. Is this a permanent thing? This is actually installed? It is not a temporary thing of hours and days?

Dr. COOPER. This can be done on a temporary basis, which is occasionally what happens after a heart attack. The heart slows down because of variety of reasons and yet it will resume its normal rate with adequate treatment. The way that this is done is that the wires of which I spoke are inserted through a vein into the inside chamber of the heart. The wires lie against the walls of the heart and they can be powered from an electrical source on a temporary basis and will respond. This is very good treatment for certain complications.

Mr. FLOOD. What is the size of the hardware as against, say, a half dollar or quarter or a silver dollar? What does it look like in size?

Dr. COOPER. Currently now, the ones that are most commonly used are a little smaller than a pack of regular sized cigarettes. There is design work and activity going on now to make it about the size of a half dollar or silver dollar.

Mr. FLOOD. Miniaturization?

Dr. COOPER. Yes.

HYPERTENSION

Mr. FLOOD. For many, many years we have been hearing about hypertension. What is hypertension?

Dr. COOPER. Hypertension is high blood pressure, the pressure in the arterial system that is actually the driving force for distributing the blood around the body. When it gets high, it becomes an important stress on the body and the problems with high pressure are the eventual bad effects it has on other organs like the brain.

Mr. FLOOD. What are the results or effects of low blood pressure? What does that mean?

Dr. COOPER. Low blood pressure, if it is low enough, is a disastrous situation. It is one of the hallmarks of the condition which is known as shock.

Mr. FLOOD. What produces it?

Dr. COOPER. The most common cause of significant low pressure, hypotension as opposed to hypertension, or shock——

SHOCK

Mr. FLOOD. What is shock?

Dr. COOPER. Shock is a clinical symptom or group of features that is not well understood which usually includes very low blood pressure, cold clammy skin, pallor, mental confusion, lack of urine output.

Mr. FLOOD. These things are all within your jurisdiction?

Dr. COOPER. Yes, sir.

Mr. FLOOD. What are you doing or trying to do, what is your research with reference to both high blood pressure and low blood pressure?

Dr. COOPER. With respect to the shock condition in low blood pressure, research is taking several directions. The most common form is related to hemorrhage or loss of blood, trauma. Therefore, the primary treatment would be restoration of the blood or the volume that is needed in the circulation.

Mr. FLOOD. Transfusion?

Dr. COOPER. Yes, sir. We have programs related to this.

The second avenue of research is to understand why some people, even in blood loss and retransfusion, if it is done at a late enough period of time, even though they get restored blood volume, they go on and do not survive, and this is called irreversible shock. The mechanism of this is not understood and what we are doing in this area is finding what organ systems are involved in the generation of the catastrophic effects which go on.

There are types of shock related to serious infection in which the primary research is directed toward the prevention of the basic infection and then there is a final kind that is related to heart attack and which we do not know the mechanism of, so-called cardiogenic shock. Our myocardial infarction research program is primarily designed for to determine what it is in the early days after a heart attack that leads to the ciculatory collapse or shock. This is how our basic research in shock is conducted.

BLOOD TRANSFUSION

Mr. FLOOD. How many kinds of transfusions are there? Is there not a new type of transfusion?

Dr. COOPER. There are many types of transfusions and I think that this development is a very good one. The administration of whole blood as a transfusion medium for every type of situation——

Mr. FLOOD. What is whole blood?

Dr. COOPER. That is the blood, if we took it from one individual, properly matched, it would be made out of the plasma, the red cells, the white cells and other cellular elements. If this is transfused, for a wide variety of reasons, some people do not tolerate the transfusion very well even though there is adequate type and cross match. So what we have now learned is that specific fractions of the blood or parts of it like the plasma——

Mr. FLOOD. What is that?

Dr. COOPER. We call it a plasma transfusion, or serum transfusion for an infusion of a specific factor isolated from the blood.

Mr. FLOOD. Can you preserve this better than whole blood?

Dr. COOPER. Yes, sir; in some cases we can, and this is a great economic benefit and a great benefit because whole blood has a limited time span for which it can be utilized for transfusion.

Mr. FLOOD. What is the span?

Dr. COOPER. About 21 days at a maximum by the current most common preservative.

Mr. FLOOD. Suppose it is beyond the time limit. Is there any danger to using the blood?

Dr. COOPER. Yes, sir. Cells in the whole blood undergo certain changes with time and there are certain metabolic changes in the cellular element of the blood which release into the fluid certain ions like potassium which, if infused, could be potentially harmful.

HEPATITIS

Mr. FLOOD. Is there a greater danger of hepatitis in the whole blood rather than the other transfusions?

Dr. COOPER. Yes, sir; there is a danger of hepatitis with whole blood transfusion. There is a danger of hepatitis with certain forms of plasma transfusion. If there are purified fractions and selected segments of the cells, particularly with adequate washing, the likelihood of transfusion hepatitis ought to be reduced.

Mr. FLOOD. I understand there is an alarming amount of infection by hepatitis in transfusions?

Dr. COOPER. Yes, sir.

Mr. FLOOD. Why do you not stop that?

Dr. COOPER. Because it is very difficult to detect by the current method that we know when a particular unit of blood would be a carrier of the virus, because it is not entirely clear how this is transferred within the cellular elements.

Mr. FLOOD. Are you examining this problem? It is a serious problem.

Dr. COOPER. Yes, sir.

Mr. FLOOD. You are on this, are you?

Dr. COOPER. Yes, sir; we are in the national blood resource program.

Mr. FLOOD. Getting any place?

Dr. COOPER. I think we do understand more about this and have plans to expand our activity, but with specific projects directed toward washing cells and seeing, for example, special types of washing to see if these problems can be reduced further.

Dr. BERLINER. On this score, there is some very promising recent work which suggests that much investigation may be on the track

of the virus which causes transfusion hepatitis and that they may be able to detect it.

Mr. FLOOD. I have had transfusions for different reasons. When I lie there and see this transfusion going on right in front of me, while I am watching this I am wondering, am I getting hepatitis. I cannot get it out of my mind. I am on the wrong subcommittee, I guess, to go to a hospital.

Dr. BERLINER. The chances from any one transfusion are not very high, but it is people who get large numbers of transfusions who are most likely to get it. I think the work currently going on is highly promising as far as the identification of the agent which produces transfusion hepatitis is concerned.

Mr. FLOOD. At least you make me feel better.

I am wondering why it should be so difficult to identify this foreign agent in the blood which should not be used for a transfusion.

Dr. COOPER. Because, as Dr. Berliner has mentioned, it usually takes a fairly large volume to do it and the amount of blood that has to be worked with is a limited factor in isolating and identifying the virus, and the location within the constituency of the blood as to how it is being transported is another problem.

By recognizing these problems and improved techniques, the virologists have provided, I think now as Dr. Berliner indicated progress will be made in identifying the virus and then a suitable test could be determined.

Dr. MARSTON. Up until now, you recall Mr. Chairman, the problem has been that you have had to use human volunteers for proper studies because experimental animals have not been susceptible to hepatitis. And several years ago there were studies that were carried on in human volunteers, and this raised very serious moral and ethical problems because this is not an innocuous disease.

Back in World War II, when the problem of hepatitis was such a great problem for the wounded in the war, then conscientious objectors and others were considered for human volunteer studies. These have been stopped because of the risk to the individuals used in the experiments, and this has been over the years the biggest single deterrent to progress in studying hepatitis because there was not a suitable animal host to test for the virus, and the use of human carried such risk.

SYNTHETIC BLOOD

Mr. FLOOD. Does anybody ever talk about artificial blood, creating blood?

Dr. COOPER. Yes, sir, in a certain sense for certain functions of the blood, there are certain liquids that are currently being considered as oxygen carriers which would serve as a form of oxygenater fluid which would help in creating a portion of the blood.

The other function of the blood that is often utilized as a synthetic is a volume expander. For many years there have been a wide number of substances which have been used, including gelatin solutions, fractions of blood as we mentioned, and substances like high molecular weight sugars called dextran, and this provides the ability to restore total volume so that the pressure comes up and the function of the heart and blood vessels remains suitable for a given period of time.

CLOT-DISSOLVING AGENTS

Mr. FLOOD. Are you still pursuing the search for better clot-dissolving agents?

Dr. COOPER. Yes, sir, we are in the first year of the Urokinase pulmonary embolism trial in order to test the efficacy of this particular type of clot-dissolving agent.

Mr. FLOOD. Mr. Michel?

MOTIVATION TO ENTER GOVERNMENT RESEARCH SERVICE

Mr. MICHEL. What motivated you, doctor, to come into the Government service rather than practicing your profession outside?

Dr. COOPER. First off, I had been at the National Institutes of Health twice before in the intramural program, and I recognized that this is a very excellent scientific atmosphere and I had a very high regard for it.

In 1967 I was recruited to return in an administrative capacity to help direct the artificial heart myocardial infarction program, and in that capacity I found that the problems that were developing and the responsibilities that had emerged and the importance of these to the community were large enough that I felt that when I had the opportunity to take my current position, it was one which I should accept.

FORMATION OF BLOOD

Mr. MICHEL. Most of us at one time or another are blood donors. Am I right in saying that it takes only 24 or 48 hours for the human body to reproduce a pint of blood taken from it?

Dr. COOPER. No; I think the period of time is somewhat longer.

Mr. MICHEL. I think I got that figure from a letter soliciting our son's giving blood at school, and because he was not 21 he needed the old man's OK, and it was nothing to worry about, it is replenished within 24 or 48 hours.

Dr. COOPER. The volume is replenished within that period of time. The blood is made up of two constituents and the body mechanism for replenishing various fractions of the blood react at different rates. The blood cells that are generated in the bone marrow have a given life span. The plasma is generated by another source, and the total liquid in the blood comes from another source. There is such a good margin of safety in a normal individual for oxygen-carrying capacity for the blood that the restoration of volume could well occur within that period of time and the donor would have no ill effects.

Mr. MICHEL. But if you were to suffer a profound loss of blood such as being in an accident, would it not take longer proportionately?

Dr. COOPER. Yes, sir; and if the patient is left with low blood pressure or in shock, the sequence of events that occurs further impedes the ability of the body's natural defenses to replenish it.

BLOOD PRESSURE AND BLOOD COUNT

Mr. MICHEL. What is the figure considered normal in measuring blood pressure? Is there a standard for normal count?

Dr. COOPER. The blood count and the low blood pressure are two different elements, and the blood count refers usually to the amount

of red cells or hemoglobin that is available to carry oxygen in the blood. This is usually described in millions of cells per unit volume. When one is anemic, he usually has a hemoglobin count of 10 or nine, depending on what standards you use.

Blood pressure, on the other hand, is the actual amount of hydraulic pressure in the vascular system and usually measured by a cuff on the arm, and this is normally 130 or 120 over 80, with the peak pressure when the heart beats and the low pressure before the next beat. Consequently, when somebody has high blood pressure, we mean that there is a significant elevation of at least the lowest figure, that is the 80, to somewhere over a hundred. When we go to low pressure, we usually mean that the patient, if he is walking around and is not in shock or has been in an accident, doctors will often tell a patient he has some low blood pressure when his systolic blood pressure or peak pressure during the cycle is under 90.

Mr. CASEY. Will the gentleman yield?

Mr. MICHEL. Yes.

USE OF BLOOD FRACTIONS

Mr. CASEY. There is less use of whole blood now, is there not, except when there is a big loss of blood?

Dr. COOPER. In most medical centers—for loss of whole blood?

Mr. CASEY. I say unless there is a large loss of blood.

Dr. COOPER. Yes; that is correct. The preference would be that if we knew the specific absent factor, then we would like to restore that factor which is absent, say any hemophilia factor, certain other fractions of blood or certain types of cells, either red cells or platelets or that sort of thing.

Mr. CASEY. Then you separate it and sometimes you give the donor part of his blood back, do you not?

Dr. COOPER. The ability to give a donor part of his blood back requires a very careful way of taking the blood out of the patient so there is insurance in the cycle of handling it it is not contaminated, and since most donors are normal individuals and they have a very active capability for regenerating themselves and restoring their volume, it is not a usual practice to restore.

Mr. CASEY. When I was in a hospital they told me they got most of their supply from the personnel there at the hospital and gave part of it back to them. That way they could make more donations.

Dr. COOPER. I think this may be a unique situation. The common form, since most people are not within the hospital confines, is to go out and seek in the communities people to volunteer, that would not be a practical way to deal with the problem.

The other fractions of the blood, if only selected portions are used, are then used for other purification processes to get other fractions which can be stored well.

Mr. MICHEL. What is the going rate for blood now if one needs a transfusion of a pint?

Dr. COOPER. The hospital charge?

Mr. MICHEL. Yes.

Dr. COOPER. I would not be able to answer that in any precise way. I think it all depends on what additional costs the patient bears for the service involved, and not only the cost of the blood that the donor is paid, but also for the handling of the blood and administration of

the blood in the hospital setting. I would guess there is a wide spectrum of costs.

Mr. MICHEL. Somewhere I read some arbitrary figure of $60.

Dr. COOPER. I do not think that figure would be unusual but I think there is a wide range from some place between $15 or $20 up above $60.

ARTERIOSCLEROSIS

Mr. MICHEL. In your testimony you say that arteriosclerosis is still the leading cause of heart disease mortality. What is the principal cause of hardening of the arteries?

Dr. COOPER. I wish I could answer that question in a definitive scientific way.

There are a lot of risk factors and correlated factors that have been identified in patients who suffer this process. At the present time there is no complete understanding of the basic mechanism of what the total arteriosclerotic process is. Some of it is related, apparently, to metabolism in various parts of the body and in the vessel walls. Some of it is related to the permeability of the vascular wall; some of it is related to clotting factors that may be involved in injuring the vascular wall. I cannot give a very definitive answer.

Mr. MICHEL. We are spending some sizable amounts on it. By your own testimony you say that about 59 percent of the available $57 million is used to support research on the prevention of the disease and about 32 percent you say for research on treatment and so on.

Is there anything really significant we can point to by way of accomplishment in the last several years for this expenditure?

Dr. COOPER. Yes, sir; there is. Although I was guarded in my statement about understanding the total etiology of the disease or cause of the disease, there have been significant instances in understanding of certain aspects of it.

At our own laboratories at Bethesda, in the laboratory of Molecular Diseases headed by Dr. Fredrickson, the former Director, there have been significant developments in understanding the role of blood lipids and lipoprotein substances in the blood in patients who have arteriosclerosis in various forms. This refinement and understanding, that the patterns of the fats in the blood are related to different forms of diseases and different rates of progress of the disease and the susceptibility of the disease to management, has been a most signficant advance.

So I think we have gained this understanding, we have gained understanding of the metabolism of cholesterol which is one of the blood fats, of the role of cholesterol's place in the body.

Mr. MICHEL. Haven't the more recent findings with respect to cholesterol changed considerably from what we thought a few years ago?

Dr. COOPER. There is no question still that patients who have elevated blood cholesterol in a correlative way have higher risks for experiencing complications of arteriosclerosis. What we have learned is a good deal about how cholesterol is made in the body, what the role of outside cholesterol might be and how it might be controlled, and how this cholesterol might be transported in the body, and how it is related to this total pattern of fats in the blood.

So I think our understanding of the total impact of knowing about cholesterol has changed but the importance of cholesterol still remains an important point of focus.

Mr. MICHEL. On the artificial heart program, do I understand that research in transplanting of the human heart, your total research effort on that aspect of it is $1.7 million?

Dr. COOPER. In the past fiscal year, yes, sir.

Mr. MICHEL. And then in the mechanical aspect, $8 million.

Dr. COOPER. Yes, sir.

Mr. MICHEL. What have we really done about moving in the direction of a total mechanical heart? We have talked about some assistance. I have heard we do not have one scientist or one technician working on the prospects for a total mechanical heart. Is that true?

Dr. COOPER. No, sir; it is not. There are several investigators working on the concept and on actual models and designs of the total implantable artificial heart. This work has not gone as rapidly as perhaps one might like it to go because of the basic technological difficulty I expressed before. That is the absence of a suitable material out of which to make the basic pump, because to test the long term effect of a pump in the circulation and miniaturize it as a result of the information gained from it requires that we have to have a compatible material that does not make the blood clot of itself when a foreign substance like glass comes into contact with the blood. It is more than just a clotting problem as blood hits a foreign surface made out of the plastic, it will denature the protein, change it in a significant way or injure cells and change patterns of regulation of the circulation.

So that until we can get a suitable substance that can be tolerated for a long period of time, the progress in further pump design must wait.

On the other hand, however, we have not been inactive in work in developing energy systems for total implantation, nor in developing and implementing control systems.

The problem of temporary assist has many of the same fundamental problems. In other words, better assist devices, better heart-lung machines can be made if we make them out of better material. So that the whole family of assist devices will be benefited as soon as we can develop the best material we can for long term use in the body.

Mr. MICHEL. Since it has become quite obvious that one of the principal problems in the human heart transplant is the rejection factor, do you think we should speed up the research on the total mechanical heart as a substitute?

Dr. COOPER. I think these two programs are not competitors in the real sense, they are really complementary programs.

It is important that we recognize that to do a transplant we have to use an artificial circulation device. When the donor heart is resuscitated, it is done on an artificial circulation system as well. So that the better systems we have for artificial circulation, the better techniques we will have for transplantation.

If a patient is very ill and dying, the ability to put him on a machine at least temporarily while he can be adequately matched with a donor heart in itself would be a great advance.

As I mentioned in my testimony, even if we were able to maximally use all of the available donor hearts that come to us through cerebral accidents, strokes, or trauma, there would not be enough

donors to serve the group of patients who would be potentially recipients for a transplanted heart.

Therefore, we would think that the development of the artificial heart must go on.

INFORMATION ON HEART TRANSPLANTS UNDERTAKEN TO DATE

Mr. MICHEL. You spoke, I believe, of a total of 121 heart transplants to date.

Dr. COOPER. Yes.

Mr. MICHEL. Sixty-seven of those being in the United States and 54 in foreign countries?

Dr. COOPER. Yes, sir.

Mr. MICHEL. Since there are so few, Mr. Chairman, would it be agreeable to have a list placed in the record of these heart transplants, the name of the patient, the age, where the operation took place, and the current status of the patient and, if he died, how long he lived, the name of the surgeon?

Dr. COOPER. We have such information.

Mr. MICHEL. Of both U.S. and foreign instances?

Dr. COOPER. Yes, sir.

Mr. MICHEL. Can we have that supplied for the record, Mr. Chairman?

Mr. FLOOD. Yes.

Dr. COOPER. With this caveat, that our source for the total information is largely from the press, particularly on the foreign information. We have some direct connection with some of our own grantees. To try to improve the precision of this information, the National Institutes of Health have recently initiated a registry with the American College of Surgeons which will be international in scope and which will be the mechanism by which to collect and collate all of this information in a comprehensive form which will be available both to the public and to the scientific community on an ongoing basis.

This was started in February. In the meantime, the Heart Institute as best it can from the clipping service, has a list of these 121 cases, where they are done, what the patient's age was, what the cause of failure was, and how they survived.

Hence the accuracy of the information may need to be checked.

Mr. MICHEL. This would be in chronological order probably.

Dr. COOPER. Yes.

Mr. MICHEL. Fine.

Mr. FLOOD. There would be no danger of violating any confidential relationship by use of the names?

Dr. COOPER. I think if it is made public information, this probably would be a consideration that would have to be taken.

Mr. SMITH. You got it out of the newspaper?

Dr. COOPER. Not all of the information.

We have called when we have seen cases, and in certain instances, as you know, the information in the newspaper did not identify the surgeon or the patient or the donor. We do not have names of donors. We have names of practically all of the recipients.

What the sensitivities here would be I think would have to be in-

vestigated for public distribution, but the basic information of age, sex, type of heart disease, the operation date, the length of survival, and the casue of death we could provide within those limits of precision.

Dr. MARSTON. Mr. Chairman, if we may supply as complete a list as we feel is possible and appropriate for inclusion in the record, I think that is the best course we could take.

Mr. MICHEL. That is perfectly all right with me. I do not want to be spreading on the record anything that ought not be there, but we read about it so frequently. I think it would be important to have collected in one place an up-to-date résumé of where we are or how far we have gone.

Dr. MARSTON. We will do that in suitable form.

(The information follows:)

REPORT OF HUMAN HEART TRANSPLANTS, AS OF APRIL 1, 1969

No.	Recipient Age	Recipient Sex	Donor Age	Donor Sex	Date of transplant	Survival	Reported cause of death	Country
1	53	M	25	(1)	Dec. 3, 1967	18 days	Pneumonia	South Africa.
2	[2]17	M	[2]2	M	Dec. 6, 1967	6½ hrs	(1)	United States.
3	58	M	24	M	Jan. 2, 1968	Surviving		South Africa.
4	57	M	43	(1)	Jan. 6, 1968	15 days	Internal hemorrhage	United States.
5	58	M	29	F	Jan. 10, 1968	8½ hrs	Heart failure; donor heart ½ size.	Do.
6	27	M	19	F	Feb 17, 1968	3 hrs	Pulmonary hypertension	India.
7	66	M	23	M	Apr. 27, 1968	53½ hrs	Embolism/brain damage	France.
8	40	M	43	M	May 2, 1968	3½ days	Pulmonary embolism	United States.
9	47	M	15	F	May 2, 1968	[3] 6 mos., 6 days	See No. 87	Do.
10	45	M	26	M	May 3, 1968	46 days	Lung/kidney infection	England.
11	48	M	15	M	May 7, 1968	8 hrs	(1)	United States.
12	62	M	36	M	May 7, 1968	7 days	(1)	Do.
13	65	M	35	M	May 8, 1968	2 days	(1)	France.
14	56	M	39	(1)	May 12, 1968	Surviving		Do.
15	54	M	17	M	May 21, 1968	4 mos., 23 days	Rejection/cardiac arrest	United States.
16	54	M	58	M	May 25, 1968	7 days	Total rejection	Do.
17	23	M	41	M	May 26, 1968	28 days	(1)	Brazil.
18	56	(1)	38	(1)	May 30, 1968	4 hrs	Lung/kidney complication	Canada.
19	54	M	47	M	May 30, 1968	5 days	Neurological complication	Argentina.
20	39	M	29	M	May 31, 1968	Died on table	Malfunction of right ventricle	United States.
21	41	(1)	20	(1)	June 10, 1968	1½ hrs	(1)	Do.
22	49	M	23	M	June 28, 1968	5 mos., 2 days	Asphyxiation following indigestion.	Canada.
23	24	F	32	(1)	June 28, 1968	4 mos., 13 days	Brain infection	Chile.
24	48	(1)	50	(1)	July 2, 1968	4 mos., 26 days	Heart attacks due to rejection	United States.
25	49	F	46	M	July 9, 1968	5 hrs	(1)	Czechoslovakia.
26	58	M	33	F	July 20, 1968	Surviving		United States.
27	57	(1)	16	(1)	July 23, 1968	5 mos., 2 days	Tissue rejection	Do.
28	48	M	32	M	July 25, 1968	58 hrs	Congestive heart failure	England.
29	49	F	40	F	July 29, 1968	25 days	Cardiac arrest	United States.
30	18	M	20	M	Aug. 7, 1968	80 days	Acute respiratory insufficiency	Japan.
31	5	F	11	M	Aug. 18, 1968	9 days	Cardiac arrest/acute rejection	United States.
32	50	M	37	F	Aug. 19, 1968	68 days	Cardiac arrest	Do.
33	43	M	21	M	Aug. 22, 1968	46 days	Pneumonia	Do.
34	43	M	17	M	Aug. 24, 1968	Surviving		Do.
35	58	(1)	35	(1)	Aug. 30, 1968	11 days	Stroke	England.
36	50	M	20	(1)	Sept. 1, 1968	Surviving		United States.
37	46	M	22	M	Aug. 31, 1968	do		Do.
38	50	M	39	M	Aug. 31, 1968	do		Do.
39	42	M	39	M	Sept. 2, 1968	do		Brazil.
40	50	M	25	F	Sept. 4, 1968	do		United States.
41	47	M	17	M	Sept. 5, 1968	8 days	Cardiac arrest	Do.
42	52	M	36	F	Sept. 8, 1968	Surviving		South Africa.
43	48	F	27	M	Sept. 10, 1968	4 mos., 6 days	Hepatitis	United States.
44	21	M	24	F	Sept. 13, 1968	14 hrs	Kidney trouble	India.
45	52	M	20	M	Sept. 15, 1968	3 mos., 20 days	Pneumonia	United States.
46	[4]2	F	[4]1	F	Sept. 15, 1968	14 hrs	Cardiac arrest	Do.
47	45	M	27	F	Sept. 16, 1968	6 hrs	Cerebral hemorrhage	Venezuela.
48	44	M	46	F	Sept. 17, 1968	2 days	Acute kidney insufficiency	Spain.
49	16	M	36	M	Sept. 17, 1968	Surviving		United States.
50	49	M	37	M	Sept. 17, 1968	do		Do.
51	57	M	46	M	Sept. 19, 1968	88 days	Lung infection	Do.
52	46	M	17	M	Sept. 23, 1968	12 days	Cardiac arrest	Do.
53	51	M	19	M	Sept. 27, 1968	67 days	Infection/kidney complications	Canada.
54	58	M	16	M	Sept. 29, 1968	4 mos., 1 day	Rejection	Do.
55	21	M	17	(1)	Oct. 1, 1968	Surviving		Chile.

See footnotes at end of table.

REPORT OF HUMAN HEART TRANSPLANTS, AS OF APRIL 1, 1969—Continued

No.	Recipient Age	Recipient Sex	Donor Age	Donor Sex	Date of transplant	Survival	Reported cause of death	Country
56	46	M	43	M	Oct. 2, 1968	5 days	Acute heart seizure	United States.
57	54	F	28	F	Oct. 5, 1968	61 days	Pneumonia	Do.
58	54	F	28	F	Oct 3, 1968	5 mos., 15 days	Inflammation of the small intestines.	Do.
59	19	F	35	[1]	Oct. 15, 1968	15 hours	Complication in blood coagulation.	Argentina.
60	50	M	20	M	Oct. 17, 1968	Surviving		United States.
61	42	M	29	[1]	Oct. 19, 1968	do		Canada.
62	45	F	20	[1]	Oct. 21, 1968	47 days	Acute rejection	Do.
63	49	F	30	M	Oct. 21, 1968	Surviving		United States.
64	57	M	29	M	Oct. 22, 1968	44 days	Hemorrhage following surgical complications.	Australia.
65	19	F	19	M	Oct. 23, 1968	6 days	[1]	United States.
66	42	[1]	41	[1]	do	6 hrs	Cardiac arrest	Do.
67	52	[1]	49	[1]	Oct. 25, 1968	4 mos., 3 days	do	Do.
68	35	[1]	25	[1]	do	2 mos., 2 days	Rejection	Canada.
69	54	[1]	20	[1]	Oct. 26, 1968	Surviving		United States.
70	[1]	[1]	[1]	[1]	Oct. 27, 1968	do		France.
71	45	[1]	20	[1]	Oct. 28, 1968	8 days	Pneumonia	Canada.
72	32	[1]	24	[1]	Oct. 30, 1968	18 days	Rejection	United States.
73	40	[1]	42	[1]	Nov. 3, 1968	4 days	Failure of liver/kidneys	Do.
74	53	[1]	28	[1]	do	Surviving		Canada.
75	50	[1]	27	[1]	Nov. 5, 1968	7 days	Rejection	United States.
76	25	F	19	[1]	do	33 hrs	Progressive weakness of heart complicated by changes in lungs and liver.	Russia.
77	55	[1]	27	[1]	Nov. 9, 1968	48 days	Bacterial pneumonia	United States.
78	53	[1]	15	[1]	Nov. 11, 1968	38 days	Acute rejection	Canada.
79	34	[1]	[1]	[1]	Nov. 12, 1968	15 days	[1]	France.
80	54	[1]	22	[1]	Nov. 13, 1968	7 days	Stroke	Canada.
81	40	[1]	40	[1]	do	14 hrs	[1]	Australia.
82	50	[1]	38	[1]	Nov. 16, 1968	Surviving		United States.
83	53	[1]	50	[1]	Nov. 17, 1968	40 days	Rejection	France.
84	54	[1]	18	[1]	Nov. 17, 1968	Surviving		Canada.
[5] 85 [5] 86	56	[1]	[1]	[1]	Nov. 20, 1968	3 days	Stroke	United States.
[3] 87	47	M	[1]	[1]	Nov. 20, 1968	do	Rejection	Do.
88	49	[1]	[1]	[1]	Nov. 22, 1968	Surviving		Do.
89	30	[1]	[1]	[1]	Nov. 22, 1968	3 hrs	[1]	Chile.
90	40	F	14	[1]	Nov. 22, 1968	18 hrs	Liver ceased functioning	Turkey.
91	37	[1]	47	[1]	Nov. 24, 1968	14 hrs	Irreversible kidney failure	France.
92	48	[1]	[1]	[1]	Nov. 24, 1968	Surviving		Do.
93	26	[1]	51	[1]	Nov. 25, 1968	39 hrs	Cardiac insufficiency	Turkey.
94	56	M	26	[1]	Nov. 25, 1968	10 weeks	Rejection	United States.
95	33	[1]	57	[1]	Nov. 26, 1968	20 hrs	Cardiac arrest	France.
96	48	[1]	25	[1]	Nov. 27, 1968	Surviving		Do.
97	54	[1]	40	[1]	Nov. 29, 1968	13 days	Rejection	United States.
98	54	M	23	[1]	Nov. 29, 1968	3 mos. 13 days	Cerebral thrombosis	Canada.
99	38	[1]	22	[1]	Dec. 2, 1968	Surviving		United States.
100	40	[1]	[1]	[1]	Dec. 6, 1968	14 days	Kidney failure/pneumonia	Israel.
101	22	M	21	[1]	Dec. 16, 1968	43 days	Congestive heart failure	United States.
102	28	[1]	30	[1]	Dec. 22, 1968	Surviving		France.
103	[2] 8	[1]	[2] 2	[1]	Dec. 25, 1968	5 hrs	[1]	United States.
104	50	M	24	[1]	Dec. 27, 1968	91 days	Progressive failure of heart	Do.
105	62	[1]	48	[1]	Jan. 1, 1969	Surviving		Do.
106	35	[1]	[1]	[1]	Jan. 4, 1969	Died on table	[1]	Poland.
107	59	[1]	14	[1]	Jan. 5, 1969	37 days	[1]	United States.
108	44	[1]	54	[1]	Jan. 5, 1969	7 days	Lung ailment	Do.
109	48	M	47	[1]	Jan. 6, 1969	6 days	Brain hemorrhage/pneumonia	Do.
110	52	[1]	23	[1]	Jan. 7, 1969	Surviving		Brazil.
111	49	[1]	38	[1]	Jan. 17, 1969	3 hrs 52 min	Progressive pulmonary hypertension.	United States.
112	47	[1]	13	[1]	Jan. 23, 1969	3 days	Brain damage/edema of brain	Do.
113	7	F	6	M	Feb. 8, 1969	30 days	Lung infection/rejection	Do.
114	43	M	[1]	[1]	Feb. 8, 1969	Surviving		Do.
115	36	[1]	35	[1]	Feb. 13, 1969	1 day	Vital functions of organs destroyed.	Germany.
116	55	M	24	M	Feb. 15, 1969	10 days	Rejection	United States.
117	36	M	57	M	Feb. 20, 1969	Surviving		Do.
118	58	M	23	F	Feb. 20, 1969	do		Do.
119	56	M	26	M	Mar. 3, 1969	do		Do.
120	43	M	24	M	Mar. 17, 1969	do		Do.
121	38	M	[1]	[1]	Mar. 22, 1969	1 day	[1]	Germany.

[1] Information not available.
[2] Age in days.
[3] Received 2d transplant Nov. 20, 1968. See No. 87.
[4] Age in months.
[5] This patient received 2 transplants.
[6] Received 2 transplants. See No. 9.

SPECIALIZED RESEARCH CENTERS

Mr. MICHEL. Under this item of specialized research centers, Doctor, you say that the 1970 request of $925,000 will be adequate to continue the planning effort and to provide minimal operation support for perhaps one such center. Does that mean one additional over the 14 that are apparently in existence?

Dr. COOPER. No, sir. It is one of the group of 14 or a suitable competitor. The fact that these people have had an opportunity on a competitive basis to look at the resources and to make the plan would not exclude any institution from competing for the designation of a specialized center. So it would be one of the 14 or one other such institution.

Mr. MICHEL. What is the difference then? What have we not done in the past in the 14 that we are going to do in the 1970 budget? You say here in 1969 the Institute has provided support for planning for specialized research centers at 14 medical schools and other institutions.

I see in the 1970 request: "Continue the planning effort and to provide minimal operation support." I think that is about the same terminology used up here for the 14. I am a bit confused here.

Dr. COOPER. This does not mean that we would plan to continue planning in ones that have completed their planning. Several of these have finished planning. They now wish to support operational applications. These take a wide variety of forms depending on the specialized interest and competence of the given institution and group of investigators. There are some that have been initiated more recently of the 14 that would continue and finish planning, and we would hope to provide one such center with operational support.

Mr. MICHEL. Would all 14 be competing to be this one?

Dr. COOPER. At their option, yes, sir, they could do that.

Mr. MICHEL. And it takes that much money, nearly a million dollars, to get the one school to become operational?

Dr. COOPER. The school is operational, sir.

Mr. MICHEL. I realize that. I mean effectively operational.

Dr. COOPER. Yes; several hundred thousand dollars. A concerted effort for the solution or the attack on a given problem would probably be in that order of magnitude. This would be in addition to other competitive research grants. The core investigators would work in collaboration with these other researchers.

We view this as a core that would be reviewed on its own merit with collaboration to avoid overlap support from other individual investigators who would work in concert with these core workers.

For example, if we had an arteriosclerosis center or emphysema center, the establishment of the core or group facility for investigators would probably take several hundred thousand dollars initially, and this would be supplemented by the special work by the investigators which is done on a competing basis, with the usual method of surveillance by the usual research grant mechanism.

CONTRACTUAL RESEARCH ON THE ARTIFICIAL HEART

Mr. MICHEL. One further question on the totally mechanical heart. How is most of the research on this carried on, by grants? By contract?

Dr. COOPER. Most of it is carried on by contract, some is carried on by grant.

We feel that we must not close the avenue to the creative imaginative investigator to develop his own ideas, because this has been the source really of our own ideas for the organized program.

On the other hand, it is necessary to do certain types of fabrication, production, development of different parts of the system, and certain engineering features of the ideas which are developed by academic investigators which need to be done in the industrial sector, and I think to exclude the important group of industrial scientists would not be profitable to the program. Therefore, we support a great deal of work.

Mr. MICHEL. Is there much competition for contract awards for this?

Dr. COOPER. Yes; indeed. The response to the request for proposals is always vigorous and we have never suffered from a paucity of proposals.

Mr. MICHEL. How many firms would be bidding on a contract of this kind?

Dr. COOPER. I would say 200 or 300.

Mr. MICHEL. And how many would be let in a given year like last year?

Dr. COOPER. Last year we supported 97.

INCREASE IN TRANSPORTATION COSTS

Mr. MICHEL. On page 33 of the justifications I note: "Transportation of things," and it shows a $9,000 increase, which is about a 10 percent increase.

Have transportation costs gone up that much since last year?

Dr. COOPER. I suppose the costs have gone up, sir, and I believe the amount of things have gone up.

Mr. MICHEL. Is that just a figure picked out of thin air?

Mr. REEDER. It is largely for the transportation costs of people leaving and coming on at the beginning of the year, their household effects and so on. It is in the main for commissioned officers coming and going—their transportation costs.

Mr. MICHEL. But a 10-percent increase in 1 year; does that suggest there is a more rapid turnover expected in this coming year?

Mr. REEDER. No, sir. This relates specifically to an increase of 12 positions and $100,000 requested on page 85 of the justifications for our intramural research effort. This increase relates to additional laboratory space newly assigned to this institute. The $9,000 is included in that amount to move the household effects of these requested new scientists and technical personnel entering on duty during 1970. In subsequent years it would be diverted to help annualize the research bench costs of these scientists.

Mr. MICHEL. That is all.

Mr. FLOOD. Mr. Natcher?
Mr. NATCHER. No further questions, Mr. Chairman.
Mr. FLOOD. Mr. Shriver?

CARDIOVASCULAR RESEARCH CENTERS

Mr. SHRIVER. I want to get clear in my mind the conversation you had a moment ago with Mr. Michel concerning the cardiovascular research centers.

It is my recollection that last year this committee expressed the hope they would all be operating in 1973. Now I understand there is just going to be one.

Dr. COOPER. We would like to have several, 12, 14, but at the current level of funding we would only be able to initiate one. We would hope with the addition of available resources by 1973 we could get the network.

Mr. SHRIVER. It is a question of money?

Dr. COOPER. Yes, sir. Again, this is a program which the academic community and other institutions are greatly interested in and would be interested in competing for, but I think this is a matter of available resources.

HEART COOPERATIVE DRUG STUDY

Mr. SHRIVER. Can you estimate the total cost now of the heart cooperative drug study described on page 74?

Dr. COOPER. For 1970?

Mr. SHRIVER. The total costs.

Dr. COOPER. The total costs with our current projections will probably remain in about the $43- to $45-million figure originally planned.

DISSEMINATION OF RESEARCH RESULTS

Mr. SHRIVER. Can you tell me how the positive results of the institute research projects are disseminated among the regional and local medical service centers? How do you get this out?

Dr. COOPER. We do this currently by the heart information service, which is involved in a vigorous program of providing to the physicians and to the community at large synopses of the developments in research that have taken place, and we have had recent publications of this type that have been distributed by way of meetings, by requests for mail, by distribution to regions.

Some of the publications and exhibits deal with hypertension, spare parts for surgery, nomenclature for disease, and general heart disease and the like.

In addition, we have been in active conversations with the regional medical programs for ways in which we could correlate our activities in order that we may more effectively and more rapidly bring the research developments to the regions as they are made available.

We have a pilot project pending on this in the field of arteriosclerosis and lipid typing, for example.

NATIONAL REGISTRY OF ORGAN TRANSPLANTS

Mr. SHRIVER. In the justifications you mention the need for a national registry of all pertinent information regarding organ transplants.

Dr. COOPER. Yes, sir.

Mr. SHRIVER. Is there anything being done on this?

Dr. COOPER. Yes. The registry is now operational. There are six institutes participating with us because this is comprehensive and involves, hopefully, all organs. We have initiated activity on heart transplantation, liver transplantation, and bone marrow transplantation in a program in conjunction with the American College of Surgeons and, as you may know, there is already a kidney registry which has been functioning for some years now. This program was initiated on February 14.

NATIONAL BLOOD RESOURCE PROGRAM

Mr. SHRIVER. How much of your fiscal 1970 budget will be devoted to the national blood resource program?

Dr. COOPER. Approximately $2.8 million, sir; $2,792,000.

REDUCTION IN FELLOWSHIPS AND TRAINING GRANTS

Mr. SHRIVER. On page 82 of the justification it says,

> This decrease reflects the Department priorities in the 1970 President's budget related to national health programs, which gives emphasis to the development of health services personnel.

Is that still a priority? I am talking about President Johnson's budget.

Dr. COOPER. Yes, sir, to my knowledge there has not been a revision of our fellowship and training line. I think this will reflect that level of decrease, although we would concur with the notion that the total manpower program will probably be commensurately increased to help service the whole cardiovascular community.

ADDITIONAL POSITIONS FOR PROGRAM DIRECTION

Mr. SHRIVER. Your programs are not really being substantially increased, are they?

Dr. COOPER. No, sir.

Mr. SHRIVER. But you have asked for four additional positions in the area of program direction.

Dr. COOPER. Yes, sir.

Mr. SHRIVER. Why? What kind of people are they?

Dr. COOPER. Basically, what we need to have in our office, and which was not available when I became Director last year, is the capability for an organized and systematic planning effort. It was pointed out to us by the leadership at NIH and the Department and other committees that have investigated NIH that we should have an active planning concept that would help us in the selection of priorities and in the development of these programs. This is what we hope to do.

Mr. SHRIVER. It is not because of an increase in programs?

Dr. COOPER. No, sir, to meet the need and be more responsive, to help us use our resources better.

Mr. SHRIVER. Thank you.

Mr. FLOOD. Mr. Smith?

EMPHASIS ON HEART TRANSPLANTATION

Mr. SMITH. Doctor, a number of doctors have told me, and I would like you to comment on it, that they think we are putting too much attention, relatively speaking, on the heart transplants and not nearly enough attention, relatively speaking, on the kind of techniques that will assist the heart, especially during shock periods after an accident and would help relieve the heart and give it pumping assistance. What do you think about this?

Dr. COOPER. I think the impression that we are giving our attention——

Mr. SMITH. When I say "we," I mean not just NIH, I mean everybody.

Dr. COOPER. I think the community at large would take the view that they are not providing primary focus on transplantation. I think it is the most dramatic development in this area that has occurred, but I would think you would find the community of cardiovascular sciences, and certainly the Institute would support the position, that there needs to be a concerted effort and balanced effort and a substantial focus on the problem of assisting the shock stage as a most important feature.

This is important mainly because there are more people who can be helped potentially by availability of new therapies for the complications of heart attack and shock.

MECHANICAL HEART ASSISTANCE DEVICES

Mr. SMITH. What are the limitations at the present time upon providing pumping assistance to the heart during these stress periods?

Dr. COOPER. As you know, there has been a tremendous success in the use of heart-lung machines as an adjunct to heart surgery. This gives us the encouragement that the use of mechanical assistance devices for other states will be a beneficial thing, but the time that the patient is on the pump during a heart operation is relatively short, a couple of hours. When it gets to 4 or 6 hours the complications from pumping become a threat to the patient's life itself, so that the reason that not more devices and more types of devices are available for general clinical use at the present time is that we have not solved the problem of prolonged pumping, and in my opinion the reason for this is the absence of a suitable material which will not damage the molecules in the blood, the cells in the blood, and initiate clotting. I think this is the primary scientific problem that we need to develop for improving the whole field of mechanical assisted circulation.

Mr. SMITH. What is the period of time beyond which this becomes a danger?

Dr. COOPER. I would guess now, depending on the initial vitality of the patient—the more ill the patient the shorter his tolerance for a prolonged profusion—but 4 to 6 hours would seem to be in general the maximum for total profusion.

There have been several patients, and by several I mean you can count them on two hands, who have been pumped by various techniques for several days.

Mr. SMITH. Included in my question, and this would be the vast majority of the people I include, are those people who are brought to the hospital as a result of an accident and they may not really have a chronic heart condition or perhaps have not had a heart attack but merely need pumping assistance during a period of stress.

Dr. COOPER. Resuscitation and assistance; yes, sir.

Mr. SMITH. Is there any real problem of giving them help for an hour or two?

Dr. COOPER. This has been done in several centers for people who have had electrocution and other forms of trauma, and other forms of acute respiratory arrest. Indeed there is a monograph written on the subject.

Mr. SMITH. Suppose somebody just had his legs broken in an automobile accident.

Dr. COOPER. And goes into shock and needs to be supported. This has been attempted and the results have not been outstanding. However, in some cases the resuscitation of the patient has been dramatic.

Mr. SMITH. Do you speak now also of the devices where they merely plug into the veins rather than opening the chest?

Dr. COOPER. Yes, sir; the necessary technology there, and the desirable thing is not to have to do a major surgical operation in the operating room but the sterile incisions could be done through the arteries and veins of the leg. This is under investigation and it has been accomplished with some success.

Mr. SMITH. Are we far enough along to promote this type of help?

Dr. COOPER. This is the primary focus of our mechanical and circulatory assistance program. Where we might be able to serve from 10 to 50 or 80,000 patients with total cardiac replacement, the figure that we could rehabilitate through the use of mechanical circulatory assist devices of the type of which you speak, which could go for hours, days or weeks, might be 10 times that figure. Our focus then is on the total family of devices with priority given to the mechanical and circulatory assistance devices.

Mr. SMITH. Has the computer problem been pretty well worked out with regard to these devices?

Dr. COOPER. Using the computer for controls?

Mr. SMITH. Yes.

Dr. COOPER. Where the device is dependent upon a relatively simple signal from the body a computer-like device can and has been used to control the performance of the pump. However, where the signals are more complex requiring fine measurements at various sites within the body a suitable computer system has not been perfected or used in part because we do not have the instruments available which are safe and effective if left in the body for long periods of time. However, we are working on this problem of instrumentation.

Mr. SMITH. Then an infusion of time—and money means time—and specialists in this area might well yield good results in the very near future. Is that a correct summary?

Dr. COOPER. I think additional time will have promise for mechanical circulatory assistance in various disease states; yes, sir.

Mr. SMITH. Should this aspect be speeded up in comparison with other things we are doing or do you think we have the right balance now?

Dr. COOPER. At the expense of our other programs I would not recommend taking away from the other disease areas. In its totality the problem of cardiovascular disease is a very large one, and each one of the segments has a very large number of potential patients involved.

I think I would not recommend at this time a disbalance of our current resources in order to accelerate that activity.

Mr. SMITH. Of course they become cheaper if several of these were produced, but how expensive are the devices, such as the computer and other devices involved?

Dr. COOPER. They cover a wide range in their developmental form from several hundred dollars up to $25,000 in their total form.

Mr. SMITH. But still we are talking about something in the range of possibility of any metropolitan area to have, that is to have one or more. On many of these things we are doing research on, it will be clear out of the reach of most people in the United States, anyway. Is that not correct?

Dr. COOPER. The last part of the question I do not understand, sir.

Mr. SMITH. Many of these things we are working on, if successful, will be out of the reach financially of a great many people.

Dr. COOPER. These would not be out of the reach if we could understand the basic mechanism of arteriosclerosis and in effect the significant changes in the basic lipid metabolism. This could be an inexpensive program.

Mr. SMITH. I would like to see us invest money, which means to invest the time of scientists which are in short supply, on things which, if we have success, would result in health care being available for people on a mass scale rather than in an isolated dramatic case.

Dr. MARSTON. The policy at NIH has been right along the lines that you have outlined here. You remember back a few years ago when the question of putting the major effort only into either total replacement or transplantation came up. Dr. Shannon and others took the stand to do what you suggest, to broaden the program so that it did as a policy matter include the possibility of getting the results that you speak to.

In actual fact the commitment to the transplantation area of your funds, Dr. Cooper, is less than 1 percent of the dollars in the Heart Institute.

As I understand your line of questioning I would say that we are in complete sympathy with your objectives.

Mr. SMITH. If you do allocate resources in that manner, is it fair to say, then, that these types of devices are likely to get considerable attention and become available to many people in a few years?

Dr. COOPER. Several types are moderately simple and could be made available. I think we could accelerate even within that resource line if we could solve that materials problem.

However, I think until we solve the materials problem it would not be profitable to accelerate the program in its totality.

Mr. SMITH. As I understand it, you have the materials problem but it is still not so acute that it affects someone just for an hour or two?

Dr. COOPER. Yes, sir; and those devices are already available and are in several medical centers and are in some use.

Mr. SMITH. But replacement with a new device with new material in it would be relatively inexpensive if everything else has been accomplished. In other words, all you do is to substitute a new material, such as plastic which is not very expensive.

Dr. COOPER. Our plan at this point has been exactly along the lines you mention. We have research in progress on the design, on the control of the pumping mechanism, on the pickup for information to put on the control, and the energy source to drive it. We can put these all together and demonstrate a wide spectrum of types of activity, and we can do this.

Mr. SMITH. It seems to me that somehow we should be able in the next year or two to get a lot of these devices with materials we now have spread throughout the country and when a better material comes along, it could be substituted.

Dr. COOPER. That is exactly our plan. We have a family of devices which are being assembled in their component parts and ready for testing so we can be sure they have the safety features which are requisite as well as the biologic features, and then we would be in a position to do this. This is the other point of my testimony.

One of these devices is a balloon, for example. It has to be inflated. Not only does the reaction in toxicity of the balloon need to be investigated but its tolerance to rupture within the aorta. So we have a lot of mechanical bench testing we must go through in order that we can put it out to the pracitioner with instructions to say how it can be used safely.

If it is used improperly it can be a detriment. If it is out of phase with what needs to be done or if it is overinflated and explodes this could worsen the patient's condition, so our test program is absolutely essential and it is the prelude to the program you have indicated.

I do think a small and partial success is possible with partial progress.

SEPTICEMIA

Mr. FLOOD. What is septicemia?

Dr. COOPER. Septicemia is a condition of infection which is widely disseminated by carrying the infected process through the bloodstream. The bloodstream actually shows evidence of infection throughout the body.

Mr. FLOOD. Can you identify the source of the infection?

Dr. COOPER. Sometimes. Many times it can be. Sometimes it remains——

Mr. FLOOD. What seems to be the main source?

Dr. COOPER. An infected part of the bowel, such as in diverticulitis, an infected part in the leg from injury, an infected abscess in the lung. It could be an infected tooth.

Mr. FLOOD. What is a gram negative septicemia?

Dr. COOPER. An infection caused by an organism which has certain staining properties when the organism is prepared on a slide and stained with what is called a gram stain. It has certain characteristics and looks red on the slide. These organisms are then further identified

as to their chemical properties and a general group of organisms taking a negative gram stain are called that.

Mr. FLOOD. Is low-blood pressure identified with this?

Dr. COOPER. Often in a severe form it is.

Mr. FLOOD. Septicemia can be a very serious condition, I suppose?

Dr. COOPER. Absolutely, sir.

RISK OF HEART ATTACKS IN MEN AND WOMEN

Mrs. REID. Do you have statistics to show the number of men versus women who have heart attacks?

Dr. COOPER. Yes; we do. I do not know whether we have them available with us.

Mrs. REID. Will you supply that for the record?

(The information follows:)

RELATIVE RISK OF HEART ATTACKS IN MEN VERSUS WOMEN

Age	Relative risk of suffering a heart attack [1]		Relative risk of dying from a heart attack [2]	
	Men	Women	Men	Women
35 to 44	20	1	5	1
45 to 54	6	1	5	1
55 to 64	4	1	3	1
65 to 74	2	1	2	1

[1] Based on information from the Framingham Heart Study on coronary heart disease.
[2] Based on information from the National Center for Health Statistics on mortality from arteriosclerotic heart disease in the United States in 1966.

Dr. COOPER. The general trend is that in males between the ages of 30 and 65 the incidence of heart attack is substantially greater than in the females.

After the menopausal period as the female ages the incidence of heart attack seems to increase and past the age 65 to 75 there is even less of a difference.

There is no question but that the incidence of heart attack in the young female is substantially less than that of the male.

Mrs. REID. At what age would you say a man could expect, according to statistics, to have a heart attack? Certainly not 30. Would it be the forties?

Dr. COOPER. If you plotted it statistically it would be toward the mid and late 40's and in the 50's as the most serious form of premature heart attack but this does not exclude the group of patients, young males who have a predilection for having heart attacks in the thirties. There are some.

MEDICAL ASSISTANCE FOR HEART ATTACK VICTIMS

Mrs. REID. I know from personal experience that it is difficult at times to get medical assistance quickly. Why couldn't a man carry a tablet of the type which is placed under his tongue and be informed of the symptoms of a heart attack so that if he had one he could take this tablet? It seems to me it would save lives.

Dr. COOPER. This is a complex question, Mrs. Reid. Let me answer it this way: One of the biggest problems in heart attack is in that

period immediately surrounding the heart attack before the patient comes to the hospital, as you indicate. This is where more than half of the deaths occur.

Part of the problem is that the patient has a great deal of difficulty in making the decision that he is sick enough, either needs his own pill or should seek medical aid. If he were a known cardiac and could be alerted to the conditions involved, in many cases there are emergency procedures which he is aware of that he can take advantage of. It is a question of whether it is indigestion or something of this sort.

Mrs. Reid. If he took this pill and it was not a heart attack would this harm him in any way?

Dr. Cooper. Depending on what type of pill it is. It would not necessarily harm him but it would not solve the type of problem in the initial attack, which is the large and important problem. It would be very difficult to give all males between that age group a set of pills and say, "When you have pain in your chest of a certain type put this in your mouth."

I think we would have to think very carefully of the effect of this on making a cardiac neurotic out of many people and whether or not they would actually carry it in their pockets or take too many at one time in which case it could be serious. There are a lot of logistical problems surrounding that episode.

Mrs. Reid. The doctor would have to know the patient.

Dr. Cooper. If he has had a previous heart attack——

Mrs. Reid. I am not talking about that.

Dr. Cooper. Then the doctor advises him. If he has not had a heart attack and many of these patients have seen no doctor and have no inklings as far as they know that they have a heart condition at all, they therefore would not be given the medication.

The second point is that the general form of medication that is given which is inserted under the tongue, like nitroglycerine, would not prevent the heart attack nor abort it nor prevent the lethal complications which occur after that, an unusual rhythm of the heart.

However, the Institute is investigating the capability of designing emergency kits for known cardiacs which could then give us the basis for some competence regarding certain types of complications and the symptoms of heart attack and means which could be self-applied while the patient calls the physician and gets medical attention.

Mrs. Reid. But is it not true that if a person would take nitroglycerine, for instance, it might keep him from going into a state of such terrible pain that would increase the attack? Is that not true?

Dr. Cooper. It may help with regard to the pain. Nitroglycerine is most effective in the condition known as angina pectoris, which is not necessarily occlusion with subsequent damage of the heart muscles. In these cases the application of nitroglycerine does abort the pain and the patient feels better.

In the case of a complete occlusion the characteristic is that you give him nitroglycerine and maybe it has no effect at all and that becomes just a severe and persistent pain, and therefore this is not sufficient even to relieve his pain.

It is a very complex problem.

COMPUTERIZED BLOOD BANKS

Mrs. REID. Last year during the hearings mention was made of the computer base for blood donors and blood products. Is this in operation?

Dr. COOPER. Yes. There are contracts let to test the feasibility of working this in metropolitan centers. There is some evidence that if the blood banking system is well developed and there is good cooperation amongst the various blood banks in a region that maximal resource use can be made of a computerized system and perhaps you could reduce the loss of shelf blood down to 5 or 10 percent from about 25 percent.

EFFECT OF DIET ON CHOLESTEROL LEVELS

Mrs. REID. Your coronary drug experiments seem to demonstrate the effect of cholesterol in blood. This is something about which many people are concerned. I understand that cholesterol can be controlled by diet and drugs. However, lately I have heard that there are some doubts about the effectiveness of diet. Has your research shed any light on this?

Dr. COOPER. There is a body of evidence, as you have mentioned, that supports the view that the level of cholesterol in the blood can be influenced by the diet. What we have learned recently is that in certain individuals this effect is more pronounced than in others and the selection out of these particular patients is absolutely fundamental if we are to seek a method for controlling blood cholesterol by the dietary method, so that this becomes a refinement in understanding what the role of cholesterol is in the process of coronary artery disease, for example.

There is no question but what there is a statistical relationship between very high cholesterols and the incidence of heart disease.

Mrs. REID. That is all, Mr. Chairman.

Mr. HULL. I have no questions.

MECHANICAL HEART DEVICES

Mr. CASEY. Is anyone working on this material for the mechanical heart which seems to have a technological block?

Dr. COOPER. Yes, sir. We devote a large sector of our resources to the mechanical circulatory assistance problem in the artificial heart program to the problem of materials solution. There have been some significant new ideas which have developed in the last year or two.

I might mention only two. One is the covalent bonding of heparin to a surface, that is, take an anticoagulant substance and by a physical-chemical process bind it on to a synthetic. In some circumstances this has proven to be a relatively long protection against clotting but it does not prevent the denaturization of other proteins, the effect of which we are still not aware of and where research is going on.

The other important element is the use of tissue culture techniques for the lining of the synthetic material with living cells and living tissue, particularly from the patient's own body, which would then be

much more compatible and nontraumatic to the blood. This is in a very early stage and I think that the results will be available soon. We are expending good effort in this area.

I think we need an expanded effort here on the basic problem of the atomistic and physical and chemical changes at the interface between the blood and the foreign substance. This is where we hope to increase our effort.

Mr. CASEY. It would take a lot of tissue, would it not?

Dr. COOPER. Tissue grows rapidly. The pump volume would not be prohibitive.

Mr. CASEY. It would be a good trick if you can do it—line the whole thing with living tissue.

Dr. COOPER. Yes, sir. This is feasible.

Mr. FLOOD. What is that?

Mr. CASEY. Line the mechanical heart and the pump and tubing with living tissue.

Mr. SMITH. I assume you are working on the red blood cells, too?

Dr. COOPER. What we are seeking to accomplish here is this: Since the fabrics in the materials are made up of either projected rough surfaces even in a highly polished condition or a matrix that the ability to allow tissue to grow into this and develop a very smooth lining like the normal lining of a blood vessel is a very promising aspect. We have a lot of work to do on it yet and we have to be sure it does not crack and cause clotting, but this is a very interesting avenue of pursuit.

Mr. CASEY. How many different types of mechanical hearts are there?

Dr. COOPER. Total implantable artificial hearts? There is basically only one.

What most investigators have done is to try to reproduce the analogy of the structure of the human heart, in other words, four chambers—two for receiving and two for pumping. The right side, or the one side, pumps blood to the lungs where it is oxygenated and purified and the other side pumps to the rest of the body. Although there are differences in how these two parts are put together and how they are designed from an engineering standpoint, and these are many, a dozen, the basic design is an analogy of the four chambers of the heart.

Mr. CASEY. What you speak of is just an assist.

Dr. COOPER. There are about five types of assists currently under investigation.

Mr. CASEY. I believe that is all, Mr. Chairman.

Mr. FLOOD. Thank you, Doctor.

You obviously made a very favorable impression on the subcommittee.

Did you get that feeling?

Dr. COOPER. It was very interesting, sir.

PACEMAKER

Dr. MARSTON. Sir, the pacemaker has arrived. You wanted to see it.

Dr. COOPER. This is the portion that is inserted in contact with the muscle of the heart, and the impulse comes off here and drives the

electrical stimulus into the heart muscle. Heart muscle, like any living tissue, responds with its normal reaction. In the case of muscle it is to beat and contract.

This is the power pack back here.

Mr. FLOOD. You must open the chest. There is surgery involved.

Dr. COOPER. This type is inserted down through the jugular vein into the heart and then it is implanted under the pectorial muscles here.

Mr. FLOOD. It does not call for open surgery?

Dr. COOPER. Certain types do not but other types do. There are types where there is an incision made into the chest and the device is sewn directly on the outside of the heart and then it is planted subcutaneously here.

Mr. FLOOD. You could cut the arm at this point and put it through the neck.

Dr. COOPER. But it is usually done through the large vein in order not to break it off while you are flexing.

Mr. FLOOD. Open the vein in the neck?

Dr. COOPER. Yes.

Mr. FLOOD. The pack you show can be inside or outside the body?

Dr. COOPER. It can be either way. It can be implanted easily in a pocket right here. As you notice there is a depression right under the clavicle. It can be implanted very nicely right here.

Mr. FLOOD. Who determines whether it is outside or inside? What condition would determine whether you would have it outside or inside?

Dr. COOPER. It would be the clinical decision as to the permanence of the heart block or the slowness of the heart beat. If it is going to be a permanent thing it is important that it be a permanent implantation so that the patient cannot traumatize it or fool with it and yet not to have to be concerned with adjusting anything.

Mr. FLOOD. Is this an expensive thing, this piece of hardware?

Dr. COOPER. A couple of hundred dollars, $250 to $300.

Mr. FLOOD. This one instrument I hold in my hand?

Dr. COOPER. Yes.

Mr. CASEY. How long do batteries last?

Dr. COOPER. It was to have been 5 years. This has not proven to be necessarily the case under living conditions in the body because although the bench tests might be the same in a different environment where there are other chemical forces at work they have not always lasted that long at the level necessary to drive the pacemaker at varying conditions of requirement.

However, they last several years. Some are 5 years, some are 2, some are 3, they can be easily replaced. It is not a major surgical procedure to replace the batteries.

SPECIAL REPORT ON HEART DISEASE

Mr. FLOOD. We will place your special report in the record at this point.

(The report follows:)

SPECIAL REPORT:
NATIONAL HEART INSTITUTE
ATHEROSCLEROSIS AND CORONARY HEART DISEASE:
DRUG AND HORMONE THERAPY

There are presently no cures for atherosclerosis or coronary heart disease. However, there is reason to hope that the disease process is reversible and that therapeutic agents will eventually be found that will be able to cause regression of established atherosclerotic lesions and to restore health to diseased arteries. Meanwhile, with existing therapeutic measures, it may be possible to halt or slow down the progress of the disease and thus avert or delay the onset of such disabling or deadly manifestations as heart attacks. For heart-attack victims, the outlook for immediate and long-term survival has been improved by new concepts of intensive medical care, improved resuscitative measures, and anticoagulant therapy. Clot-dissolving agents such as urokinase may provide still other powerful weapons against coronary thrombosis and other thromboembolic complications of atherosclerosis. But our greatest hope for substantially reducing mortality from coronary heart disease lies in devising effective means of prevention.

Therapeutic Approaches to Prevention

Through epidemiological studies on many human populations, we have learned much about factors in the individual or in his environment that increase his risk of developing coronary heart disease. From this information has emerged a highly useful portrait of the coronary-prone individual, a "coronary profile" that is helping physicians to spot the coronary candidate early and to initiate countermeasures that may reduce his risk and help to prolong his life.

Against some of these risk factors, the physician is helpless. For example, heart-disease risk increases steeply with age; is considerably higher for males than for females; and also appears to be higher for individuals with a strong family background of coronary heart disease, though conclusive evidence for this point is lacking. However, the physician can do something about many of the others.

In general, the coronary candidate tends to have elevated levels of cholesterol and other fatty substances (lipids) in the blood; to have elevated blood pressure; and to smoke too many cigarettes. He may be a hard-driving, aggressive (but sedentary) type who reacts strongly to emotional stress. He may also be overweight, although this does not appear to appreciably increase his risk unless it is associated with an increase in blood pressure.

Elevated Blood Lipids. The factor most consistently associated with increased susceptibility to coronary heart disease is elevated blood cholesterol. Excessive blood cholesterol levels may stem from certain metabolic disorders, such as hereditary hypercholesterolemia, hypothyroidism, or diabetes; but these are relatively uncommon causes. In most instances, moderate hypercholesterolemia can be traced to habitual dietary patterns.

In general, diets high in total fat, most of it saturated fat, tend to raise blood cholesterol, especially if the diet also contains excess calories. Conversely, diets containing less total fat, with polyunsaturated fats substituted for saturated fats wherever possible, tend to lower blood cholesterol. There appears to be a direct relationship between the degree of saturation of a given

fat and its effects on blood cholesterol: the more unsaturated the fat, the greater its cholesterol-lowering effects. But how polyunsaturated fats work their magic is still incompletely understood.

Most therapeutic diets and drugs for the management of elevated blood lipid levels have been aimed at the reduction of blood cholesterol. However, elevated blood cholesterol is only one facet of the larger clinical problem of hyperlipidemia. In turn, NHI studies have shown, hyperlipidemia is not a single entity but at least five, several of which include hypercholesterolemia as one of their manifestations.

The NHI studies have resulted in a rational system for identifying and classifying hyperlipidemias on the basis of serum lipoprotein patterns easily obtained by low-cost electrophoretic techniques. Under this system, most patients with elevated blood lipids fall conveniently into one of the categories of hyperlipoproteinemia designated as types I-V.

This is an important step toward a more systematic approach to clinical management, for standard "cholesterol lowering" regimens are not uniformly effective against all types of hyperlipoproteinemia and may actually aggravate rather than ameliorate one or another of these disorders. In fact, lumping patients with different types of hyperlipoproteinemia under the general heading of "hypercholesterolemia" may be responsible in large measure for wide individual variability in response to diet or drug regimens frequently observed in clinical trials.

Currently, NHI scientists are attempting to determine which mode of therapy is best suited to each of the five types of hyperlipoproteinemia. The two most common are type II and type III.

Type II is characterized by a relative excess of low-density lipoproteins. It may be an inherited condition, it may be of dietary origin, or it may be a secondary manifestation of certain other metabolic disorders, especially hypothyroidism. It is probably responsible for most cases of "hypercholesterolemia" that the physician is called upon to treat.

Type III, though less common than type II, is by no means rare. It, too, is characterized by an excess of low-density lipoproteins, especially the very-low-density ones that transport chiefly cholesterol and triglycerides in the blood. Both of these blood lipids are commonly elevated in type III patients.

Both type II and type III hyperlipoproteinemia are associated with accelerated development of atherosclerosis. In addition, a common characteristic of both types, if severe, is the appearance of fatty deposits called xanthomas in various soft tissues of the body, particularly around tendons of the hands and feet.

Good to excellent results have been achieved in both types with therapeutic diets containing 40 percent of total calories as fat, chiefly polyunsaturated; 40 percent carbohydrate; 20 percent protein; and severely limiting cholesterol intake. Such a diet substantially improves the blood-lipid pattern in type II and nearly normalizes it in type III.

Further blood lipid reductions have been achieved by supplementing the therapeutic diet with the lipid-lowering drugs.

Although effective in some patients, therapeutic diets may fail completely in others. Moreover, only relatively modest reductions in blood cholesterol usually result from dietary modifications that do not also produce major upheavals

in habitual dietary patterns.

The limitations inherent in diet therapy have spurred research seeking drugs or hormones that might lower blood cholesterol safely and effectively by some direct action on processes involved in the absorption, synthesis, transport, or excretion of cholesterol by the body. A number of the more promising lipid lowering agents developed thus far are described in the following section.

Nicotinic acid, an inhibitor of cholesterol synthesis, usually brings about moderate reductions in blood cholesterol. Its effectiveness is enhanced when it is used in conjunction with diet therapy. Its toxicity appears to be relatively low. Although the drug produces flushing, gastro-intestinal disturbances, or increased pigmentation of the skin in some patients, these side effects are seldom intolerable enough to force discontinuing the drug.

Estrogenic compounds may confer significant protection against recurrent heart attacks and increase long-term survival among middle-aged males who have previously suffered one or more heart attacks.

In one study, estrogen therapy produced a very high incidence of feminizing side effects (breast enlargement, loss of sexual drive), but sharply reduced the incidence of recurrent heart attacks and increased five-year survival rates by 50 percent.

In another study, significant protection was conferred by conjugated equine estrogens in doses that produced none of these undesirable side effects. Protection appeared to be greatest during the first 18 months, when mortality among estrogen-treated subjects was more than fifty percent lower than among controls. Thereafter, the effects were less spectacular; but, after three years, mortality in the estrogen-treated group was still one-third lower than that in the control group.

The findings of these studies suggest that middle-aged males, and possibly postmenopausal females who have overt heart disease or who appear to be coronary prone might derive substantial protection against first heart attacks or recurrent attacks from estrogen therapy. They further suggest that this protection need not entail intolerable side effects. However, more extensive scientific evaluation will be needed to determine the place of estrogens in the prevention and clinical management of coronary heart disease.

Thyroid hormones lower blood cholesterol, but the doses required also raise metabolic rates; cause nervousness, tremors, and other signs of hyperthyroidism; and very often cause angina pain in patients with coronary heart disease. Much research has been directed toward developing chemical analogs that would retain the cholesterol-lowering action of thyroid hormones, but produce fewer of the other metabolic effects. The most promising of the preparations developed thus far is D-thyroxine. In clinical trials with the compound, moderate reductions (15-25 percent) in blood cholesterol have been achieved. The drug is well tolerated by most patients, although increased heart rates, weight loss, angina, and other complications have occasionally attended its use.

Clofibrate (Ayerst) is a new drug that has shown great promise in clinical trials conducted to date. Not only does the drug reduce blood cholesterol, but it also produces even greater decreases in blood triglycerides, another lipid fraction strongly implicated in the development of coronary heart disease. There is some evidence that the drug also reduces the tendency of blood platelets to clump, and so it might confer some protection against certain of the thromboembolic complications of coronary heart disease that are so often responsible for its disabling

or lethal consequences. Although little evidence of toxicity has been observed in short-term clinical studies, clinical experience with the drug has been too limited to predict whether it will retain its effectiveness and freedom from adverse side effects during long-term use.

SaH-2348 (Sandoz) is a very new agent structurally akin to clofibrate and apparently, on a weight basis, considerably more potent. Experiments in rats have indicated that at only about one-tenth the dose SaH-2348 produces lipid-lowering effects similar to those achieved with clofibrate.

Four-week clinical trials in 31 patients with elevated blood lipids showed that a daily dose of 450 mg. of SaH-2348 significantly reduced blood cholesterol levels (mean reduction: 19%) in 25 patients and reduced triglycerides (mean reduction: 36%) in 22 patients.

The drug appeared to increase the metabolic destruction of cholesterol without much affecting synthesis or absorption. More elaborate and definitive studies will be needed to determine the clinical potential of the new agent.

Cholestyramine is a resin that combines with bile acids in the intestine to form a non-absorbable complex that is subsequently excreted in the feces. Bile acids are the major pathway of cholesterol excretion, but a substantial proportion of the bile acids derived from the oxidation of cholesterol are normally reabsorbed. By blocking this reabsorption step, cholestyramine stimulates increased bile-acid production by the liver at the expense of blood cholesterol. In most patients, the drug has reduced blood cholesterol levels by 15 percent or more; and more recent studies indicate that the drug can reduce blood triglyceride levels as well. The drug itself is not absorbed from the gut and is non-toxic; but large daily doses are required to reduce blood lipids significantly.

Neomycin and certain other antibiotics, when given orally, have brought about reductions in blood cholesterol comparable to those achieved with diet therapy or with other cholesterol-lowering agents. These drugs apparently increase the excretion of bile acids and bile salts, thereby causing additional cholesterol to be diverted for bile-acid production by the liver. The drugs may act by killing off normal bacterial inhabitants of the intestine, which appear to be important in normal bile-acid metabolism even though their role has not been precisely defined. More recent evidence indicates that Neomycin also forms chemical complexes with bile acids, and so may act in a manner similar to cholestyramine. Diarrhea has been a common, though seldom serious side effect of Neomycin therapy.

The "combination of ingredients" approach to therapy, previously employed with considerable success in the treatment of hypertension, may also be applicable to the drug treatment of elevated blood lipids, recent NHI grantee studies suggest. Using clofibrate and D-thyroxine separately, then in combination, the scientists found that the combination was more effective than either drug alone in reducing blood cholesterol levels. Clofibrate alone reduced these levels by about 12%, D-thyroxine by 14%, but the combination achieved a reduction of 20%. Clofibrate also reduced blood triglycerides, but this effect was not enhanced when D-thyroxine was added.

To summarize: At present, both dietary manipulation and certain drugs and hormones have proved feasible for reducing elevated blood cholesterol levels, although none of these will work in all cases, nor are any of them as effective against severe hypercholesterolemia as one might wish. Less is known about measures for controlling hyperlipoproteinemias that may be relatively common among Americans and that also appear to increase heart-disease risk.

And it remains to be proved that lowering of serum lipid levels by any means--drugs or diet--affects incidence or mortality rates in coronary heart disease. However, data relevant to this question may be forthcoming from the Coronary Drug Study, a large-scale research project designed to assess the effects of various lipid-lowering drugs and hormones on heart-disease mortality among men aged 30-64 who have previously suffered one or more heart attacks. Subjects under treatment with these agents are being compared with a control group which also will receive standard medical care but will not receive these drugs.

Four drugs have been selected for this clinical trial: D-thyroxine, nicotinic acid, conjugated equine estrogens, and clofibrate. These agents were chosen on the basis of their promising performance in earlier clinical trials and because they produce their lipid-lowering effects through different mechanisms.

Subjects will be followed for five years to determine the effectiveness of these agents in reducing plasma levels of cholesterol, triglycerides, and phospholipids and to evaluate the resultant effect (if any) of reduced lipid levels on heart disease mortality. If the effectiveness of these drugs is, in fact, related to their ability to lower blood fats, it can be calculated that such drugs might be able to reduce 5-year mortality rates by 30 percent.

Although the development of effective means of prevention may provide the ultimate solution to the problem of premature atherosclerosis and coronary heart disease, the Heart Institute must also continue to seek more effective means of treatment for those already afflicted by the disease.

An estimated 1,548,000 American adults already have angina pectoris and an additional 1,421,000 have already sustained one or more heart attacks. The number of new cases of coronary heart disease occurring in the U.S. population each year is estimated at 627,000. Thus, even if proven means of prevention were available and widely applied today, the problem of coronary heart disease and such clinical manifestations as angina pectoris and acute heart attacks would remain a major health problem for many years to come because of the large number of Americans already afflicted by advanced stages of the disease.

Plainly, the prospects of achieving any substantial reduction in death and disability from coronary heart disease in the immediate future are dependent on the development of improved modes of therapy for angina pectoris and acute heart attacks.

Many thousands of patients with angina are partially or completely disabled by the condition. Moreover, because angina is usually a manifestation of far advanced coronary atherosclerosis, the angina patient is at extremely high risk of acute heart attacks.

Acute heart attacks strike an estimated 750,000 Americans each year and currently account for more than half of the 560,000 annual deaths due to arteriosclerotic heart disease. For the hospitalized heart-attack victim, however, the prospects of survival and recovery are steadily improving, thanks to new concepts of intensive coronary care, improved procedures of patient monitoring, and better drugs for coping with heart failure, arrhythmias, and other complications of the acute illness.

New therapeutic agents for improving coronary bloodflow or for reducing the workload of the heart are providing more effective means of relieving the pain of angina pectoris and often permit patients to undertake activities that formerly would have brought on severe chest pain.

Coronary Heart Disease: Clinical Management

Angina Pectoris. The crushing chest pain of angina pectoris is a consequence of an inadequate supply of oxygen to the heart muscle to support its metabolic requirements. The usual cause is severe atherosclerosis of the coronary arteries, which sharply restricts the blood supply to the heart.

This condition frequently forces patients to lead sedentary lives. Severe pain may be triggered by exposure to cold, emotional upset, ingestion of large meals, and even the most moderate exercise, for example, bathing.

Drug therapy for angina pectoris is aimed at increasing coronary bloodflow by dilating the coronary arteries, or else decreasing the heart's need for oxygen.

Nitroglycerine remains the drug most widely used against angina. The drug dilates atherosclerosis-narrowed coronary arteries and also appears to reduce heart work, thereby reducing its oxygen requirements.

A newcomer, dipyridamole, appears to combine an artery-dilating action similar to that of nitroglycerine with an inhibitory effect on the formation of blood clots.

Beta adrenergic blocking agents are a highly promising new family of drugs for the relief of angina. These drugs selectively block those receptors in the sympathetic nervous system that normally increase heart rate and heart work in response to exertion or stress. By curbing these increases, beta blocking agents such as propranolol substantially increase the exercise tolerance of angina victims. Used alone or in combination with nitroglycerine, they have often enabled such patients to resume activities that formerly would have brought on disabling chest pain.

A recent study involving propranolol indicates that the short-term outlook for survival and recovery of coronary patients with angina is also definitely improved by this beta adrenergic blocking agent. These findings are based on a 2-year review of 135 patients with angina and coronary disease verified by x-ray visualization.

During this period, the control group consisting of 43 patients receiving standard medical therapy--including nitroglycerine and related agents for relief of chest pain--had 6 deaths, 5 heart attacks, and a 56.8 percent incidence of congestive heart failure. Among 55 propranolol- treated patients, there was only one death, 3 heart attacks, and a 35.8 percent incidence of congestive heart failure.

Myocardial Infarction. Acute heart attacks are nearly always the result of the blockade of vital coronary arteries by blood clots. These clots usually form on atherosclerotic lesions in diseased coronary arteries, especially in narrowed segments where the blood flows more slowly.

Anticoagulant drugs cannot dissolve clots, but they do help to minimize heart damage resulting from coronary thrombi. By preventing the growth or extension of the clot, anticoagulants may prevent it from completely obstructing a partially occluded vessel or from sealing off other branches arising near the site of blockade. They help to prevent the formation of additional clots in other coronary branches or in collateral vessels that may be supplying blood to the ischemic area. Anticoagulant therapy also reduces the risk of additional infarctions, pulmonary or cerebral embolism, and venous thrombosis, which may complicate the acute phase of myocardial infarction.

Anticoagulant therapy has its complications and its critics. But available clinical evidence favors the use of anticoagulants during the acute phase of heart

attacks. In most clinical studies, these drugs have increased survival anywhere from 30 percent up to more than 50 percent. When patients have been carefully screened to exclude those with disorders that would increase the hazards of anticoagulant therapy and when therapy has been properly and closely supervised, there have been few serious bleeding episodes or other complications attributable to anticoagulant therapy.

There is also a preponderance of clinical evidence that the risk of recurrent heart attacks is reduced and long-term survival increased by keeping patients on continuous anticoagulant therapy during the first year or two after their attacks. To date, however, there have been too few long-term studies to establish conclusively whether the degree of protection conferred by anticoagulants beyond this period is sufficient to justify the risk, inconvenience, and expense of continuing this treatment indefinitely.

Fibrinolytic agents, which bring about the dissolution of blood clots--either by attacking them directly or by activating the body's own clot-lysing mechanisms--may well turn out to be even more effective than anticoagulants in reducing mortality among heart-attack victims. At present, however, this is theory, not established fact; for the value of fibrinolytic therapy in the clinical management of coronary thrombosis has not been convincingly demonstrated.

A number of investigators have employed various fibrinolytic preparations in the clinical treatment of heart attacks. Many of their results have indicated that fibrinolytic therapy reduced the extent of heart-muscle damage, improved the clinical course, and increased survival among these patients. But many of these studies were not adequately controlled and involved too few patients to justify strong statements concerning the worth of fibrinolytic therapy. Further undermining confidence in the results of earlier clinical studies was the lack of suitably purified fibrinolytic preparations.

A number of the difficulties that had hampered clinical progress in this field have now been overcome, and definitive clinical studies now appear feasible. The fibrinolytic agent selected is urokinase, derived from human urine. Urokinase is a "native" substance. Being non-antigenic, it has distinct advantages over earlier fibrinolytic agents (streptokinase, staphylokinase) derived from bacteria. Anyone who has ever had a streptococcal or staphylococcal infection has developed antibodies against streptokinase or staphylokinase. Thus, in using these agents, the dosage must be increased sufficiently to neutralize the antibodies and still have enough activator left over to bring about clot dissolution. The intense antibody response elicited by these agents also makes it extremely hazardous to use them more than once. However, results with urokinase indicate that infusions of this agent can produce intense fibrinolytic activity in the blood without the undesirable side effects of earlier fibrinolytic agents.

Currently NHI is supporting a carefully controlled clinical trial of urokinase at a number of cooperating institutions. The drug is being tested against clots obstructing bloodflow to the lungs (pulmonary embolism). However, if urokinase performs up to expectations, it is anticipated that definitive studies will subsequently be done to determine the value of urokinase against coronary occlusion and strokes resulting from clots or emboli.

Death from a heart attack is due to one or more of three mechanisms. Often the death-dealing mechanism is an abnormal, chaotic rhythm of the heart or an actual arrest of cardiac contraction. Cardiac defibrillators, external electrical pace-making and driving devices have already proven life-saving in many instances by returning the heart rhythm to normal. Drug control of cardiac rhythmicity is another avenue of research holding great promise for preventing or controlling the rhythm complications of myocardial infarction.

The second mechanism of death in acute myocardial infarction is a profound

derangement of the nerve reflexes which integrate heart function with general body physiology. The often fatal circulatory collapse or "shock" which results from this reflex disturbance is little understood and its clinical management is largely empirical. But drugs for controlling such shock are under intensive study.

The third mechanism of death is the damage to the heart muscle resulting from the blockage of its arterial nourishment. This occurs to a greater or lesser extent in every heart attack. It is also one of the principal causes of the chronic disability, the shortness of breath, the pain accompanying effort, and other evidences of diminished heart function so frequently seen in patients who have recovered from one or more heart attacks. For these patients, drugs capable of providing continuous support to their failing circulation are essential for restoration to more normal living.

Antiarrhythmic drugs are used to correct variations from the normal rhythm of heartbeat. Arrhythmias upset the smooth contraction sequence of the heart, often compromise its pumping efficiency, and may progress to cardiac arrest. They are a dreaded complication of heart attacks and are often the immediate cause of death among heart-attack victims.

Fortunately, if promptly detected and treated, many arrhythmias stemming from heart attacks can be corrected or controlled by drugs such as digitalis, quinidine, diphenylhydantoin, procaine amide, isoproterenol, and others. Serious arrhythmias that fail to respond to drug therapy can often be corrected by precisely timed shocks delivered to the heart by electrical defibrillation equipment.

Propranolol, the beta adrenergic blocker cited earlier for its anti-anginal effectiveness, has also proved to be an effective anti-arrhythmic drug as well. It not only prevents arrhythmias stemming from sympathetic hyperactivity but also seems to possess a "quinidine-like" effectiveness against a variety of rhythm disturbances. This latter anti-arrhythmic effect may be separable from the drug's adrenergic blocking action, since experiments have shown that propranolol continues to act as a broad spectrum anti-arrhythmic agent when its adrenergic blocking effects have been overcome by other drugs.

The local anesthetic lidocaine now appears to be a safe and effective agent for treating and preventing ventricular arrhythmias in patients who have experienced acute myocardial infarctions. Earlier surgical studies have indicated that lidocaine reduced heart-muscle irritability after open-heart surgery and effectively curbed ventricular arrhythmias during the postoperative period. The drug also performed well in 21 patients with ventricular arrhythmias following heart attacks. Each received a dose of 25-100 milligrams, then was maintained by intravenous infusions of 0.5-4 milligrams per minute for periods of up to 72 hours. Excessive ventricular rates were controlled in 20 instances and the frequency of premature contractions was reduced in 17 of the 21 patients.

Bretylium Tosylate, originally developed as anti-hypertensive agent, has also shown promise against ventricular fibrillation and other heart rhythm problems in recent studies.

Animal studies had demonstrated the value of bretylium in reducing the vulnerability of the heart to arrhythmias resulting from heart biopsy, electrical shock, or hypothermia. Subsequently a pilot clinical trial of the drug was carried out among 30 patients with serious arrhythmias following heart attacks, open-heart surgery, or digitalis intoxication.

It proved to be a valuable adjunct to treatment of patients with ventricular arrhythmias that had been resistant to other drugs or countershock. In 27 patients, suppression of the arrhythmia occurred within 5 minutes to several hours; in the other 3, correction was delayed or required a second dose, but all were brought under control. The anti-arrhythmic effects of bretylium persist for 10-20 hours;

and, unlike most anti-arrhythmic drugs, which in large doses depress contractility, bretylium actually improves heart output.

The quest for new and better anti-arrhythmic drugs continues, as does basic research to define more precisely the mechanisms of action, the advantages, and the limitations of currently available drugs. Knowledge gained from such studies is enabling the physician confronted with a particular type of arrhythmia to choose from among a fairly wide selection of agents the drug or combination of drugs most likely to be effective in coping with the problem.

Cardiogenic Shock. An extremely dangerous complication of acute heart attacks, cardiogenic shock formerly carried mortality rates as high as 95%. Improved therapeutic measures have reduced this appalling toll somewhat.

Often, an important factor in cardiogenic shock is extensive heart muscle damage sustained as a result of the attack, which may severely compromise the pumping effectiveness of the heart. Frequently, heart output may be further diminished by the loss of normal blood-vessel tone.

Widespread relaxation of blood vessels increases the capacity of the vascular system, especially the venous bed, and thus reduces the amount of blood returning to the heart.

When both of these factors are operative in cardiogenic shock, the drugs most frequently used are norepinephrine, metaraminol, or mephenetermine. These agents act directly on the heart to improve its pumping performance and to increase its output, and they also increase blood-vessel tone. This dual action tends to raise systemic blood pressure and to increase effective bloodflow to the organs and tissues of the body.

Other drugs, such as methoxamine, phenylephrine, and angiotensin, also increase blood-vessel tone; but their effectiveness in cardiogenic shock is limited by the fact that they have no direct effect upon the heart. Thus, while blood pressure may be raised by these drugs, heart output and systemic bloodflow may actually decrease.

In other instances of cardiogenic shock, there may be widespread blood-vessel constriction rather than relaxation. This may sharply reduce heart output and systemic bloodflow by forcing the damaged heart to pump against a higher resistance. In such instances, vasopressor drugs that increase blood-vessel tone may only make the situation worse.

Recently, NHI grantees tested several treatment regimens in animals with heart attacks induced by injecting plastic microspheres into the coronary circulation. Of animals developing cardiogenic shock, 85% died within 24 hours if untreated. But 75% survived when treated with infusions of low-molecular-weight dextran, a plasma expander, plus phenoxybenzamine, a drug that selectively blocks nerve receptors that mediate blood-vessel constriction. By increasing circulatory blood volume and decreasing blood-vessel resistance, the combination boosted heart output and effective systemic bloodflow. It has since been used, with similar gratifying results, in selected patients with cardiogenic shock.

Norepinephrine increases heart rate and the vigor of heart-muscle contraction by stimulating beta receptors of the sympathetic nervous system. But this drug also stimulates sympathetic alpha receptors. Alpha adrenergic stimulation causes blood-vessel constriction that reduces the overall effect of norepinephrine on heart output and coronary bloodflow while increasing the cardiac workload. NHI grantees report that using norepinephrine to augment cardiac output plus phentolamine to achieve partial blockade of alpha receptors increased coronary bloodflow by as much as five times without significantly increasing the workload on the heart in animals with induced cardiogenic shock.

Dopamine, the chemical precursor of norepinephrine, is a potent beta adrenergic stimulating agent that also dilates the blood vessels of the kidney. Preliminary studies by NHI grantees indicated that infusions of dopamine lasting up to 35 minutes increased heart output and decreased peripheral blood-vessel constriction in 7 patients with hypotension, 3 of them in clinical shock.

Subsequently the drug was infused for periods of 2-51 hours in 14 other patients with severe hypotension and reduced kidney function due to heart disease. Both peripheral bloodflow and urinary output improved markedly in 7 patients, while one or the other function was improved in 6 others. The grantees suggest that dopamine may prove superior to certain other vasopressor drugs in the clincal management of shock of cardiac origin. Their good results with dopamine have subsequently been duplicated in clinical studies elsewhere.

Chronic Congestive Failure. Congestive heart failure may develop as a consequence of a long-standing circulatory disorder, such as hypertension, that places a prolonged, heavy circulatory burden on the heart, or it may stem from the loss of functioning heart muscle tissue as a result of one or more heart attacks. Whatever the cause, the failing heart is incapable of coping with the circulatory demands of the body. Heart failure is commonly attended by abnormal salt retention, and the accumulation of fluid in the lungs (pulmonary edema) can be a serious and life-threatening complication. The treatment of congestive heart failure entails reducing the workload on the heart; using cardiac stimulants to improve its pumping efficiency and output, and preventing or eliminating edema.

Digitalis, used against congestive heart failure since 1785, is still the drug of choice, although crude digitalis preparations have been largely supplanted by digitoxin and digoxin, purified active ingredients of digitalis plants.

In patients with congestive heart failure, digitalis slows heart rate, but increases the vigor and efficiency of heart-muscle contraction so that more blood is expelled per beat. In normal subjects, digitalis increases heart output only slightly if at all, because the drug causes blood-vessel constriction that largely negates its cardiac stimulant effects by forcing the heart to work against a higher resistance. However, for reasons that are not clear, this blood-vessel constriction does not occur in patients with failing hearts treated with digitalis, so that the drug substantially augments heart output and systemic bloodflow.

Glucagon, a pancreatic hormone long known for its role in elevating blood sugar, has only recently been identified as a heart stimulant of considerable clinical promise. Its mechanism of action in this new role is still obscure, but in the liver glucagon activates some of the same enzymes which are activated in the heart by norepinephrine. Glucagon produces a sustained and striking increase in heart output while causing only slight and transient increases in heart rate. It does not increase heart irritability (with the resultant threat of arrhythmias) and its only side effect observed thus far is occasional nausea. Its major drawback for long-term use is that it must be given by injection.

Heart stimulants and low-sodium diets may provide adequate control of edema in many patients with congestive heart failure; but, should edema be severe or refractory, the physician has at his disposal a wide variety of clinically proven diuretic agents from which to select the one best suited to the needs of the individual patient.

Although these agents may differ in mode or site of action, potency, onset and duration of action, and route of administration, diuretic drugs promote the elimination of excess fluid primarily by increasing urinary sodium excretion. Most also increase urinary losses of both potassium and sodium so that patients on diuretic therapy are usually given supplementary potassium to prevent potentially dangerous deficits.

Organomercurial agents were among the earliest diuretic agents. Usually

given by injection, though some are suitable for oral use, they are extremely potent, fast-acting drugs employed primarily in clincal situations requiring that the patient be rid of a lot of water in a hurry, such as severe pulmonary edema.

Chlorothiazide, developed by Merck, Sharp and Dohme in 1955 and introduced commercially in 1958, is the most widely used diuretic. It is an oral agent well suited for long-term control of edema. Its diuretic action is most pronounced in severe edema, then usually diminishes as the edema clears, thereby reducing the threat of fluid and electrolyte imbalances. The drug is also widely used in the treatment of hypertension, since it has a mild hypotensive action and also potentiates the effects of a number of other blood-pressure-lowering drugs. Chlorothiazide has spawned a large number of thiazide derivatives, each a more potent diuretic than the thiazide that preceded it. But these derivatives provide few clinical advantages over chlorothiazide other than requiring smaller doses to achieve the same clinical result.

Triamterene, a diuretic recently introduced by Smith, Kline and French, is reportedly highly useful in the treatment of edema due to congestive heart failure and/or excessive production of aldosterone, a hormone that promotes sodium retention by the kidney. This drug also promotes the excretion of sodium without causing undue potassium losses, a distinct advantage over the thiazide diuretics.

Amiloride, a diuretic with unusual potassium-conserving effects, was recently introduced by Merck, Sharp and Dohme for clinical investigation. Preliminary studies in 14 subjects--3 of them normal, 6 with various edematous conditions, and 5 with essential hypertension--indicated that amiloride alone consistently showed potent sodium-losing and potassium-retaining effects while producing mild diuresis.

Amiloride, used in combination with other diuretics, consistently enhanced their sodium-losing effects while strongly or completely blocking their potassium-losing effects. Thus, in combination with other diuretics, amiloride facilitates treatment of the most difficult edematous states while lessening the attendant danger of potassium depletion. No toxic effects were noted in any of the subjects treated.

Ethycrynic acid, introduced by Merck, Sharp and Dohme, is a new, orally administered agent that, in speed and potency of action, rivals the organomercurial agents. In clinical trials it has proved extremely useful in the clinical management of severe edema, especially life-threatening pulmonary edema, and has often proved effective against edema refractory to other diuretics.

Aldosterone Antagonists, such as spironolactone, are steroids that counter the salt-retaining action of aldosterone. They are expensive, and their clinical value is limited to those relatively rare clinical situations where excessive aldosterone production is directly responsible for the edema or else is a significant aggravating factor.

Conclusion

Heart damage due to atherosclerosis is typically a late, often unexpected, largely irreversible consequence of a slowly progressive condition initially acquired in early life, possibly in childhood or early adulthood. The greatest hope for effectively combatting this massive and growing health problem resides in identifying and eliminating primary and antecedent causes, so that attempts to halt or reverse the secondary and multiplied consequences in patients may ultimately be unnecessary. Meanwhile, the essential pursuit of more effective means for treating patients already victimized by coronary heart disease is yielding abundant practical results.

The Coronary Drug Study, previously described, is an example of a targeted

research program concerned primarily with the prevention of recurrent heart attacks. But, if these drugs confer significant degrees of protection in patients with clinically manifest heart disease, their benefits are likely to be even greater among subjects who are coronary prone but who have not yet experienced clinical complications.

The salvage and rehabilitation of patients who have already sustained heart attacks is the goal of the Institute's Artificial Heart-Myocardial Infarction Program. While the Artificial Heart Branch is driving toward the development of effective, reliable devices to provide temporary or permanent circulatory assistance to damaged or failing hearts, and, if developments warrant it, a total replacement for hearts damaged beyond salvage, the Myocardial Infarction Branch is directing a program of intensive biomedical research on the acute heart attack and its medical management. The goals of the medical program are to learn more about acute heart attacks, their presently unpredictable clinical course, and the mechanisms underlying potentially lethal complications such as arrhythmias and shock. It will seek improved techniques for diagnosis and for the evaluation of irreversible heart muscle damage, devise and evaluate methods for the continuous monitoring of patients, develop and test new drugs and therapeutic procedures, and define the place of heart-assist devices in the clinical management of heart attacks. The ultimate goal is to reduce the necessity for heart-assist devices by providing less drastic, equally effective therapeutic alternatives.

The achievements of these realistic goals could have a dramatic impact on our presently appalling death rate from coronary heart disease and its complications.

Mr. FLOOD. Do you do any research yourself with your own hands or are you just an administrator? Do you do any research?

Dr. COOPER. Yes, sir; I do a little bit.

Mr. FLOOD. What are you doing now?

Dr. COOPER. My field——

Mr. FLOOD. What is your pet?

Dr. COOPER. I am interested in the role of the nerves and the control of the heart. I was involved previously in transplantation of the heart myself.

I was also involved in artificial circulation.

Mr. FLOOD. You have been a fine witness.

Dr. COOPER. Thank you very much, sir.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Heart Institute

Amounts Available for Obligation

	1969	1970
Appropriation	$166,927,500	$163,141,000
Comparative transfer to "Salaries and expenses, Office of the Director, National Institutes of Health"	-919,000	---
Cutback required by P.L. 90-364	-4,999,000	---
Total obligations	161,009,500	163,141,000
Disposition of cutback:		
To be returned to the Treasury	4,999,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
72	Research		$99,666,000		$101,307,000		+$1,641,000
	General research support grants		(9,425,000)		(9,425,000)		.....
	Scientific evaluation and planning		(163,000)		(163,000)		.....
	Categorical clinical research centers		(4,500,000)		(4,500,000)		.....
74	Heart cooperative drug study		(3,820,000)		(4,820,000)		(+1,000,000)
	Specialized research centers		(925,000)		(925,000)		.....
82	Fellowships		7,604,000		7,309,000		-295,000
83	Training		18,150,000		17,442,000		-708,000
	Direct operations:						
84	Laboratory and clinical research	375	13,168,000	387	13,641,000	+12	+473,000
85	Collaborative research and development	31	17,354,000	35	18,148,000	+4	+794,000
87	Biometry, epidemiology, and field studies	64	1,692,000	64	1,724,000	0	+32,000
88	Training activities	4	225,000	4	204,000	0	-21,000
88	Review and approval of grants	99	2,561,000	99	2,723,000	0	+162,000
89	Program direction	27	589,500	31	643,000	+4	+53,500
	Total obligations	600	161,009,500	620	163,141,000	+20	+2,131,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions.....	600	620	+20
Full time equivalent of other positions..	28	30	+2
Average number of all employees.....	583	602	+19
Personnel compensation: Permanent positions.....	$6,309,000	$6,481,000	+$172,000
Positions other than permanent.....	223,000	242,000	+19,000
Other personnel compensation.....	52,000	52,000	---
Total personnel compensation.....	6,584,000	6,775,000	+191,000
Personnel benefits.....	703,000	715,000	+12,000
Travel and transportation of persons.	281,000	285,000	+4,000
Transportation of things.....	100,000	109,000	+9,000
Rent, communications, and utilities..	242,000	242,000	---
Printing and reproduction.....	118,000	118,000	---
Other services.....	24,924,500	26,169,000	1,244,500
Supplies and materials.....	1,691,000	1,706,000	+15,000
Equipment.....	946,000	964,000	+18,000
Grants, subsidies, and contributions.	125,420,000	126,058,000	+638,000
Total obligations by object.....	161,009,500	163,141,000	+2,131,500

Summary of Changes

1969 estimated obligations	$161,009,500
1970 estimated obligations	163,141,000
Net change	+2,131,500

Increases	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
A. Built-in				
1. Annualization of 1969 pay increase	...	...	...	$11,000
B. Program				
1. Research grants	...	$99,666,000	...	1,641,000
2. Laboratory and clinical research	375	8,270,000	12	100,000
3. Collaborative research and development	31	17,333,000	4	778,000
4. Program direction	27	568,000	4	50,500
Total program increase	...	.....	20	2,569,500
C. Payment to "National Institutes of Health management fund" for centrally-furnished services	...	6,222,000	...	554,000
Decreases				
A. Program				
1. Fellowships	...	7,604,000	...	-295,000
2. Training grants	...	18,150,000	...	-708,000
Total decreases	...	.....	...	-1,003,000
Total net changes requested	...	.....	+20	+2,131,500

Explanation of Changes

Research grants--The increase provides $641,000 for the noncompeting continuation of existing regular research grants and $1,000,000 for complete patient enrollment in the heart cooperative drug study.

Fellowships--The decrease of $295,000 will result in an estimated 365 awards in 1970 compared with 418 in 1969.

Training grants--The decrease of $708,000 will result in an estimated support of 266 graduate research and clinical training programs in 1970 as compared with 285 in 1969.

Laboratory and clinical research--The program increase of $100,000 and 12 positions will permit expansion into laboratory space to be newly assigned to this Institute.

Collaborative research and development--The program increase of $778,000 and 4 positions will permit further systematic biological testing and evaluation of the family of circulatory assist devices currently under development by the artificial heart program and for the continuation of existing myocardial infarction research units.

Program direction--The program increase of $50,500 and 4 positions is needed for professional staff in the Office of the Director, National Heart Institute.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action Taken or to be Taken
1969 House Report	
The Committee Report again noted that of more than one million deaths which result annually from heart disease, over half were due to arteriosclerosis and its most common consequence, the acute heart attack. (Page 19, 20)	The National Heart Institute is attacking this urgent health problem on a number of fronts.
(1) Myocardial Infarction Research Units are being established to develop more effective salvage techniques that could be widely applied to heart-attack cases. (Page 19)	(1) Nine such units have been established out of a planned network of 12. Attempts are also being made to develop satisfactory animal models of the acute heart attack; also planned are vital studies to attack the problem of sudden pre-hospital cardiac death, which accounts for one half of all deaths from heart attacks.
(2) Supported was research concerned with the development of heart-assist devices and techniques. (Page 19)	(2) Much progress has been made in the past year. While one of the major problems remains the development of suitable materials, several kinds of assist devices are ready for testing; the next step is the refinement of a critical test and evaluation program so that these circulatory assist devices can be subjected to thorough test and evaluation during the period of development and before they are made available to the practicing physician. Research is aimed at the eventual development of a totally implantable artificial heart.
(3) The Coronary Drug Project is to demonstrate whether the sustained reduction of cholesterol and other fatty substances in the blood, by use of drugs, will improve the long-term survival among heart-attack victims. (Page 20)	(3) Another approach to the heart-attack problem, the 55 participating clinics will have enrolled the necessary 8,000 patients by July, 1969. An additional $1 million is requested in 1970 to permit funding at the level of full operation.
(4) Because elevated blood lipids appear to be a major risk factor in heart attacks, the Institute supports projects that deal specifically with the reduction of blood lipids through dietary modification, as well as drugs. (Page 20)	(4) Intensive, controlled studies are receiving continuing particular emphasis by the Heart Institute: over $6 million in research projects deal specifically with the reduction of blood lipids through dietary modification or drugs.

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action Taken or to be Taken
1969 House Report (Continued)	
(5) The Committee again noted that the Heart Institute has supported planning for the eventual establishment of 10 to 12 Cardiovascular Research Centers--of the sort envisioned by the President's Commission on Heart Disease, Cancer, and Stroke. It is hoped all will be operating by 1973. (Page 20)	(5) The Heart Institute has provided support for planning for specialized research centers at 14 medical schools and other institutions. Funds available in 1970 are adequate to continue the planning effort and to provide minimal operational support for perhaps one such center.
1969 Senate Report	
(1) The Committee Report again discussed at length the purposes, history, and potential of the Artificial Heart-Myocardial Infarction Program and recommended an increase of $4 million for the program. This increase was not included in the 1969 enacted appropriation. (Page 41)	(1) See items (1) and (2) in the 1969 House Report.
(2) The Committee Report again discussed at length the concept, background, and role of Specialized Cardiovascular Research Centers and recommended increased funds for this program by $4 million to allow several of these cardiovascular research centers to move into the operational phase. These operational funds were not included in the 1969 enacted appropriation. (Page 41, 42)	(2) See item (5) in the 1969 House Report.
(3) The Committee Report noted that the Heart Cooperative Drug Study is proceeding: that the total 55 participating clinics have been enrolled and that patient recruitment is proceeding. (Page 42)	(3) See item (3) in the 1969 House Report.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action Taken or to be Taken
1969 Senate Report (Continued)	
(4) The Committee Report noted that the National Blood Resource Program, in its second year of operation, continued research on blood preservation and fractionation and planned a computer-based inventory system for blood products and blood donors for more equitable and more efficient distribution of blood products. (Pages 42, 43)	(4) The principal goals of this program are concerned with improved methods for storage, distribution, and utilization of blood and blood components, and development and evaluation of therapeutic agents to counter disorders of the blood-clotting mechanisms. Specific goals are described in the narrative justification.
(5) The Committee Report noted that another major project soon to get underway is the clinical evaluation of a clot-dissolving agent, urokinase. (Page 43)	(5) This project was begun in 1968 against clots obstructing blood flow to the lungs; this clinical trial is an essential prelude to further evaluation of clot-dissolving agents in the treatment of heart attacks, certain strokes, and other clotting complications of heart and blood vessel disease.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act Section 301--Research and Investigation, in General.....	Indefinite
Title IV, Part B--National Heart Institute.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Title IV--National Research Institutes, Part B,
National Heart Institute

Section 411. There is hereby established in the Public Health Service a National Heart Institute (hereafter in this part referred to as the "Institute").

Section 412. In carrying out the purposes of section 301 with respect to heart diseases the Surgeon General, through the Institute and in cooperation with the National Advisory Heart Council (hereafter in this part referred to as the "Council"), shall--

(a) conduct, assist, and foster researches, investigations, experiments, and demonstrations relating to the cause, prevention, and methods of diagnosis and treatment of heart diseases;

(d) make grants-in-aid to universities, hospitals, laboratories, and other public or private agencies and institutions, and to individuals for such research projects relating to heart diseases as are recommended by the Council, including grants to such agencies and institutions for the Council, including grants to such agencies and institutions for the construction, acquisition, leasing, equipment, and maintenance of such hospital, clinic, laboratory, and related facilities, and for the care of such patients therein, as are necessary for such research; (g) in accordance with regulations and from funds appropriated or donated for the purpose (1) establish and maintain research fellowships in the Institute and elsewhere with such stipends and allowances (including travel and subsistence expenses) as he may deem necessary to train research workers and procure the assistance of the most brilliant and promising research fellows from the United States and abroad, and, in addition, provide for such fellowships through grants, upon recommendation of the Council, to public and other nonprofit institutions; and (2) provide training and instruction and establish and maintain traineeships, in the Institute and elsewhere in matters relating to the diagnosis, prevention, and treatment of heart diseases with such stipends and allowances (including travel and subsistence expenses) for trainees as he may deem necessary, the number of persons receiving such training and instruction, and the number of persons holding such traineeships, to be fixed by the Council and, in addition, provide for such training, instruction, and traineeships through grants, upon recommendation of the Council, to public and other nonprofit institutions.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and expenses, Office of the Director," National Institutes of Health".....	-$919,000	.....	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH management fund.

National Heart Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$45,594,000	$52,744,000	$89,500,000	$62,237,000
1961	63,162,000	71,762,000	125,166,000	86,900,000
1962	97,073,000	105,723,000	160,100,000	132,912,000
1963	126,898,000	143,398,000	149,398,000	147,398,000
1964	130,108,000	129,325,000	130,545,000	129,325,000
1965	125,640,000	124,521,000	125,171,000	125,171,000
1966	141,412,000	146,212,000	143,462,000	141,462,000
1967	148,407,000	154,770,000	164,770,000	164,770,000
1968	167,954,000	167,954,000	177,954,000	167,954,000
1969	169,735,000	164,120,000	172,120,000	166,927,500
1970	163,141,000			

Justification

National Heart Institute

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	600	$7,287,000	620	$7,490,000	+20	+$203,000
Other expenses	...	153,722,500	...	155,651,000	...	+1,928,500
Total	600	161,009,500	620	163,141,000	+20	+2,131,500

General Statement

The special province of the National Heart Institute is the cardiovascular system and its diseases. Its primary mission is the conduct and support of research to increase knowledge of the structure and functions of this system and to search for means of preventing, alleviating, and curing the diseases that afflict it. It is a complex system, vulnerable at many points, and prey to a large family of diseases. In many instances, the causes of these diseases are not known. Some may be inherited, others may arise from adverse factors affecting the fetus at critical stages of development, and still others from subtle abnormalities in the complex processes of metabolism. In addition, there may be many factors--within the person himself, his surroundings, or his mode of life--that affect susceptibility to these diseases, accelerate their development, or else trigger their often devastating complications.

The complexities of the cardiovascular-disease problem dictate a research program of considerable scope and diversity. It includes studies which yield basic information on the cardiovascular system, the blood, on the lungs and kidneys that oxygenate the blood and purify it of waste products, and on the nervous system and endocrine glands and their secretions, which influence cardiovascular performance. Some probe deeply into the metabolic reactions occurring within individual cells, the enzymes involved with these reactions and genetic mechanisms that dictate the form and regulate the production of structural proteins and enzymes.

The primary goal is prevention; however, in reality approximately 15 million Americans already have some form of heart disease and an additional 14 million are suspected of having the disease. For this reason, an attempt is made to balance the allocation of available resources in three ways: prevention, diagnosis, treatment.

For purposes of program planning and operations, the heart diseases are categorized into several types. These disease areas are described briefly in the narrative justification which follows. These activities are supported in the laboratory and clinical facilities at the National Institutes of Health in Bethesda, by nationally organized programs supported largely by contracts to industrial and non-profit organizations, and by grants to universities and other non-profit organizations.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research projects	$80,833,000	$81,474,000	+$641,000
Special programs	18,833,000	19,833,000	+1,000,000
Total research grants	99,666,000	101,307,000	+1,641,000

Research Projects

During 1968, the NHI obligated $86,007,447 in support of 1,783 cardiovascular research projects at universities, hospitals, and other institutions throughout the country. The results of these projects were disseminated to the scientific

and medical communities in more than 4,000 scientific papers and abstracts on a multitude of cardiovascular subjects published during the year by NHI grantees. The following is a brief summary of research grant support programs in major cardiovascular disease areas. Plans for 1969 and 1970 are for the most part a continuation of current research in these areas, as indicated in the research grants program analysis table at the end of the research grant justification. The 1970 budget request for regular research projects includes an increase of $641,000 for noncompeting continuation requirements. This summary centers around major on-going research problems; recent accomplishments are reported separately under Highlights of Research Progress during 1968 from the National Heart Institute.

Arteriosclerosis

The prevention of arteriosclerosis, hardening of the arteries, and its complications continues to be one of the highest priority goals of the Institute and, in terms of research grant funds, it is the largest single program category. Arteriosclerosis may involve the arteries of the heart itself in coronary artery disease, those of the head in stroke, as well as other parts of the circulatory system. Major research efforts are described below under the areas of atherosclerosis, coronary artery disease, cerebrovascular disease, and a special program, the Heart Cooperative Drug Study.

Atherosclerosis. This is, by far, the most prevalent of all cardiovascular disorders. It was responsible for over half of the one million deaths due to heart disease last year in this country. This excessive mortality rate is not only unnaturally high and abnormally premature, but one which should be amenable to reduction. A 25% reduction below age 65 appears realistic and would save 40,000 productive lives each year. If it could be entirely eliminated in the American population, or even if only some of its complications (such as heart attacks, strokes, and congestive heart failure) could be prevented, hundreds of thousands of lives might be spared or prolonged each year.

Research in atherosclerosis has grown rapidly in the past decade. Since 1956 there has been nearly a tenfold increase in the number of research projects in this field. Major projects include:

- Studies on lipid metabolism and lipid disorders that predispose to atherosclerosis.
- Therapeutic diets and drugs for reducing blood lipid levels.
- Epidemiologic studies to identify and quantitate coronary heart disease risk factors.
- Improved techniques for diagnosis of coronary heart disease in susceptible but asymptomatic individuals.
- Monitoring techniques, resuscitation measures, emergency drugs for management of acute heart attacks.
- Drugs and surgical techniques for relief of angina.

Coronary Artery Disease. Death and disability from coronary atherosclerosis represents the greatest single challenge to modern medicine. Before the treatment of heart attack can be developed to its optimum there must be a greater understanding of the organ in its normal state, in the stress of decreased blood supply or increased metabolic demands, and in the episode of ischemia or infarction. The acquisition of data in the following areas will certainly help to impede or prevent coronary disaster:

- Functions of heart muscle in health and disease.
- Influences of decreased blood supply on heart metabolism and the mechanisms by which acute cessation of blood flow injures the heart.
- Cardiac rhythm and the many factors affecting it.
- Drug studies for the improvement of blood supply and for the management of arrhythmias.
- Better rehabilitation of the psychic and the somatic heart attack victim.

The Heart Cooperative Drug Study

The goal of the NHI Coronary Drug Project is to improve long-term survival among recovered heart-attack victims by using lipid-lowering drugs to protect against recurrent heart attacks and other complications of pre-existing coronary heart disease.

Elevated blood levels of cholesterol and other fatty substances are the factors most strongly suspected of increasing susceptibility to coronary heart disease. Elevated blood lipids may also adversely affect long-term survival among heart-attack patients by increasing their vulnerability to recurrent heart attacks and other complications. The Coronary Drug Project hopes to establish that long-term reduction of blood lipids with drugs will confer some degree of protection against these complications and reduce 5-year mortality rates by 25% or more in this highly vulnerable group of male coronary patients between the ages of 30-64. The drugs being tested are estrogens, nicotinic acid, clofibrate, and dextro-thyroxine, all previously shown to reduce blood lipid levels and all previously cleared for prescription use by FDA. Furthermore, demonstration of the principle that drugs which lower blood lipids can improve survival would stimulate the development of still more satisfactory lipid-lowering drugs for the treatment and prevention of coronary heart disease.

The present study was undertaken after several years of planning by experts in important disciplines of cardiology, lipid research, toxicology, epidemiology, and biostatistics. A model study protocol has been established, competent investigators have been recruited and the project is proceeding with a high degree of success toward its scientific objective. More than 6,000 patients have now been enrolled toward a goal in July 1969 of 8,000 calculated as necessary for statistical validity of the final measured results over a 5 year period of follow-up. The $1,000,000 increase provided in this budget is a direct result of additional patient enrollment which will reach peak level of full operations in the beginning of fiscal year 1970. This growth in patient enrollment establishes a higher level of operational costs for participating clinics, laboratory, toxicity monitoring and diagnostic confirmation of new events which will be developing in this population.

Cerebrovascular Diseases. Blood-vessel diseases affecting the central nervous system which result in strokes account for about 200,000 deaths a year--a toll exceeded only by heart disease and cancer. There are no reliable statistics on the number of persons partially or completely disabled by cerebrovascular disease, but it may exceed a million. Although mortality is concentrated in older people, the mid-life toll is also high.

The most common cause of stroke is blood clots forming in the arteries supplying the brain. Initial mortality from acute cerebral thrombosis exceeds 15 percent, and fully half of the survivors are left with permanent disability. Mortality from cerebral hemorrhage, another common cause of stroke, is considerably higher than this.

A stroke is not a disease. It is usually the consequence of other circulatory diseases. Hypertension, for example, both predisposes patients to a stroke and aggravates its clinical effects. Atherosclerosis can weaken affected blood vessels supplying the brain, predispose them to rupture, and create conditions favorable to the formation of blood clots.

Within recent years there have been many significant advances in the clinical attack on the stroke problem: objective techniques for measurement of blood flow to the brain have been developed; new X-ray techniques provide safe and effective means of detecting obstructive disease in the large vessels of the head and neck. There has been a sharper definition, and hence a basis for more appropriate therapy, of a variety of stroke syndromes. Most importantly, there has been major progress in the surgical reconstruction of occluded vessels supplying the brain.

With the Neurological Institute, the Heart Institute has developed and supported a series of stroke research centers. The research programs of the two Institutes are complementary: the Neurological Institute supports a cooperative study of strokes due to brain hemorrhage, while the Heart Institute supports a large cooperative study of strokes due to diseased neck vessels supplying the brain.

The great majority of grant supported research deals primarily with human patients afflicted with cerebrovascular diseases, relatively few with animal studies. Research progress to date has been seriously hampered by the lack of a satisfactory disease model in animals. The preponderant investigative effort has been in the treatment and palliation of cerebrovascular diseases. Attempts to prevent these diseases must await a fuller understanding of underlying processes involved in atherosclerosis, clot formation and lysis, and blood pressure control. Major current research areas include:

- Epidemiological studies to identify host and environmental factors that increase susceptibility to stroke.
- Development of safe, sensitive techniques for locating sites of blood vessel obstruction or rupture and assessing extent of brain damage.
- Development of reliable diagnostic methods for differentiating among various types of stroke.
- Evaluation of anticoagulants, clot-dissolving agents, and other therapeutic measures.
- Development of diagnostic and surgical techniques for cerebral insufficiency due to potentially operable blood-vessel obstructions localized outside the central nervous system.

Cardiorespiratory Diseases

Despite significant research progress in the past two decades, there is an urgent need for expansion and acceleration of cardiorespiratory research. This is made more acute by an alarming upsurge of the obstructive respiratory diseases, demonstrated by a sixfold increase in mortality in the last 25 years, an approximate 10% prevalence in middle-aged American males, and a disability rate exceeded only by heart disease under age 65. Expanded research into the pathological processes of the lung is required, and better clinical-pathologic correlations are needed for the identification of pulmonary heart disease, and for the differential diagnosis of two conditions as dissimilar as bronchitis and emphysema. Recent developments, more specifically the intense and coordinated efforts to accomplish cardiac replacement (artificial or transplant), have added critical new dimensions to the need for better understanding of the respiratory component of the cardiopulmonary system. Many advances have been made in knowledge of the lung as a mechanical, gas exchange unit; yet little is known about the intimate physiology of the organ, its biochemistry, its interrelationship to the vascular network and to heart

function, and its role as a detoxifying organ. Intensified cardiopulmonary research will be mandatory in the immediate future as a complement to heart replacement efforts. Examples of ongoing research projects in this area include:

- Search for the causes of emphysema and its mode of development, about which little is yet known.
- Studies on the causes, consequences, and clinical management of pulmonary hypertension.
- Development of diagnostic techniques for evaluating pulmonary blood-flow and gas exchange.
- Development of simple, reliable techniques for evaluating lung function and for early detection of chronic respiratory diseases.
- Safe effective techniques for diagnosis of pulmonary embolism and for evaluating therapy with anticoagulant or clot-dissolving agents.
- Development and evaluation of mycolytic agents, bronchodilators, respiratory stimulants for relief of respiratory distress.
- Development of respiratory assist devices, blood oxygenators, etc., for management of respiratory crises.
- Search for more effective means of managing circulatory implications of chronic lung disease (right heart failure, secondary polycythemia, etc.).

Hypertension

Hypertension is one of the most commonly encountered forms of cardiovascular disease, affecting an estimated 17-22 million adult Americans. Of these, 10.5 million suffer from heart disease as a consequence of hypertension. Hypertension aggravates and accelerates the development of atherosclerosis and is a major cause of strokes, heart failure, and kidney failure.

As many as 15 percent of all cases of hypertension are secondary to other pathologic processes and are potentially curable if promptly diagnosed. Most often, these cases involve obstruction of the normal blood flow to the kidney due to atherosclerosis or other diseases of the renal arteries. Many of the victims of such renal hypertension can be cured or substantially benefited if the condition is detected in time and either the normal kidney blood flow restored or a severely damaged kidney removed. Improvement of the diagnosis of such renal disease, or of certain adrenal disorders that can also cause hypertension, and the selection of patients who may benefit from surgery are important goals of the Institute's research program.

Most victims of hypertension, however, suffer from a "primary" or "essential" form of hypertension, thus far of unknown origin; and intensive research continues in this area. This lack of knowledge has not prevented the development of a steadily growing number of potent drugs that are remarkably effective in reducing blood pressure. Although these drugs do not cure the disease, they are able to control hypertension of all degrees of severity.

As a result of the development of improved diagnostic and surgical techniques, a variety of effective drugs, and other advances, the death rate from hypertension has fallen by nearly 50% during the past 10 years. Major current research areas include:

- Possible causes of essential hypertension, still unknown.
- Development and evaluation of blood pressure lowering drugs and long-term effectiveness of drug therapy.
- Diagnosis and treatment of hypertension secondary to kidney disorders, tumors, etc.
- Physiology of the kidney and role of fluid and electrolyte disturbances in hypertension.
- The possible role of endocrine disorders in hypertension.
- Biologically active amines and the sympathetic nervous system as determinants of blood-vessel tone.
- Heredity and environmental factors affecting susceptibility to hypertension.
- The treatment of severe kidney disease through kidney transplants, artificial kidneys.

Thrombosis and Hemorrhagic Diseases

Clotting components may play an important role both in the development of atherosclerosis and in precipitating heart attacks, strokes, and other manifestations of blood and blood-vessel diseases. Indeed, thrombosis may well be the largest single cause of fatality in man. NHI supported research in this area includes studies on

- coagulation mechanisms and the many blood and tissue factors that participate in the clotting process.
- elevated blood lipids and other factors that may predispose the victim of cardiovascular disease to clotting complications.
- anticoagulant and clot-dissolving drugs as prophylactic or therapeutic agents against clotting complications of blood and blood-vessel diseases.

At the other end of the scale are hereditary or acquired clotting factor deficiencies that prevent normal clotting and pose the constant threat of massive hemorrhage. NHI supports a large body of research concerned with

- the diagnosis of these disorders.
- their mode of inheritance.
- the development of clotting factor concentrates and other therapeutic measures for preventing or controlling bleeding episodes in affected patients.

Congenital Heart Disease

Congenital heart disease still causes about 10,000 deaths a year, one-third of them during the first month of life and most of these in the first week. Although surgical treatment has continued to improve, it is still extremely risky in infants less than six months of age.

Furthermore, congenital heart disease is unquestionably one of the costliest of all diseases from the point of view of its medical care. For example, there are over 300 surgical teams in the United States specially trained and equipped for open-heart surgery of congenital heart diseases and more than 500 diagnostic centers elaborately equipped for its diagnosis. The annual cost of this equipment, personnel, and services runs to many millions of dollars. The costs of these services to the patient often exceeds $2,000.

The Heart Institute's research program has placed heavy emphasis on the improvement of methods for the diagnosis and evaluation of congenital heart defects and on the perfection of surgical methods of correcting them.

As a result, corrective or palliative operations have been developed for most of the recognized types of congenital heart disease. Moreover, improvements in heart-lung machines and other life-support techniques provide surgeons with prolonged access to the heart, so that they can undertake the correction or palliation of even very complex or multiple malformations. These advances have steadily increased the surgeon's prospects of success while reducing the risk of open-heart procedures, although it remains high for complex or multiple malformations, especially in infants. Current research projects include:

- Studies to identify potentially preventable causes of congenital heart defects (diseases, teratogenic agents, etc.).

- Studies on the natural history of congenital heart defects. Development of reliable criteria for determining which defects require immediate surgery; which allow postponement of surgery until the child is older and surgery less risky; and which can be managed successfully without surgery.

- Development of improved techniques for detecting and evaluating congenital heart defects.

  Development of more effective surgical procedures for palliating or correcting such defects and better life-support techniques (heart-lung machines, hyperbaric, oxygenation, etc.) for sustaining patients during prolonged open-heart operations.

Rheumatic and Infectious Heart Disease

During the past several decades, there has been a steady fall in the number of deaths each year from acute rheumatic fever and its complications. But even though the full application of existing knowledge and techniques could, in theory, prevent almost all recurrent attacks of rheumatic fever and a large proportion of initial attacks, rheumatic fever and rheumatic heart disease continue to occur in significant numbers. This is explained by several apparent deficiencies: existing methods of disease control fall short of the ideal, gaps remain in current methods of prevention, and existing knowledge is not applied.

There has been steady improvement in surgical techniques for restoring or replacing heart valves damaged by rheumatic fever. A variety of clinically proven artificial valves have been devised and valve homografts (from persons dying of non-cardiac causes) are finding increased clinical application. Today, surgeons can undertake single or multiple valve replacements with a better than 80 percent prospect that the patient will be substantially benefitted by the operation.

Besides continuing improvements in surgical procedures and prostheses, current research areas and objectives include:

- The mechanisms by which streptococcal infections (and perhaps other infectious diseases) lead to rheumatic fever.

- Factors underlying susceptibility and relative immunity to rheumatic fever as to heart damage resulting from rheumatic-fever episodes.

- Search for more effective means of identifying susceptible individuals and protecting them against rheumatic fever and/or recurrent attacks.

- More effective means of diagnosing the extent of heart muscle inflammation during rheumatic fever attacks and preventing or minimizing permanent heart damage.

Heart Failure and Shock and Circulatory Regulation

Circulatory failure is generally classified into acute and chronic forms. The acute form includes shock, some types of fainting, and some forms of sudden death--often due to profound disturbances of heart rhythm. The chronic form of circulatory failure is generally known as congestive heart failure and denotes prolonged impairment of the ability of the heart to maintain an adequate blood flow to the tissues.

Most of the research support in this disease category is concerned with causation. It is not yet known whether heart failure represents a "weakness" of the heart muscle cells or is the result of defective energy production or utilization. The answer may be found in intensive studies:

- on the ultrastructure and arrangement of the heart muscle fibers and contractile proteins,

or

- in the complex biochemical mechanisms by which the heart generates chemical energy and harnesses that energy to drive the contractile process.

Other research projects concern:

- The bases of abnormalities in heart rhythm; the development and evaluation of countershock techniques and antiarrhythmic drugs for correcting arrhythmias.

- Artificial pacemakers for the control of heart block or chronic rhythm disturbances.

- Cardiac stimulants for supporting a failing circulation.

- Diuretic agents for combatting edema secondary to congestive failure.

- Mechanisms regulating cardiovascular performance and tissue perfusion; neural, mechanical, and biochemical determinants of heart-muscle contractility.

Organ Transplantation

The realities of organ replacement offer potential for treatment of several cardiovascular diseases. For that reason it is discussed separately. Currently, NHI is supporting research in organ transplantation (heart, kidney, lung, and liver transplants) at somewhat over $3 million, plus additional support for tissue immunology and tissue typing--studies basic to organ transplantation in general. This program will be strengthened and expanded as available funds permit.

In order that the best care may be offered to patients in critical need of new therapies, it is imperative that patients currently receiving cardiac transplantations be assessed and followed with great care. Studies are needed to establish valid parameters for recipient selection, for donor match, for post-transplantation evaluation and for long-term care. The very real and finite limit to the number of potential donors demands that these be optimally utilized. The logistics of donor registration, organ transportation, and recipient preparation must be delineated and resolved. The establishment of a registry of all transplanted organs would provide an overview of the transplantation field. The kidney registry has already documented some of the benefits to be derived from this type of ongoing assessment. Finally, with each new underlying disease process for which transplantation becomes a possible cure, real opportunities arise to study underlying disease mechanisms and pathological pathways.

Of critical importance to the success of cardiac transplantation and hence to the patient himself are studies in four key areas:

- The determination of the specific antigenicity of the heart tissues and related phenomena of immunological rejection.
- The physiologic and clinical manifestations of rejection of the heart.
- The effects of immunosuppressive drugs on heart function.

The preservation and storage of donor hearts.

Other Cardiovascular Diseases

The research activities placed in this category are diverse and cover a number of important disease areas. They include 20 large multidisciplinary program project grants concerned with cardiac diseases; studies of aging; liver diseases; hypothermia; environmental factors, especially as they affect the circulatory system; and peripheral vascular diseases, including the development of improved diagnostic techniques and better methods of treatment.

Special Programs

Funds are carried forward to 1970 at the same level of support as in 1969 for General Research Support Grants, a program included in each NIH appropriation containing research grant projects but administered by DRFR; for Categorical Clinical Research Centers, which provide the research resources for in-depth, multidisciplinary investigations in many of the research areas outlined in the presentation above for regular research projects; for Specialized Cardiovascular Research and Training Centers for continued planning of such centers; and an increase of $1,000,000 is provided for the Heart Cooperative Drug Study which is discussed under Arteriosclerosis (above).

Research Grants Program Analysis

	1969 Estimate	1970 Estimate	Increase or Decrease
Arteriosclerosis:			
Atherosclerosis	$14,250,000	$14,358,000	+$108,000
Coronary artery disease	6,656,000	6,706,000	+50,000
Cerebrovascular disease	1,451,000	1,461,000	+10,000
Subtotal	22,357,000	22,525,000	+168,000
Cardiorespiratory diseases	3,925,000	3,955,000	+30,000
Hypertension and kidney disease	11,861,000	11,950,000	+89,000
Thrombosis and hemmorrhagic diseases	11,349,000	11,435,000	+86,000
Congenital heart disease	5,120,000	5,158,000	+38,000
Rheumatic and infectious heart disease	1,963,000	1,977,000	+14,000
Heart failure and shock and circulatory regulation	17,835,000	17,969,000	+134,000
Other cardiovascular diseases	10,923,000	11,005,000	+82,000
Subtotal[1/]	85,333,000	85,974,000	+641,000
General research support grants	9,425,000	9,425,000	---
Scientific evaluation	163,000	163,000	---
Heart cooperative drug study	3,820,000	4,820,000	+1,000,000
Specialized research centers	925,000	925,000	---
Total research grants	99,666,000	101,307,000	+1,641,000

1/ Includes $4,500,000 in 1969 and 1970 budgeted for Categorical Clinical Research Centers.

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Noncompeting continuations	1,144	$60,000,000	845	$60,641,000	-299	+$641,000
Competing projects	356	19,158,000	386	19,333,000	-30	+175,000
Supplementals	(186)	1,675,000	(166)	1,500,000	(-20)	-175,000
Subtotal, regular program	1,500	80,833,000	1,231	81,474,000	-329	+641,000
General research support grants		9,425,000		9,425,000		---
Scientific evaluation and planning		163,000		163,000		---
Categorical clinical research centers		4,500,000		4,500,000		---
Heart cooperative drug study		3,820,000		4,820,000		+1,000,000
Specialized research centers		925,000		925,000		---
Total, research grants		99,666,000		101,307,000		+1,641,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total fellowships.....	$7,604,000	$7,309,000	-$295,000

Introduction

The primary objective of the fellowship program is to increase the number of scientists qualified to carry on independent cardiovascular research.

Program Plans in 1969 and 1970

The above objective is carried out through four means: (1) the postdoctoral fellowships are awarded in a wide variety of cardiovascular disciplines to encourage young physicians to obtain research training and experience so that the country's research potential can be maintained; (2) special fellowships are awarded to more mature individuals, often faculty members, who find it highly productive to spend a year or two in research laboratories other than their own in which they can improve current skills or acquire new ones; (3) the highly successful research career development program supports the younger investigator of demonstrated ability and provides the means whereby the grantee institutions can expand their cardiovascular potential; (4) the research career award provides stable support for the senior investigator.

Funds requested for 1970 will provide for 365 awards, compared to 418 in 1969, a decrease of 53. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Continuations:						
Noncompeting.....	234	$5,008,000	251	$5,586,000	+17	+$578,000
Competing.....	44	871,000	39	804,000	-5	-67,000
Supplementals.....	(15)	30,000	(10)	20,000	(-5)	-10,000
New.....	140	1,695,000	75	899,000	-65	-796,000
Total, fellowships.....	418	7,604,000	365	7,309,000	-53	-295,000

Fellowships (By Type of Program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Postdoctoral.....	90	$827,000	68	$649,000	-22	-$178,000
Special.....	122	1,487,000	92	1,140,000	-30	-347,000
Research career development....	175	4,390,000	175	4,635,000	0	+245,000
Research career.....	31	900,000	30	885,000	-1	-15,000
Total, fellowships.....	418	7,604,000	365	7,309,000	-53	-295,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total training grants.....	$18,150,000	$17,442,000	-$708,000

Introduction

The training grant programs of the National Heart Institute are designed to: (1) attract individuals to a career in the cardiovascular field; and (2) produce investigators who will contribute significantly to the mission of the Institute. In order to achieve these goals, the Institute makes available undergraduate training grants, graduate research training grants, and graduate clinical training grants.

Undergraduate Training Grants

Undergraduate training grants will be made to a total of 112 schools of medicine, osteopathy, and public health. These grants are utilized to strengthen the cardiovascular-teaching capabilities at the undergraduate level. By introducing students to the cardiovascular field at an early stage, a higher percentage of top students are provided with the foundation and incentive for a cardiovascular career.

Graduate Training Grants

Graduate training grants are available to institutions which can provide excellent training programs for individuals already holding a doctorate. These programs prepare both research and clinical scientists for careers in the area of cardiovascular disease. The graduate research training prepares future investigators to contribute to the research mission of the Institute. The graduate clinical training prepares physicians who are not only skilled clinicians but also specialists, able to evaluate research data critically, translate the results of research for patient care, and keep abreast of their field. While many of the training grant programs are multidepartmental in nature, high priority is now being given to training in: (1) cardiorespiratory diseases, (2) cardiovascular surgery, (3) clinical cardiology, and (4) biomedical engineering as it relates to the cardiovascular field.

Funds requested for 1970 will provide for 378 awards, compared to 397 in 1969, a decrease of 19. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Continuations:						
Noncompeting.....	322	$14,042,000	313	$13,792,000	-9	-$250,000
Competing.....	53	2,820,000	55	3,018,000	+2	+198,000
Supplementals.....	(8)	150,000	(7)	75,000	(-1)	-75,000
New.....	22	1,138,000	10	557,000	-12	-581,000
Total, training grants.....	397	18,150,000	378	17,442,000	-19	-708,000

Training Grants (By Type of Program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Undergraduate.....	112	$2,685,000	112	$2,685,000	0	0
Graduate.....	285	15,465,000	266	14,757,000	-19	-$708,000
Total, training grants....	397	18,150,000	378	17,442,000	-19	-708,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	375	$4,481,000	387	$4,562,000	+12	+$81,000
Other expenses		8,687,000		9,079,000		+392,000
Total	375	13,168,000	387	13,641,000	+12	+473,000

The Institute's laboratory and clinical research program has provided an effective blend of fundamental studies of the cardiovascular system with research aimed directly at the solution of specific clinical problems posed by the cardiovascular diseases. A staff of approximately 170 professional scientists, with about an equal number of supporting staff, is devoted to this research program.

Of the eleven laboratories and branches of the National Heart Institute, five are involved in a vigorous program of clinical research--usually conducted concurrently with laboratory research efforts. At present 100 research beds in the NIH Clinical Center are allocated to these Heart Institute studies; in addition, research subjects are studied on an out-patient basis.

The fundamental research effort of the intramural program has received deliberate emphasis. Most cardiovascular diseases have their roots in subtle and complex metabolic processes and in the mechanisms that control or regulate these processes. A fuller exploration of these processes will improve our basic understanding of these disorders and will, thereby, provide improved methods of diagnosis, treatment, and prevention.

The close association between basic and clinical research activities within the intramural program has been highly advantageous. It provides for the more rapid clinical testing and application of those findings from basic studies that show promise in the solution of clinical problems.

In terms of budget and scientific staff, the intramural research program is modest indeed, yet the findings of Heart Institute scientists have exerted profound effects in practically every major area of cardiovascular research.

Its scientists pioneered in the use of enzyme inhibitors in the treatment of hypertension, discovered and proved the therapeutic potential of several antihypertensive drugs now in wide clinical use, and have made major contributions to scientific knowledge concerning the mechanisms by which many such agents lower blood pressure.

They have also made substantial contributions to our understanding of nerve and hormonal factors that regulate heart performance, mechanical and biochemical determinants of heart-muscle contractility, and the mechanisms by which the autonomic nervous system and various cardiac stimulants provide support to a failing circulation.

They have developed important new techniques for the detection and clinical evaluation of various types of congenital and acquired heart disease and have compiled an enviable record of success in the surgical treatment of these disorders.

Their work has helped to define more fully many of the complex processes involved in the synthesis, transport, and metabolism of cholesterol and other fats, and to identify and classify certain heritable disorders of fat storage and metabolism that are frequently associated with elevated blood-lipid levels and accelerated development of atherosclerosis.

These are only a few of the major accomplishments stemming from the work of this relative small group of scientists.

The total increase of $473,000 includes a program increase of $100,000 and 12 positions which will permit expansion into laboratory space to be newly assigned to this Institute, $6,000 for annualization of the 1969 pay increase, and $367,000 for centrally furnished services from the "National Institutes of Health management fund."

Collaborative Reserach and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	31	$388,000	35	$463,000	+4	+$75,000
Other expenses		16,966,000		17,685,000		+719,000
Total	31	17,354,000	35	18,148,000	+4	+794,000

This activity includes (1) the Artificial Heart Program, (2) the Myocardial Infarction Program, (3) the National Blood Resource Program, and (4) the direct support of the Heart Cooperative Drug Study.

Artificial Heart-Myocardial Infarction Program

This program has as its goal the reduction of heart disease deaths and disability through (1) the development of mechanical devices to assist or replace the sick or failing heart, and (2) research on the treatment of acute heart attacks. An estimated 750,000 Americans develop heart disease every year, and over 350,000 die of heart attacks. This joint program combines biomedical and bioengineering approaches to this major health problem.

Artificial Heart Program

This is a goal-oriented program and incorporates the philosophy of system development found successful in other research and development programs. It represents the first application of systems development techniques to biomedical problems. Its goal is the development and utilization of a variety of therapeutically useful, safe and reliable circulatory assist devices, including (1) emergency devices to enable more heart attack victims to reach the hospital and medical care; (2) short-term assist devices to help the heart recover and rest after surgery or other acute illness; (3) long-term assist devices for hearts that cannot carry the full load by themselves; and (4) complete replacement for hearts that are too sick to carry any of the load. While problems in physiology, surgery, and engineering remain to be completely solved, much progress is being made in their solution.

Scientists with biomedical and engineering competence from academic and industrial research and development centers have developed a number of materials and components that are ready for prototype fabrication into several kinds of assist devices. While these and other componenets are being further developed and improved, plans are underway to provide full and objective tests and evaluations of them in the laboratory, in animals, and when thoroughly tested, in patients. This comprehensive test and evaluation program is designed to ensure that all devices and components developed in this program will be systematically and objectively examined so that selections of the most promising can be made; results of these tests will be used in modifying and improving the devices. Only those that pass the rigorous engineering and animal tests will be considered for use in patients. Such a systematic test and evaluation program will lead to the development of safe, effective, and reliable devices in the shortest possible time and with the least expenditure of research and development funds.

Myocardial Infarction Program

This program currently supports nine Myocardial Infarction Reserach Units of a national network which is planned eventually to be increased to 12. Each unit is located within the patient-care area of a hospital; each has a multi-disciplinary program emphasizing clinical investigation, supported by more fundamental studies. Communication and cooperation are taking place among the units. Each is specially equipped and staffed for the most comprehensive care and detailed study of heart-attack patients during the acute phase of their illness. The goal is the acquisition of new knowledge needed for improving all phases of medical care for heart-attack cases, and the evaluation of both accepted and new modes of treatment. Some specific goals:

- To learn as much as possible about the presently unpredictable clinical course of the acute heart attack.
- To determine what drugs and other measures might be used to minimize the injury suffered by the heart muscle.
- To provide more rational bases for all phases of diagnosis, treatment, and patient care.
- To develop new and more effective methods of therapy.
- To evaluate more precisely and thoroughly both accepted methods of treatment and promising new ones, including mechanical assist devices.

Laboratory and clinical research on myocardial infarction is in part dependent upon satisfactory animal models of the acute illness. The program has, therefore, recently awarded six contracts to develop and evaluate non-atherosclerotic methods of producing myocardial infarction in animals. Several different techniques are under study and development.

The Myocardial Infarction Program plans to launch vital studies to attack the problem of sudden pre-hospital cardiac death, which now accounts for one-half of all deaths from heart attacks. Studies are also being initiated to answer the critical questions of what precipitates--and what can prevent--the conversion of chronic coronary artery disease into an acute heart attack, what the derangements are early in the illness, and how their progression can be interrupted.

The National Blood Resource Program

The principal goals of this program are concerned with (1) improved methods for storage, distribution, and utilization of blood and blood components; and (2) development and evaluation of therapeutic agents to counter disorders of the blood-clotting mechanism. Some specific goals are:

- To investigate additives for prolonging the shelf life of whole blood and cellular fractions.
- To study the feasibility of a computerized national or regional daily shelf inventory system for blood and blood products.
- To develop an integrated system for the mass production of blood fractions.
- To evaluate the effectiveness of drugs for dissolving blood clots obstructing blood flow to the lungs.

During the past year, a major project was initiated to study the feasibility of an automated inventory and information system for the regional or national management of whole blood and blood products. The development of computer-based systems for the inventory control of the donation and distribution of blood by the nation's blood banks will reduce the outdating of blood by 50% - 75%. This would

effect a large annual dollar saving and, more importantly, would make blood and blood fractions available for the urgent needs of surgical, hemophilic, cancer, and leukemic patients over the country. This work will be continued in 1969 and 1970.

Another project is continuing the evaluation of the chemical additive adenine. Preliminary evidence has indicated that this additive can perhaps double the storage life of whole blood, thus substantially reducing presently unavoidable losses of this valuable resource through outdating in storage. Contract supported studies are currently assessing the effectiveness of adenine as a preservative and verifying the safety of adenine-treated blood products for clinical use.

A major project concerning the promising clot-dissolving agent, urokinase, was begun in fiscal year 1968. Included is the controlled clinical Urokinase-Pulmonary Embolism Trial on the effectiveness of this thrombolytic agent which is thought to hold great promise against crippling or lethal clotting complications. This clinical trial is an essential prelude to further evaluation of clot-dissolving agents in the treatment of heart attacks, certain strokes, and other clotting complications of heart and blood vessel diseases. Pulmonary embolism was the lesion of choice for a controlled clinical trial of the efficacy of urokinase since the effect could be most clearly and quantitatively documented.

Another concern of this program is the development of highly purified concentrates of an antihemophilic factor (AHF). An important result could be an AHF concentrate of sufficiently low cost to permit its use as a routine, rather than an emergency procedure for the treatment of individuals affected with that disease.

New projects which may begin in 1970 include studies into the detection of serum hepatitis in whole blood and blood components of which thirty thousand cases are reported each year as the result of the transfusion of blood; and research and development of chemical substances which inhibit platelet aggregation, a first step in the complex sequence of reactions which result in the formation of a thrombus (intravascular clot).

Heart Cooperative Drug Study

This is an Institute coordinated program to determine whether several lipid-lowering drugs will reduce the incidence of recurrent attacks and increase longevity among heart-attack victims. Most of the funding of this study is by research grants to approximately 55 participating clinics. Ancillary funds included under Collaborative Research and Development are for reimbursement to other agencies of DHEW for performing the required laboratory determinations and for ordering, packaging, and distributing the necessary drugs.

The program increase of $778,000 for Collaborative Research and Development provides for expansion of test and evaluation procedures in the Artificial Heart Program and for sudden pre-hospital cardiac death studies in the Myocardial Infarction Program. There are also increases of $1,000 for annualization of the 1969 pay increase and $15,000 for centrally furnished services from the "National Institutes of Health management fund."

Biometry, Epidemiology, and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	64	$875,000	64	$876,000	--	+$1,000
Other expenses		817,000		848,000		+31,000
Total	64	1,692,000	64	1,724,000	--	+32,000

This activity conducts direct studies and also participates in cooperative studies in cardiovascular research. The major thrusts of this program are in epidemiology, geographic pathology, biostatistics, and the clinical evaluation of therapeutic agents. This program provides a valuable mechanism not only for undertaking direct research in selected scientific areas, but also for collaboration with grantees, intramural research scientists, and foreign research workers conducting investigations of program importance.

As in other parts of the National Heart Institute, the programs of this activity balance studies of relatively immediate clinical usefulness with those of a more fundamental, long-range nature. Thus, the staff conducts or collaborates in epidemiologic research where "experiments of nature" have resulted in unusually high (or unusually low) rates of cardiovascular diseases, and is systematically identifying risk factors that are responsible for such differences. Also, the program assists in the development of clinical trials to study the effectiveness of drugs, diet, or other factors which may be effective in reducing heart diseases. It is estimated that 70 percent of the funds in this activity are allocated to such clinically relevant studies. The remaining activities are of a more fundamental character and deal with the design and analysis of studies and the development of new biomathematical methods for biological research.

There are increases of $1,000 for annualization of the 1969 pay increase and $31,000 for centrally furnished services from the "National Institutes of Health management fund."

Direct Training

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	4	$46,000	4	$46,000	--	---
Other expenses		179,000		158,000		-$21,000
Total		225,000		204,000		-21,000

Incorporated in this program is the training of personnel to meet the long-range and immediate cardiovascular scientific personnel needs of the Institute and the Department. This is an important and basic part of the heart research program in that it provides for the training of qualified investigators who must keep abreast of new knowledge, techniques, and methods that are constantly being developed so that they may function at the highest level of proficiency.

The $21,000 decrease reflects an adjustment in the prorated financing of centrally furnished services from the "National Institutes of Health management fund.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	99	$1,122,000	99	$1,124,000	--	+$2,000
Other expenses		1,439,000		1,599,000		+160,000
Total	99	2,561,000	99	2,723,000	--	+162,000

This activity provides professional direction for the scientific review and administration of all grant supported cardiovascular research and training programs, including the necessary operational and technical support activities and scientific and financial analysis of such programs.

There are increases of $2,000 for annualization of the 1969 pay increase and $160,000 for centrally furnished services from the "National Institutes of Health management fund."

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	27	$375,000	31	$419,000	+4	+$44,000
Other expenses		214,500		224,000		+9,500
Total		589,500	31	643,000	+4	+53,500

This activity supports the over-all administration, coordination, and direction of the varied programs and activities of the Institute. The Director and his immediate staff are responsible for introducing new knowledge into current operating programs and for the planning, development, and review of new areas of focus and interest.

The program increase of $50,500 and 4 positions will provide for additional professional staff for program planning and administrative review within the Institute. Also included is $1,000 for annualization of the 1969 pay increase and $2,000 for centrally furnished services from the "National Institutes of Health management fund."

New Positions Requested

Fiscal Year 1970

		Grade		Annual Salary
LABORATORY AND CLINICAL RESEARCH				
(2)	Scientist	GS-13		$28,818
(2)	Scientist	GS-12		24,348
(2)	Research technician	GS-9		16,924
(2)	Research technician	GS-7		13,962
(2)	Laboratory technician	GS-5		11,464
(2)	Laboratory technician	GS-3		9,200
			(12)	104,716
COLLABORATIVE RESEARCH AND DEVELOPMENT				
(1)	Scientist	GS-15		19,780
(1)	Scientist	GS-14		16,946
(2)	Administrative staff assistant	GS-11		20,406
			(4)	57,132
PROGRAM DIRECTION				
(1)	Deputy director of office	GS-17		26,264
(1)	Administrative staff assistant	GS-15		19,780
(1)	Administrative staff assistant	GS-14		16,946
(1)	Clerical assistant	GS-5		5,732
			(4)	68,722
	Total new positions, all activities		(20)	230,570

THURSDAY, MARCH 27, 1969.

NATIONAL INSTITUTE OF DENTAL RESEARCH

WITNESSES

DR. SEYMOUR J. KRESHOVER, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. RICHARD C. GREULICH, DIRECTOR OF INTRAMURAL RESEARCH, NATIONAL INSTITUTE OF DENTAL RESEARCH
DR. ROBERT M. GRAINGER, ASSOCIATE DIRECTOR FOR EXTRAMURAL PROGRAMS, NATIONAL INSTITUTE OF DENTAL RESEARCH
HERBERT C. CHRISTOFERSON, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF DENTAL RESEARCH
MRS. FRANCES H. PETTINATO, BUDGET OFFICER, NATIONAL INSTITUTE OF DENTAL RESEARCH
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY. BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Prersonnel compensation:			
Permanent positions	2,856	3,177	3,236
Positions other than permanent	102	116	116
Other personnel compensation	27	22	22
Total personnel compensation	2,985	3,315	3,374
Personnel benefits: Civilian employees	348	359	365
Travel and transportation of persons	131	141	158
Transportation of things	29	33	38
Rent, communications, and utilities	79	101	106
Printing and reproduction	35	42	47
Other services	2,243	2,347	2,661
Supplies and materials	384	453	460
Equipment	273	202	213
Grants, subsidies, and contributions	22,525	22,429	22,643
Quarters and subsistence charges	−5	−3	−3
Total obligations	29,027	29,419	30,062

PERSONNEL SUMMARY

Total number of permanent positions	321	301	306
Full-time equivalent of other positions	13	14	14
Average number of all employees	299	303	309
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,446

See footnotes at end of table.

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

Program by activities:			
1. Grants:			
(a) Research	15,521	15,055	15,559
(b) Fellowships	1,724	1,765	1,694
(c) Training	5,280	5,609	5,390
Total, grants	22,525	22,429	22,643
2. Direct operations:			
(a) Laboratory and clinical research	4,394	4,687	4,947
(b) Collaborative research and development	662	845	942
(c) Biometry, epidemiology, and field studies	735	431	436
(d) Review and approval of grants	608	689	763
(e) Program direction	294	338	331
Total direct operations	6,333	6,990	7,419
Total program costs, funded [1]	28,858	29,419	30,062
Change in selected resources [2]	169		
Total obligations	29,027	29,419	30,062
Financing:			
Comparative transfers to other accounts	256	286	
Unobligated balance lapsing	1,005	278	
Budget authority	30,288	29,983	30,062
Budget authority:			
Appropriation	30,307	29,983	30,062
Transferred to other accounts	−19		
Appropriation (adjusted)	30,288	29,983	30,062
Relation of obligations to outlays:			
Obligations incurred, net	29,283	29,705	30,062
Obligated balance, start of year	18,345	19,695	23,635
Obligated balance, end of year	−19,695	−23,635	−25,411
Adjustments in expired accounts	−1,087		
Outlays	26,846	25,765	28,286

[1] Includes capital outlay as follows: 1968, $225,000; 1969, $202,000; 1970, $263,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $852,000; 1968, $1,021,000; 1969, $1,021,000; 1970, $1,021,000.

Mr. FLOOD. Now we have the National Institute of Dental Research, Dr. Seymour J. Kreshover, who is the Director.

Have you appeared here before?

Dr. KRESHOVER. Yes; I have, Mr. Flood.

Mr. FLOOD. Do you have any new people here that we do not know?

Dr. KRESHOVER. Yes, sir; I do. One new member of our staff, Dr. Grainger, who serves as Associate Director for Extramural Programs. The other three people accompanying me have been here before and have had the pleasure of meeting you.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Mr. FLOOD. We will place your biographical sketch in the record and then you may proceed with your statement.

(Dr. Kreshover's biographical stetch follows:)

BIOGRAPHICAL SKETCH

Name.—Seymour J. Kreshover.

Position.—Assistant Surgeon General, Director, National Intitute of Dental Research, NIH.

Date and place of birth.—June 22, 1912—New York, N.Y.

Education.—New York University, Liberal Arts College, B.A., 1934; University of Pennsylvania, School of Dentistry, D.D.S., 1938; Yale University (clinical medicine and pathology), Ph. D., 1942; New York University, School of Medicine, M.D., 1949.

Professional and work experience.—1938–39, university fellow, University of Illinois Graduate School; 1942–43, assistant in oral surgery, Yale University School of Medicine; 1942–46, military service, U.S. Army; 1946–48, teaching fellow in histoanatomy, New York University; 1949–56, professor of oral pathology, director of dental research; director of graduate and postgraduate studies, the Medical College of Virginia, Richmond; 1956–60, associate trustee, Board of Medical Education and Research, University of Pennsylvania; 1956, visiting professor, the Medical College of Virginia; 1956–66, associate director, National Institute of Dental Research, National Institutes of Health; 1966, Director, National Institute of Dental Research. National Institutes of Health.

Association memberships.—American Dental Association; American Medical Association; American Association for the Advancement of Science (fellow); American Public Health Association (fellow); Diplomate, American Board of Oral Medicine; Honorary member, the New York Institute of Clinical Oral Pathology, Inc.; consultant to Council on Dental Research, American Dental Association; consultant to Committee on Research, American College of Dentists; 1961–67, chairman, Commission on Dental Research, Federation Dentaire Internationale; 1962, president, International Association for Dental Research; 1963–66, secretary, section Nd (dentistry), American Association for the Advancement of Science; 1968, regent, American College of Dentists;

Honors, awards.—1945, Commendation Award for Especially Meritorious Service with Western Pacific Base Command; 1960, Tufts University Award for Leadership in Oral Pathology; 1961, Honorary Doctor of Science Degree, University of Buffalo; 1965, Alumni Research Award Medal, the Association of Dental Alumni, Columbia University; 1965, Public Health Service Meritorious Service Medal; 1967, Honorary Doctor of Science Degree, University of Pennsylvania; 1968, Annual Lecture Award (first recipient) of the New York University College of Dentistry Alumni Association;

Author of some 50 publications.

General Statement

Dr. Kreshover. Mr. Chairman and members of the committee, it is my privilege to appear before you on behalf of the National Institute of Dental Research. In the health field today needs and opportunities are out of phase with each other. Americans are increasingly concerned with everything that harms the quality of life. Yet, while recognition of a vast reservoir of dental neglect and the importance of oral health grows steadily, limited manpower resources, even if stubstantially expanded, could not begin to meet these needs. The Dental Institute, through its programs of laboratory, clinical, epidemiologic, and applied research is seeking to identify and develop more preventive measures to preserve and maintain the maximum degree of health and function of the oral cavity.

DENTAL CARIES

In the area of dental caries, a panel of expert advisers has confirmed the growing conviction of Dental Institute scientists that bacterial plaque plays a major role in the caries process and has urged an expansion of research on plaque formation, microbiology, and control. We are moving forward to meet this need through creation of a dental caries task force. This mechanism is being used because we believe that work conducted and supported by the Institute has developed an adequate base of knowledge to justify expectations that caries can be

completely prevented within the next decade if a concerted effort is initiated now. A review of the state of the art in this field suggests that prevention should be possible by such varied means as topical antibiotic therapy, sealing of occlusal surfaces by adhesive materials, additions to the diet to alter the metabolism of cariogenic bacteria, and prevention of dextran plaque formation by substitution of other sugars for sucrose or by topical use of dextranase. In addition to proceeding in these directions, research will also continue to seek new ways of improving or utilizing fluoride to improve tooth resistance to decay.

Through the efforts of Dental Institute and grant-supported scientists, we now know, for example, that the principle of a sealant to prevent decay in pits and fissures—the most common sites of occurence—is a sound one. Already demonstrated is that sealants can penetrate effectively into enamel surfaces and prevent decalcification. We are confident that a material with the necessary biostability can be developed.

The problem of smooth surface caries is presently being attacked through the enzyme dextranase, which has proved effective in dissolving plaque and preventing this type of caries in animals. Clinical trials had been delayed pending development of a purified dextranase, but they were begun recently.

Underpinning these and other approaches to more effective caries control and ultimate prevention is the significant extension of our understanding of the disease process itself. Thus, we now know that specific micro-organisms are responsible for tooth decay and that these bacteria are not present universally from birth. Preliminary studies of preschool children, age 2 to 4 years, indicate that these specific organisms were present in only 30 percent of those examined. By following these children over a period of years, we hope to learn more about how any subsequent appearance of caries-inducing streptococci correlates with the onset and progression of tooth decay, and to observe transmission patterns within family groups.

FLUORIDES

The technique whereby a fluoride gel is applied to the teeth for a few minutes a day several times a week, via a fitted mouthpiece, is also being tested in this age group. The opportunity here is to determine whether early topical treatments provide a foundation for later defense against decay. In addition, studies of junior high school students are underway in a fluoridated community to see if this method confers additional protection. In earlier studies in a nonfluoridated area, schoolchildren had shown a reduction of 80 percent in tooth decay.

A related development reported this year by grantees concerns the use of tablets by children in the first through the third year of school in a low-fluoride area. By chewing tablets containing acid phosphate sodium fluoride once every schoolday for 2 years, these children had 23 percent less caries in their permanent teeth than those who did not get the fluoride. Moreover, the teeth which erupted during the test period had 50 percent less caries.

In view of the shortage of professional and auxiliary personnel in dentistry, it bears mention again that these caries control techniques permit supervision of hundreds of children with only a fraction of the number of personnel required by conventional methods of topical fluoride application.

FILLING MATERIALS

Current efforts by the Dental Institute to develop a new restorative material should also lead to the provision of better dentistry with less manpower. Possibly, the most significant use of a truly adhesive filling material would be to intercept the progress of the carious lesion before it penetrates into the dentin. In such a procedure, it would be necessary only to scrape away the damaged enamel. Because a drill-less procedure of this type would be relatively simple, well-trained and supervised ancillary personnel should be able to carry it out, thereby freeing the dentist for more complicated tasks.

Considerable interest in the Dental Institute's work with barnacle cement has been created by our recent booklet describing progress to date, and we hope that other investigators will build on our efforts. It is anticipated that, once the mechanism of secretion and the chemistry of the cement are known, a similar cement can be synthesized for testing as a dental adhesive.

Still another promising avenue in biomaterials research continues to be provided by studies of plastic tooth implants. Using baboons as experimental animals, grant-supported investigators have already shown that it is possible to successfully implant a plastic tooth replica in the socket of a freshly extracted tooth. More recent studies have shown that adding grated anorganic bone to the roots of the plastic teeth appears to heighten chances of the permanent survival of the synthetic tooth.

PERIODONTAL DISEASE

In the continuing puzzle posed by periodontal disease, recent findings of Institute and grant-supported scientists have helped to fit together important pieces. For example, studies have confirmed an old and previously discarded theory that a major factor in human resistance to periodontal disease is the attachment of the oral epithelium to tooth structure around the neck of the tooth.

Other studies have shown that while certain bacterial products can cause gum inflammation, an early stage of periodontal disease, these antigens do not penetrate the intact surface of the subgingival lining. Thus, our search has concentrated on bacterial products that are capable of ulcerating the pocket lining. To date, these efforts have focused on ammonia and hydrogen sulfide.

Although intraoral irritants, such as plaque and calculus deposits, are intimately associated with periodontal disease, their role is not adequately understood. Accordingly, a long-term investigation of their influence on the initiation and progression of this disorder in a stable, adult male population was begun last year.

In the important field of oral-facial growth and development, a special report on cleft lip and palate and related speech studies has been prepared for the record which discusses genetic-environmental causative factors, diagnostic techniques, and rehabilitative procedures.

MALOCCLUSION

The Dental Institute is also supporting research in malocclusion, the principal aim of which is to create a better scientific basis for the treatment of certain orthodontic problems and to establish simpler therapeutic approaches. Particular emphasis is placed on such suspected postnatal causative factors as oral muscle forces and abnormal oral habits. Among the prenatal environmental influences under study are certain drugs and agents ingested during pregnancy. For example, intake of excessive doses of vitamin D by pregnant rabbits has been found to cause malocclusion as well as other defects in the offspring.

A diagnostic index based on sound statistical and orthodontic principles has long been needed. The usefulness of one particular diagnostic index for the study in large populations of the distribution of occlusal deviations from an ideal "standard" is currently being assessed.

DENTAL RESEARCH INSTITUTES

Turning now to another major program effort that has been of particular interest to this subcommittee, I should like to report that five Dental Research Institutes are currently in varying stages of development in different parts of the country. Each in its own way is seeking to develop and support a unique, interdisciplinary assemblage of scientists working toward the solution of oral health problems. We firmly believe that developing such a critical mass of investigators and investigations will not only contribute significantly to oral health research but will also have important byproducts in professional health education.

Finally, Mr. Flood and members of your subcommittee, I am pleased to report to you that our public information program which has progressively accelerated over the past 3 years, continues to do so at an impressive pace. This year, due largely to publicity generated by the observance of the Institute's 20th anniversary, we had unprecedented coverage in the print media and on radio and television.

Mr. Chairman, I have touched on only a few of our productive areas of research and training. A greater coverage of our efforts will be found in our research highlights.

SUMMARY OF BUDGET

Our budget request for 1970 is $30,062,000, an increase of $642,500 over the 1969 operating level of $29,419,500. Included are increases of $504,000 in research grants, $260,000 in laboratory and clinical research, $97,000 in collaborative research and development, and $74,000 in review and approval of grants. We will operate at about the same level as last year in biometry, epidemiology and field studies, and program direction. There will be a reduction in level of support for the fellowship and training grant programs.

Mr. Flood and members of the subcommittee, this concludes my formal statement. I would be happy indeed to answer or try to answer any questions presented to me.

ADVERSE EFFECTS OF FLUORIDATION

Mr. FLOOD. Do you wish to comment on the article on fluoridation and the reply we referred to earlier?

Dr. KRESHOVER. Yes, Mr. Flood.

In response to your question regarding an article that recently appeared dealing with the subject of adverse effects, so stated, to the use of fluoridated water supplies, I would wish to put into the record that a statement has been prepared and released over the signature of Surgeon General Stewart that in essence points to the efficacy of fluoride in recommended levels as not only a proven measure of caries control but also one that, used in the recommended levels, does not present a health hazard.

I would wish for the record to cite one passage that is pertinent and relates in general fashion to the article in question.

"The desirable fluoride content of water to be used in dialysis has not been finally determined."

By dialysis, we refer to a mechanism by which patients with damaged kidneys are treated with an artificial kidney through which a large quantity of water flows in order to provide a clearance process for the circulating blood of the patient; in a sense substituting for the damaged kidney.

"Some clinicians have suggested that a small quantity of fluoride may counteract to a degree undesirable bone demineralization that occurs in patients with kidney failure.

"There are also some indications that the absorption of fluoride during dialysis from the approximately 900 quarts of water used each week, an amount of water 50 to 100 times the amount of fluid consumed by the average person, can result in increased storage of fluoride in the skeleton because various solutes may be absorbed from the water as it is normally supplied during long-term dialysis. Most water used in dialysis should be de-ionized."

This is the recommendation that has been made by Dr. Stewart, by the National Institutes of Health leadership and, indeed, by the scientific competency that we have in the National Institute of Arthritis and Metabolic Disease, an institute which is supporting considerable research on kidney disease.

It should be pointed out again that the need to process some water supplies before therapeutic use in large quantities in artificial kidneys has no bearing on the ingestion by anyone of optimally fluoridated water from community water supplies recommended by health authorities as a medically safe procedure for the reduction of dental caries.

I would say in a final comment, Mr. Flood and members of your committee, that Surgeon General Stewart again goes on record, as we do, that fluoridation of water is endorsed as a safe and effective public health measure and we urge all communities to make its benefits available to people at the earliest possible time.

EFFECT OF FLUORIDATION ON THE ELDERLY

Mr. FLOOD. I have here an article dated January 2, 1967, from the New York Times, page 25. It says:

Fluoride may also reduce hardening of the arteries.

The article goes on to say that:

The use of fluoride in water as a tooth-decay preventive may also aid in reducing hardening of the arteries, the American Dental Association reported today.

A group of Boston physicians have conducted research showing a "striking low incidence" of aortic calcification (a phase of hardening of the arteries) among older persons who drink fluoridated water, the dental association reported.

(The newspaper article referred to follows:)

[From the New York Times, Jan. 2, 1967]

FLUORIDE MAY ALSO REDUCE HARDENING OF THE ARTERIES

CHICAGO.—The use of fluoride in water as a tooth-decay preventative may also aid in reducing hardening of the arteries, the American Dental Association reported today.

A group of Boston physicians have conducted research showing a "striking low incidence" of aortic calcification (a phase of hardening of the arteries) among older persons who drink fluoridated water, the dental association reported.

Research has shown that the increased deposit of calcium in bone brought about the fluoridation may possibly be linked to a lessening of calcium deposits in other organs and tissues, where such deposits may be damaging, they said.

Mr. FLOOD. Do you know about this theory?

Dr. KRESHOVER. Yes, sir.

This relates to a most interesting study that the National Institute of Arthritis and Metabolic Diseases supported possibly within the course of the last 2 years. This was a study dealing with the relationship of fluoride to a disease entity we call osteoporosis, a bone-thinning lesion, particularly characteristic in elderly people and notably more prevalent in women than men.

The study in question was conducted in North Dakota. It sought to put under observation two groups of people from different community areas. There were approximately 300 people studied at ages 45 to 85 years in a northeastern area where the fluoride level ingested by these people over a lifetime of exposure to the fluoridated water was in the range of some 4 to 5.8 parts per million.

In the southwest area, a larger group approaching some 700 people was studied following again a lifelong exposure to fluoride at levels under 0.3 part per million.

The interesting observation was that the high fluoride area showed an appreciable and statistically significant lower level of aortic calcification. On the other hand, further observation showed that in the low-fluoride area there was approximately two times as great an incidence of osteoporosis than in the high-fluoride area.

Your point is well taken. This evidence, at least inferential evidence, suggests that high levels of fluoride may have beneficial effects in areas quite beyond those concerned with the teeth and the control of dental caries.

Mr. FLOOD. I have an article here from the Washington Star of April 29, 1964, page 3. The headline is:

Fluoridation Seen Aiding Elderly.

This is very much along the line of your suggestion; that is "A nutritionist declared yesterday the elderly may find themselves greater gainers than children from fluoridation of water supplies."

They go on to say the indications are that the "intake of fluoride throughout life may be helpful in preventing the abnormal porousness of bones that is a common disorder of the older."

Fewer fractures, and quicker and stronger healing when they do occur, would indeed be a boon to anybody of advancing years.

They attribute this possibly to fluoridation along the line of the argument that you are using.

Dr. KRESHOVER. Yes, sir.

High intakes of fluoride are being tried in some hospitals for the treatment of osteoporosis. As you may well recall, that is a disease entity that has markedly lower bone density and frequently is manifested by collapse of the vertebra. Some osteoporosis cases that have been followed with high levels of fluoride treatment have apparently been successful.

(The newspaper article follows:)

[From the Washington Star, Apr. 28, 1964]

FLOURIDATION SEEN AIDING ELDERLY

CHICAGO.—A nutritionist declared yesterday the elderly may find themselves greater gainers than children from fluoridation of water supplies.

There is evidence that such treatment produces stronger bones as well as stronger teeth in adults, Frederick J. Stare, M.D., chairman of the nutrition department at Harvard School of Public Health, told an American Dental Association Conference.

He said there are indications that intake of fluoride throughout life may be helpful in preventing the abnormal porousness of bones that is a common disorder of the older.

"Fewer fractures, and quicker and stronger healing when they do occur, would indeed be a boon to persons of advancing years," Dr. Stare said.

PUBLIC INFORMATION ACTIVITIES

Mr. FLOOD. I think we stated in our report last year that you people should make more widely known what you are doing in dental research, what you are as a matter of fact accomplishing. What have you done about this since last year?

Dr. KRESHOVER. Needless to say, the suggestion was a good one and one that we accepted and proceeded to make some assessments of. From the standpoint of written public inquiries made to the National Institute of Dental Research Information Office, we noted an appreciable increase of 327 percent over a period of less than 3 years. We also had an opportunity in the course of the last year to prepare two major brochures. One describes NIDR activities and disciplines under the title of "The Expanding World of Dental Science." Another one illustrates work conducted by National Institute of Dental Research grantees that we have called "A Spectrum of Dental Research." We distributed these unsolicited to a number of centers. We then were rather gratified to have many, many requests for additional copies.

I might call your attention, Mr. Flood, to the fact that we had some 2,500 requests that came from members of Congress alone in the course of the past year.

So far as other activities of our Information Office are concerned, we recently prepared an education film dealing with dental research as an exciting, challenging and rewarding career for young people.

This film was produced in cooperation with the American Dental Association, the International Association for Dental Research, and the American Association of Dental Schools. With only 125 prints available, and the film has just been released, we have, to date, received 1,300 requests for bookings. These have all been promised and will be shown between now and June. There are an additional 2,000 requests for bookings that we will be able to honor hopefully in the early fall.

I might say that the audience that we have sought to reach with this film is the senior high school and the college-level student. We believe that now that dentistry has joined—and it increasingly does this—the mainstream of biology and medicine, more and more young people can be motivated to make important contributions to problems of oral health and disease that continue to face us.

EFFECTS OF FLUORIDATION

Mr. FLOOD. We have talked a great deal about fluoridation over the years. What more do you know about the effects of drinking fluoridated water than you did 1 year ago?

Dr. KRESHOVER. You would recall, Mr. Flood, that I had an opportunity last year or the year before to cite in response to a similar question some 25 years of experience in water fluoridation in large communities where it has been controlled in a concentration of one part per million; an optimum level in the water supplies of these communities. During these years of careful study there is every evidence that there is approximately a 60-percent reduction in tooth decay, and that lifelong exposure based on studies provides no evidence of any harmful effects in the recommended quantities.

Mr. FLOOD. We are going to have at least one public witness come here to tell us about the horrible effects of drinking fluoridated water. Specifically again, what scientific evidence is there of any harmful effects, any at all? What scientific evidence?

Dr. KRESHOVER. I would merely repeat, sir, that we have no doubt whatever, based on morbidity, mortality, and necropsy evidence, that the daily intake throughout life of one part per million of fluoride, either introduced into the water in controlled systems or occurring naturally in the water supplies, harmlessly reduces caries in permanent teeth by as much as 60 percent and slightly less in deciduous teeth.

I might also point out for the record that two studies—one in Bartlett, Tex., where residents have a lifelong exposure to naturally occurring fluoride in the water at levels approaching eight parts per million, and the other in Colorado Springs, Colo., where there is approximately 2½ parts per million in the drinking water—have shown no morbidity or mortality differences between individuals in those communities and those residing in communities without benefit of fluoride in the water supplies.

Mr. FLOOD. Do you agree with that, Dr. Marston?

Dr. MARSTON. I think the important point to make, Mr. Flood, is the effectiveness of fluoride in preventing dental caries in the doses that are recommended. I think that some of the questions in terms of beneficial effects in osteoporosis would perhaps be less clearly demonstrated at present although it has been suggested.

The possible danger of large quantities of ions of various types, such as calcium or other ions that occur either naturally or added to the water, when you have the unusual situation of dialysis, is a completely different problem from the problem of adding fluoride to drinking water for the purpose of preventing caries. Water used for dialysis can be handled quite readily by de-ionizing the water to be used; this may be necessary in some areas to avoid too high a concentration of calcium as well as of fluoride.

DENTAL PLAQUE

Mr. FLOOD. You were very enthusiastic last year about developments in connection with what you refer to as dental plaque. What are the further developments since last year?

Dr. KRESHOVER. As I indicated in my opening statement, we have moved in the direction of establishing a caries task force. I believe it would be important in understanding the nature and scope of our activities if I introduced again for the record what we believe to be a proper definition of the disease entity we call dental caries.

Dental caries is a condition wherein the hard structures or the hard tissues of the teeth are destroyed by harmful acids produced by certain bacteria that have now been identified, acting on soft plaque material which accumulates and adheres to the tooth surfaces of susceptible persons. This definition emphasizes, No. 1, the resistance of the tooth so that the tissue that is attacked can be treated as one appropriate measure for the reduction of dental decay.

Secondly, the definition calls attention to acid produced by certain bacteria. If we develop techniques whereby the bacteria can be destroyed or in other ways eliminated and their harmful products accordingly prevented from accumulating on the tooth surface, a second approach becomes available for the control of dental caries.

Assuredly we have the plaque which accumulates and adheres to the tooth surface. If we can develop appropriate measures for the prevention or removal of plaque, we have a third effective procedure by which dental caries can be controlled.

Your specific question related to plaque. The plaque we have now been able to demonstrate in our studies, conducted principally by investigators at the National Institute of Dental Research, is a material that is soft, that is constituted of a variety of debris from the mouth, and that accumulates on the tooth surface, largely as a consequence of bacteria, which are streptococci. These anaerobes are given the name streptococci mutans. With these bacteria acting on substrate in the plaque, a certain type of sugar, sucrose specifically, will be metabolized.

Mr. FLOOD. How do you use the term "mutans," the same sense as mutation?

Dr. KRESHOVER. Yes, sir; it is a transitional kind of organism. The bacteria acting on the sucrose will produce a sticky, gummy polysaccharide called dextran. It is a substance of high molecular weight that will then enable the bacteria and plaque material to adhere to the tooth surface. Accordingly, when the bacteria metabolize the substrate of sugar to produce lactic acid, the acid produced will come into intimate contact with the tooth surface and cause its dissolution. The break-

down of the tooth surface permits the bacteria to make inroads into the underlying enamel and cause further destruction.

Our scientists recently, in collaboration with investigators in the Merck, Sharpe & Dohme Laboratories in Rahway, N.J., have been able to isolate and purify an enzyme that is called dextranase. This dextranase has the unique property of being able to counteract the production or the effects of the dextran. Experimental animal studies, specifically in the hamster, show that dextranase introduced either into the diet or into the water ingested by the hamsters will prevent dextran from being formed, and accordingly, and in parallel fashion, reduce and in many instances prevent the occurrence of dental caries.

We are now conducting some four clinical trials of dextranase on selected patients and selected population groups. Our initial evidence is that we may well be on the way to identifying another effective approach to the control of dental caries.

CLEFT LIP AND PALATE

Mr. FLOOD. Do you have anything new on cleft lip and cleft palate research?

Dr. KRESHOVER. We continue, Mr. Chairman, to have an interest—in both the direct operating programs of the Institute as well as programs that we support through our extramural activity—in cleft lip and cleft palate.

I might cite for you that in the cleft palate field we recognize that some 13 percent of all reported birth anomalies are of this nature. So it is no small public health problem so far as our country is concerned.

We also have evidence that cleft lip, with or without cleft palate, is very likely one specific anomaly, one specific entity. On the other hand, cleft palate alone is probably another specific entity.

Mr. FLOOD. Can this be identified with any geographic area especially; any local region of any kind?

Dr. KRESHOVER. Cleft palate, on the one hand, occurring alone is largely a disease that is caused by environmental factors. Trauma possibly, endocrine disfunctions, a variety of things may very well come into the picture.

On the other hand, cleft lip alone or cleft lip accompanied by cleft palate has a large component of genetic influence. Accordingly, if we were to examine population groups, and this is most interesting, we find a much greater prevalence of cleft lip, with or without cleft palate, among the Japanese, among the American Indians, and a considerably lower prevalence of incidence of cleft lip, with or without cleft palate, among the Caucasians and among the Negroes of this country. Accordingly, we do recognize a genetic component. On the other hand, I would be quick to say that it would be a great mistake were we to clearly pigeonhole one disease entity or one anomaly or the other as being distinguished by, on the one hand, environmental factors and, on the other hand, genetic factors. In most instances both interplay at the critical point of development of the fetus.

Mr. FLOOD. We will place your special report on this subject in the record.

(The report follows:)

Special Report Cleft Palate and Related Speech Disorders

Each year approximately one of every 800 babies born in the United States has cleft lip or palate or both. This year, over 6,000 victims and their families will need help to bear heavy medical, psychological, and financial burdens. To relieve these sufferers and to reduce ultimately the incidence of these congenital malformations, the National Institute of Dental Research conducts and supports research on the causes and treatment of oral clefts.

DEFINITION OF A CLEFT

Long before birth, certain tissues called palatal shelves fuse to form the hard and soft palate in the roof of the mouth. Shortly before the palate forms, other lateral tissues grow together making the jaws and the lips. If these tissues do not fuse permanently in the embryo, clefts result.

There are two principal types of clefts: cleft palate alone (CP) and cleft lip (with or without cleft palate CL±CP), the latter occurring about three times more frequently. While studies suggest that these are two different defects with different causes, relatively little is known about the specific causation of clefts.

OCCURRENCE OF CLEFTS

Clefts do not occur with the same frequency in all populations. Negroes have fewer clefts than Caucasians, while Mongolians have more; American Indians tend more toward the oriental incidence.

Cleft palate occurs about as often in girls as boys, whereas CL±CP is much more frequent in boys. A public Health Service survey of over 4,400 cleft babies born during a 4-year period in four widely separated States produced data showing that clefts are more frequent in multiple births, with low birth weight, and when parents are older; it showed further that cleft children are more likely to have other defects than noncleft babies. Such malformations include club foot, extra fingers, and micrognathia (very small lower jaw).

DISTINCTIONS BETWEEN TYPES OF CLEFTS

Children with CP only are more likely to have difficulty in articulation than those with both CL and CP, whereas those with CL alone often articulate normally. In addition, CP children are more likely to have trouble closing the gap between the palate and the back of the throat, to have hearing problems, and, on the average, to have lower intelligence than are CL±CP victims. Facial growth patterns also are found to differ between these two groups of cleft patients.

STUDIES ON CAUSES OF CLEFTS

Intensive study of causation began in 1960 when the National Institute of Dental Research commenced support of research on oral clefts.

Some cases of CL±CP and CP may be hereditary with the familial tendency greater in the former. However, environment appears to be more influential than heredity. For example, when one of a pair of identical twins has a cleft, 60 percent of the time the other does not.

Genetic studies indicate at least two different modes of inheritance—predominately recessive for CL±CP and dominant for CP. In an analysis by Institute geneticists of 93 Caucasian families with cleft children, both types of clefts were found to occur in only six families in which some other relative also had a cleft. Since there were cleft relatives on both sides among several of the families with CL±CP, it seemed likely that a recessive genetic trait was responsible. On the other hand, families with CP alone all traced the defect to only one side of the family which is compatible with a dominant trait.

In other research at the Forsyth Dental Center in Boston, it was shown that tooth development is retarded in clefted children. Parallel investigations at the University of Pittsburgh where recordings were made of the normal ranges of shapes and of developmental timing in human teeth from the earliest fetal stages through maturity, have shown that certain unusual tooth shapes are frequent among clefted children and that other unusual types occur among the mentally retarded.

FUSION STUDIES

In order to throw light on the specific structural changes involved in clefts, scientists at the University of North Carolina are investigating, by electron-microscopy, the normal fusion process of cells in the fusion region of palatal tissues in mice. Related studies at the University of Pittsburgh have shown by tissue culture techniques that the palatal shelves, whether from cleft or normal embryos, will fuse when they are placed in proximity to each other. Accordingly, the search continues for extraneous factors that will prevent fusion.

One area of interest continues to be in the relationship of chlorcyclizine (an antihistamine) to animal clefts. This year Institute scientists have shown that different animals convert the drug to norchlorcyclizine at very different rates. Since it has been demonstrated that the norchlorcyclizine form of the drug causes the defect, the speed of conversion from chlorcyclizine may well account for the earlier demonstrated variability of the drug's effects.

HEARING AMONG CLEFTED CHILDREN

Since hearing is essential to adequate speech development, the prevention of even slight deafness in early years, when clefted children have ear infections most frequently, is most important. Accordingly, much attention is being given today to the control of ear inflammation in cleft palate patients. In one program at Duke University, surgeons report that removing adenoids at the time of palatal surgery (usually about age three months) prevents much of the expected middle ear inflammation.

ORTHODONTIC TREATMENT OF CLEFTED CHILDREN

Clefted children frequently have either missing or extra teeth. In other instances, as an aftermath to cleft lip repair, pressure on the upper jaw can cause a retardation of its development as well as prevent normal tooth growth and eruption. So as to assure the earliest corrective procedures and maintain the best possible space relations between teeth and jaws for each type of defect, it is most essential that an orthodontist be a member of the cleft palate treatment team. Similarly, routine professional dental care must be provided so as to prevent decay in baby teeth that are so essential for the anchoring of appliances and for maintaining space in the jaw for erupting permanent teeth.

EVALUATION STUDIES OF SURGERY

Although surgery is often the key to successful management of clefted patients, sometimes it should be avoided. Diagnostic techniques are needed to help the cleft palate team decide when to operate or when an appliance or speech training would suffice. When surgery is required, there must be criteria for selection of the most appropriate operation. NIDR grantees are now watching the progress of patients for a period of years to learn which surgical techniques are best.

In one study at Duke University a 5-year appraisal has been made of 25 infants who had pieces of rib grafted into their clefts and were fitted with appliances to maintain space in the jaw for teeth. The surgeons reported that although the grafts were accepted by the body, teeth did not move spontaneously into the grafted sites, nor did the new tissue grow. Accordingly, these patients may require further surgery at a later date.

Some clinical researchers believe that operations before the age of 9 months result in longer palates and better speech, and that patients thereby avoid unlearning faulty speech patterns acquired before the palate is closed. However, much evaluation of treatment remains to be done.

SPEECH RESEARCH

Physical Adaptations.—Before surgery, people with unilateral clefts are likely to speak better than people with posterior, double, or subtle submucuous clefts. The submucuous disability is the most likely to be overlooked, since the cleft is hidden by the lining of the mouth.

Two physiological phenomena frequently appear as an expression of a cleft palate patient's attempt to compensate for the gap that occurs between palate and throat. One is the formation of a lump of tissue called Passavant's pad at the back of the throat, and the other is the appearance of nodules on the vocal cords. A frequent final symptom of this latter abnormality is hoarseness.

Diagnostic Aids.—Studies of the levels of air pressure in the nose and mouth, helpful in predicting the capacity for good speech in cleft palate patients are receiving particular attention at the Eastman Dental Center in Rochester, N.Y. Highly sensitive equipment, including X-ray motion pictures synchronized with a high fidelity sound recorder and a photographic recording of an oscillograph, is used to pick up on separate channels the air pressure, air flow, and air volume in the mouth and in the nose. These records are then analyzed to evaluate the sequence of certain sounds, as well as to help determine good speech capacity.

Muscle Studies.—An important aspect of speech research is the study of the muscles involved. Scientists at the Haskins laboratories in New York City have recorded normal muscular patterns in speech as a basis for comparison with muscle reactions in subjects with impaired speech. These studies have led to the finding that production of a particular sound (phoneme) used in speech often requires more than one pattern of muscular motion.

Another comparative study has shown that while deaf persons may have normal muscle patterns, their tongue motions are commonly exaggerated and inadequate. However, even a minimum of hearing greatly helps the deaf person. Thus, those with speech imperfections (dysarthria) due to defective nerves, are found to have muscle patterns that often vary even when they repeat a particular syllable. Fortunately though, the dysarthric patient can usually manage fairly intelligible vowls.

In order to record muscle changes and improvements after speech training, a grantee has designed a so-called capacitator which records electrically how close the moving tongue comes to the hard palate, and can discriminate between vowels and consonants. This instrument can be a helpful adjunct to speech training programs.

Training Methods.—It is estimated that about 40 percent of clefted children speak nasally after the first operation and that some 20 percent still have this trouble after a second. Special exercises often help to improve speech when there is adequate physical capacity. Careful diagnosis is needed to identify which children can be helped and scientists at Duke and Northwestern Universities are studying speech training methods. Improvement from training exercises usually will be reflected in terms of fewer mistakes in articulation.

How Speech is Perceived and Coded.—Some insight into the role of speech codes has been provided by efforts of scientists to devise sound alphabets suitable for converting print into sound to help the blind read. The fact that, despite 50 years of experimentation, sound alphabets have achieved only about a tenth of the speed and information that comes easily through speech suggests that the only way the slow machinery of the ear can handle many signals rapidly is through code. English, for instance, requires about 40 separately identifiable sounds or "acoustic shapes" lasting about 50 milliseconds each. A sound alphabet would require at least 30 such signals per second. However, many sounds would be perceived only as a buzz because the ear cannot handle this load.

Investigators at the Haskins Laboratory consider that most encoding takes place below the level of consciousness, and before the neuromotor command is given to the articulatory muscles. This view is borne out by the fact that electromyography shows that some of the muscle action is always the same for making each sound, whereas the spectrographic pictures of sound perceived as the same actually differ. Since there is no single way that any sound is perceived, some sort of "decoder" identifies incoming sounds by referring them to the commands for producing them by moving muscles.

MOTOR DEFICIENCIES ASSOCIATED WITH CLEFTS

This year a study of communication skills made at the University of Pittsburgh has thrown new light on the puzzling passiveness and lack of creativity of many cleft palate patients. The research shows that afflicted children are more likely to be deficient in motor responses than in vocal ones. Even normal speakers among them use few gestures. When hearing is normal, clefted children have as good an auditory memory and understanding of words as others. However, their ability to do something in response to visual or auditory stimuli is below normal. For example, clefted children find it more difficult to select similar objects from a group of pictures; to pantomime the use of an object; to duplicate, from a pile of pictures, a set of pictures previously shown and removed; or even to repeat a series of numbers. Tests of these communication skills show no improvement with age. Rather, they retrogress.

PSYCHOLOGICAL STUDIES OF CLEFTED CHILDREN

Scientists at the University of Pittsburgh have found that children who couple bad temper with speech that is not nasal but full of articulation errors need psychological rather than physical help for speech improvement. One hundred and seventy clefted children, aged 3 to 10 years, were grouped according to type of articulation in a study of psychological problems. All the subjects had normal hearing and intelligence, although the IQ of poorer speakers was slightly lower.

Speech performance was correlated with the absence or presence of 29 behavioral problems as rated by the children's mothers. The good speakers had fewer behavioral problems although they showed a greater tendency to fight, than others involved in the study. The scientists believe that children who can control closure of the gap between palate and throat often fail to speak well because they need psychological help to manage their emotions.

Patients and parents were asked to evaluate the effects of surgery on speech and social adjustment in a psychological study at the Eastman Dental Center. Parents and patients both felt that speech had improved more than professional tests showed. Both groups also felt that social adjustment had improved, although the parents appeared to be more impressed with this factor than did the patients.

INTERDISCIPLINARY TEAM APPROACH

Because of their surgical, dental, speech and psychological aspects, problems arising from clefts require a team approach for successful management. The National Institute of Dental Research supports a number of cleft palate centers in which treatment and research are designed to help patients and families as a whole. Research findings, in time, will help cleft children everywhere.

To help focus attention upon the areas where research is needed, the NIDR has held conferences to assess the "state of the art" in two areas of cleft palate research: genetics and embryology. A summary of the embryology conference was published in Science, December 1967, and reprinted in the Cleft Palate Journal and Teratology in 1968. In this way, experts from many disciplines are apprised of the frontiers in cleft palate research, and more scientists can be attracted to make new contributions.

TOOTH TRANSPLANTATION

Mr. FLOOD. On this matter of transplanting of teeth, I have an article here dated February 13, "Wisdom Teeth are Transplanted." Transplanting of wisdom teeth to replace decayed first molars was done with 92 percent success for more than 500 teenagers. This is a report from the University of Southern California School of Dentistry.

The speaker there said he felt the transplants were successful because the wisdom teeth are the last permanent teeth to develop. They seldom are fully developed until the late teens, making them the best subject for molar transplantation.

Will you tell us something about transplanting the molars?

Dr. KRESHOVER. Yes, sir. I believe, first of all, that the subject of transplantation and implantation in the field of dentistry has been of no less interest or an area of no less challenge than it has been in the broad field of medicine down through these many centuries.

I would say furthermore, that our experience insofar as transplantation of teeth is concerned gives us a comparable body of experience as is the case with other tissues. The search by man for replacement of lost tissues, parts, and organs by parts secured from other men or from lower forms of species of life is one that we have been both interested in and challenged by in the field of dentistry.

We recognize three kinds of transplants we have had experience with. One is a transplant of a tooth taken from one site and introduced

into another site of the same individual. This is what we call an antogenous transplant; one that is most disposed to success.

A transplant of a tooth or another tissue from one man to another man; that is, within the same species, is less successful. This is a so-called homogenous transplant. And finally, there is the homologous transplant, from one species to another species, which has been notably unsuccessful.

Our experience with dental or tooth transplants is very much like that of other organs of the body. We have a rejection phenomenon—an immunologic response—and accordingly, our greatest efforts—and you touched on this in your query of Dr. Cooper this morning in regard to the heart—much of our efforts in recent years have been to obtain a synthetically fabricated, porcelainlike, artificial tooth that could be introduced and retained effectively in an individual who has lost his tooth. This has a number of favorable characteristics.

On the one hand, the utilization of the inert substance does not cause irritation to the tissue, and is nonimmunizing. A second characteristic of great importance is that it is nonabsorbable. A third characteristic of great importance is that it can be made esthetic. And a fourth, of course, is the one that we believe is also quite important, and that is, we can fabricate it upon demand.

Our studies to date have been largely at Brown University, and our experience has been largely in the baboon. A period of many years now of retention of these plastic teeth introduced into tooth sockets shows that they are retained as firmly as is a natural tooth, and indeed we believe that the evidence is such now that we may well be prompted to go into clinical trials.

Mrs. REID. Will the gentleman yield?

Mr. FLOOD. Yes.

Mrs. REID. My son several years ago had his tooth knocked out while playing football. His coach happened to see the tooth on the field and picked it up and put it back in his mouth. We were there and took him immediately to the dentist. He kept that tooth for about 6 years but it started to darken and now he has a capped tooth.

Dr. KRESHOVER. He retains the same tooth?

Mrs. REID. Yes.

With the progress which has been made since then, would you think there would be a possibility that the tooth could be kept alive under similar circumstances now?

Dr. KRESHOVER. Certainly it is like citing the evidence of 5-year cures for cancer. The longer one is able to avoid a recurrence of a disease, the more the likelihood is of not having a recurrence at a later period. With a period of some 6 years of retention of this tooth, I would say the likelihood of his continuing to retain it is quite good.

Presumably your dental practitioner continues to follow your son with X-ray examinations and other procedures, and I would say the likelihood of retention is quite good. That is an example, by the way, of the autogenous tooth transplant I referred to earlier.

Mr. FLOOD. Mr. Michel?

Mr. MICHEL. I will defer right now, Mr. Chairman.

Mr. FLOOD. Mr. Smith?

Mr. SMITH. No questions.

Mr. FLOOD. Mr. Shriver?

BUDGET FOR INFORMATION ACTIVITIES

Mr. SHRIVER. You have discussed at quite some length dental research and how you are making known to the general public what you have been doing.

Dr. KRESHOVER. Yes.

Mr. SHRIVER. How much of your budget request is planned for this purpose?

Dr. KRESHOVER. Mr. Shriver, I might point out in response to your question that the information office activity of our institute comes under the general category of what we call program direction. It is contained within the Office of the Director.

We show in our budget breakdown a reduction in the 1970 President's budget compared with the 1969 budget of $7,500. This is a minus figure in program direction. Accordingly, our information office activity would be essentially at the same level of support, possibly a slight decline in contrast to the current fiscal year.

Mr. SHRIVER. How much is it?

Mr. CHRISTOFERSON. I would say it is in the area of $115,000.

Mr. SHRIVER. I am bringing this up because of the interest last year of the committee and the impetus the committee gave to you to do more.

ORGANIZATION OF DENTAL HEALTH ACTIVITIES IN NIH

On page 98 of the justifications, it is stated that the matter of developing a more rational arrangement of the dental health activities is being discussed and studied.

Can you be more explicit on what you mean by that?

Dr. KRESHOVER. Dr. Marston, since assuming the directorship of the National Institutes of Health, has had a series of conferences with the leadership of the National Institute of Dental Research, and with the leadership of the Division of Dental Health, Bureau of Health Manpower, newly added to the broad based National Institutes of Health. In addition to these meetings, Dr. Marston has also had the input from leaders representing the broad base of the dental sciences and dental education throughout the country.

I would believe that the best answer I could give you at this time, speaking for the dental institute, is that we are assured and most confident that this is being examined critically and carefully by Dr. Marston and his staff, and at this time I do not believe we can report beyond this so far as a reordering of dental activities within total NIH.

Dr. MARSTON. Mr. Chairman, I might just add to what Dr. Kreshover has said, that we have taken the recommendation of the committee very seriously on its own merit, and also, in recognition and general agreement, that we do need to look at the relationship within the NIH, its relationship to health services and mental health administration.

I met with Dr. English on this item and we are pursuing it and will continue to pursue it along the lines suggested here.

CARIES TASK FORCE

Mr. SHRIVER. You explained in greater detail a while ago the statement about the caries task force.

Dr. KRESHOVER. Yes, sir.

Mr. SHRIVER. How much of the research budget is for that particular project?

Dr. KRESHOVER. At the present time, Mr. Shriver, the budget that can be applied specifically for the utilization by the task force is in the range of some $630,000. This represents largely an effort that emanates from our intramural research activity.

ORAL CANCER

Mr. SHRIVER. Will any of your requests be used for oral cancer research?

Dr. KRESHOVER. Yes, sir; they will. We do have an interest, as would be quite understandable, in the entire mouth and adjacent structures. Oral cancer, as you well know, is a serious problem in this country. It constitutes some 4 to 6 percent of all cancers. If we were to examine an average population group of some 100,000 adults in this country, we would find that 16 males and three females are afflicted with oral cancer.

There are some 7,000 deaths that occur each year from oral cancer alone, and some 25,000 new cases of oral cancer each year. We do not profess to take full responsibility within our institute for oral cancer alone. We do, on the other hand, cooperate and coordinate our efforts very closely with allied efforts in the National Cancer Institute, just as we do in appropriate programs that we relate to the Child Health Institute.

Mr. SHRIVER. Thank you, Doctor.

That is all, Mr. Chairman.

Mr. FLOOD. Mr. Casey?

UNIVERSITY DENTAL RESEARCH INSTITUTES

Mr. CASEY. Thank you, Mr. Chairman.

Doctor, how many dental research institutes do you have in operation now?

Dr. KRESHOVER. Five, Mr. Casey.

Mr. CASEY. Are they in operation?

Dr. KRESHOVER. Yes, sir; they are.

Mr. CASEY. Last year you had two fully in operation, did you not?

Dr. KRESHOVER. No, sir; we had five in operation last year.

Mr. CASEY. Last year you stated in your justification that you might have two or possibly three more initiated in 1968 and 1969. Are there any more being initiated?

Dr. KRESHOVER. I recall very well making that statement last year, Mr. Casey. We were optimistic at that point in time. We recognized what seemed to be some nonrecurring costs that accrued out of the support of the then existing five institutes.

On the other hand, our anticipation of requests for the support of additional institutes did not materialize. With an increase in the President's budget specifically earmarked in the fiscal 1970 appropriation of $400,000 above the $3 million that appears in our 1969 budget, with the increase in costs for the support of expanding productive institute activities that we recognize now, it would be rather unlikely, sir, that we might be able, hope as we would, to support additional institutes in the course of the next year.

But I would qualify this statement by saying we would nevertheless hope that this could be done. We would very dearly like to exploit the unusual environments that many universities have for the broadening of the base of dental science that these institutes are designed to achieve. And we would look forward with some optimism that meritorious proposals would nevertheless be submitted in the course of the next year.

Mr. CASEY. Where are these five? One is at the University of Pennsylvania and one is in Washington.

Dr. KRESHOVER. At the University of Washington in Seattle.

The third one is in Birmingham at the University of Alabama, the fourth one is at the University of North Carolina in Chapel Hill, and the fifth is in Ann Arbor, Mich., at the University of Michigan.

Mr. CASEY. How many institutes do you think you will need, or do you have any projection of how many institutes you should have?

Dr. KRESHOVER. I would like to recall to Mr. Flood and Mr. Casey and other interested members of the subcommittee that we began this program in 1965 when a critical appraisal of research and education in dentistry in this country showed an inadequate science base in our dental schools reflected in deficient critical masses of researchers and teachers.

Accordingly, a special advisory committee was constituted at that time to define the scope of the program that would be desired to correct this deficiency and to identify the conditions needed to carry out a program successfully.

In this effort, a geographic deployment, strategically speaking, was recognized. It was our judgment that established dental institutes in university centers indeed became national resources and, as such, we had optimistically projected some nine institutes that would meet our purposes most beneficially.

We would like to see an additional institute some place in the great Southwest. Most assuredly we would like to see one in the Far West, and we believe this would appropriately round out for the course of the next few years our important effort in this regard.

Mr. CASEY. I believe that is all, Mr. Chairman.

Mr. FLOOD. Mrs. Reid?

PREVENTION OF CARIES IN CHILDREN

Mrs. REID. Thank you, Mr. Chairman.

Doctor, in your statement you expressed an optimistic view that general caries can be completely prevented within the next 10 years if a concerted effort continues.

Are you speaking about all age groups in the population or just the rising generation?

I ask this question because dental problems in the elderly I think are quite different and often more severe than those of youth, particularly in these days with better oral hygiene. Of course, much of this was not known and within reach of many of our older citizens. Am I correct in my impression that the major portion of your research is centered on children and young adults and those who benefit most and longest from your research?

Dr. KRESHOVER. This is correct, Mrs. Reid.

We of course recognize the fact that dental caries is in general a childhood disease. We recognize that even before the age of 2 years some 50 percent of the children are afflicted by dental caries.

Mr. FLOOD. Before the age of 2?

Dr. KRESHOVER. Yes, sir. There has been a study, for example, at the Guggenheim Clinic in New York City which shows that before the age of 2 some 50 percent of children within this very, very young age bracket have dental caries.

Obviously in a city like New York at the present time, and in some eight others of the 10 principal and largest cities in this country that are now receiving the benefits of fluoridation of communal water supplies, this statistic may no longer obtain.

Mr. FLOOD. The baby teeth all fall out, anyhow, and the permanent teeth then come in.

Dr. KRESHOVER. This is true, of course. This is another subject, Mr. Flood, that relates to malrelations of the teeth and the jaws as the consequence of the early loss of the deciduous teeth and eruption of permanent natural teeth.

Mr. FLOOD. I am surprised that the caries are a problem before the age of 2 in those so-called baby teeth.

Dr. KRESHOVER. Yes, sir. It is extremely important in establishing a permanent dentition that man and woman would carry hopefully throughout their lives, that the teeth erupt at the proper ages, and that they come into proper alinement.

If a deciduous tooth is lost prematurely, then your assessment is perfectly correct; that is, the likelihood of an early eruption of the permanent tooth. In doing this, it would come in a malaligned position. Malalinement of teeth is a very common cause of periodontal disease; it is a very common cause of dental caries; it is a very common cause of trauma to the articulating mechanism of the jaw. Accordingly, one could ultimately have very serious consequences so far as nutrition is concerned, so far as speech is concerned, so far as respiration is concerned.

So we believe that the best kind of health practices would dictate the utmost care for the primary teeth.

Our efforts we believe up to the present time, Mr. Flood, and Mrs. Reid, in connection with our projection of a preventable measure for dental caries in the course of the next 10 years are quite realistic. We believe the scientific advances that have been made to date are such that if we were to gather all of our information, and apply this new knowledge appropriately in a considered fashion, we could very well have the disease completely in control in a 10-year period.

Indeed, we have sufficient information today that if the patient were in a position to accept full advice to the letter, dental caries could be prevented.

CONDITIONS PRODUCING DENTAL CARIES

There must be in the production of dental caries three conditions present at one and the same time. There must be the specific kind of diet ingredient, specifically sucrose—a dissacharide kind of sugar. We

must have present at the same time a specific organism. We know today, for example, that dental caries is an infectious and transmissible disease in the experimental animal; and presumably this is now being confirmed in clinical evidence so far as man is concerned.

Thirdly, we know that the tooth must be susceptible; it must have a built-in susceptibility to dental caries. We are reminded here of the Ballantine ale three rings; where all three rings come together, that is the point in time when dental caries can develop.

We know that by eliminating sucrose we can cut out dental caries even with the other two factors present. If the specific bacteria are present and we treat the mouth with an antibiotic, penicillin for example, we can remove that factor and again prevent dental caries.

Third, if we can increase the tooth resistance—as the fluoride ion is disposed to do—rendering the tooth, so far as its crystalline structure is concerned, more impervious to the action of the acid, we can control dental caries this way.

If we can take all of this knowledge we have to date and pool it and attempt to apply it in appropriate public health measures, we believe over the period of the next half a dozen years or so we can prevent caries.

PREVENTIVE MEASURES

Mrs. Reid. Is it not true that merely teaching children to brush their teeth is not going to, for one thing, keep their teeth clean and free of bacteria? Should there not be more of a program to teach children to use, for instance, dental tape or something of that nature? More thorough oral hygiene?

Dr. Kreshover. This matter of supervision and the kinds of important contributions it can make to oral health and general health is well illustrated, I believe, by what an auxiliary can do; somebody at a subprofessional level supervising school children in the proper routines of oral hygiene.

Mr. Flood, last year for example, queried me on the matter of a study we were supporting at that time—we just terminated this study by the way—in a suburban area of Buffalo, N.Y. Utilizing a mouthpiece, and I mentioned this in my opening statement, to which can be introduced a fluoridated gel, one hygienist or intelligent young lady being present with the children in the classroom can actually supervise the fabrication of the mouth appliance, which the children, incidentally, made themselves, as well as the introduction of the fluoride gel into the mouthpiece, and placing it and leaving it in the mouth for a matter of 6 minutes every school day. In a 2-year period of time, without a dentist being present, but supervising the study as described, we were able to demonstrate an 80 percent reduction of caries in these schoolchildren, age 11 through 14 years.

So this is another important direction I am sure you would explore with our colleagues in the Division of Dental Health regarding how we can apply some of this new knowledge to the betterment of our people in the community and the country.

UNIVERSITY DENTAL RESEARCH INSTITUTES

Mrs. REID. Do you feel the Dental Research Institutes have met your specification?

Dr. KRESHOVER. I would answer with a "Yes" to that question, Mrs. Reid.

While the time is short indeed, the level of productivity and the acceleration of advances made by the established five institutes is such—and this is not to raise the point of budget but merely to use this as an example of where they are—that they have projected collectively in these five institutes a deficit of support for the next fiscal year of something approaching $2⅓ million. This means that were these other times, the advancement of the institutes is such they could effectively develop additional programs with this kind of projected increase in fiscal support.

Mrs. REID. You listed the centers a moment ago—I did not hear all of them. Is there one in Illinois?

Dr. KRESHOVER. No, there is not. We have been in long discussion with four universities in the greater Chicago area—Loyola University, Northwestern University, the University of Illinois, and the University of Chicago. In consultation with these universities plus the American Dental Association, we wish to see whether at some appropriate time in the future we might be able to see developed in the greater Chicago area a consortium of universities in a regional concept that would tap the unique talents of each of these universities in a Dental Institute research program.

Mrs. REID. Thank you.

Mr. FLOOD. Mr. Michel?

TRAINING OF DENTISTS

Mr. MICHEL. How many dental schools do we have in the country, Doctor?

Dr. KRESHOVER. There are 50 dental schools today that are in operation with classes accepted, the most recent one being the Medical College of South Carolina.

Mr. MICHEL. How many graduates have we had in the past year?

Dr. KRESHOVER. I cannot give you an exact figure, sir.

The last figure that I would cite that would be reasonably correct is about 3,500 graduates in a period of 1 year.

Mr. MICHEL. How does that compare with 10 years ago?

Dr. KRESHOVER. It has increased fairly much. Our dental schools of 10 years ago, as I recall it, were turning out approximately 3,000 dental students per year. Our dental schools have been expanding their physical facilities so they are able to admit many more students.

I might say also that in addition to the 50 dental schools currently in operation, there are seven others that are being established and developed to the point where deans have actually been appointed and faculty added.

Mr. FLOOD. Are we not about to lose one or two?

Dr. KRESHOVER. Yes, sir. This brings up another point I am very

happy to put into the record, because we are very, very much concerned about the declining support for dental schools.

I believe that today people who are knowledgeable have been able to cite some 30 private universities in the United States that are in serious financial difficulties and many of these universities have dental schools.

We know, for example, that St. Louis University Dental School has already announced the closing of its doors. We know that many dental schools are running a deficit of some $1,000 per student per year. If we recognize that the average dental school may have something in the range of 400 students—a hundred per class for a 4-year curriculum—the deficit can range for many dental schools all the way from a quarter million dollars to a half million dollars.

This is a lot of deficit when we consider that the average budget for the support of a dental school today is something under $2 million. The private schools particularly are in jeopardy. We are very concerned about this. The private schools of course bring an ingredient to dental education that we must retain at all costs. They are true national resources. We know this. The private dental schools are in a position to do more things more quickly sometimes than State-supported schools, and they can be rather innovative in their approaches to educational experimentation and curriculum design.

So we are very much concerned about this. Of the some $90 million, by the way, that is in support of dental education today, some 25 percent is provided by the Federal Government. I do not know what the figure is from philanthropy, from private benefactors. But someone has cited to me a figure in the range of some 10 percent emanating from private sources.

Mr. MICHEL. What is the average length of schooling required for a dentist today?

Dr. KRESHOVER. Most dental schools today, of the 50 that are in operation, require a baccalaureate degree for admission. In some instances an outstanding student with 3 years of accredited time toward the acquisition of a baccalaureate degree may be admitted. By and large, the admission requirements by schools of dentistry today are quite comparable to those of schools of medicine.

Mr. MICHEL. So beyond the baccalaureate degree, the additional time required——

Dr. KRESHOVER. Is 4 years of dental school, as it is in medicine.

Mr. MICHEL. Four years?

Dr. KRESHOVER. Yes.

ORTHODONTISTS

Mr. MICHEL. How about orthodontists?

Dr. KRESHOVER. Orthodontics of course is a specialty of dentistry, as you know. Orthodondists are invaluable as specialists in the health professions because of the great magnitude of dental abnormalities or orthodontic needs we recognize in our country today.

Again, to cite a figure to possibly dramatize the seriousness of this problem, it has been estimated that some 50 percent of our young

school-age population in this country require orthodontic care for disturbances and dysfunctions that are beyond the esthetic. This is not to become prettier, but rather to acquire an important function that has been lost as a consequence of malrelations of the teeth and malrelations of the jaws. The estimated cost per year for orthodontic treatment in this country is something approaching $100 million.

And again, this projection is one that meets only about one-tenth of the need for orthodontic care in this country. So we need our orthodontists.

Mr. MICHEL. Orthodontists are in very short supply, are they not?

Dr. KRESHOVER. Yes.

Mr. MICHEL. You have to wait a month or more for an appointment.

I think in our whole community we have two. Because of our own children, I have come to see what good can be accomplished by it. While normally one would appear to have very good looking straight teeth, you have a real professional look at the bite once in a while he finds out what often meets the eye on first smile looks very good but there may be something in the long run that can cause some very, very serious problems.

Dr. KRESHOVER. Yes, sir.

Mrs. REID. Will the gentleman yield.

Mr. MICHEL. Yes.

PERIODONTISTS

Mrs. REID. Is it not true there is a shortage of periodontists also?

Dr. KRESHOVER. Yes, there is a shortage across the board of dentists, and increasingly dentistry today is assuming responsibility for a variety of specialty areas.

Mrs. REID. Is this fairly new, periodontist treatment, as such?

Dr. KRESHOVER. I believe we use the words so often, "state of the art." Nevertheless, I will use it one time here today to say that our state of the art, our understanding of the periodontal diseases emphasizes how little we continue to know, how much more we must know. The utilization in public health of the knowledge that we do have is such that more and more we require people skilled in periodontal treatment procedures.

Periodontal disease, as you may well know, is one that we customarily associate with the aged. We recognize, for example, that over the age of 65 almost no one is spared from periodontal disease. Of some 90 million adults in the United States with teeth, I would recall that 67 million have periodontal disease of some type.

Mrs. REID. Are they actually treated?

Dr. KRESHOVER. The treatment of periodontal disease is rather analogous, I would suggest, to the treatment for any kind of dental ailment or oral ailment; namely, there is some 60 percent of our population who never see a dentist or who are unable to avail themselves of the services of a dentist. So if we can extrapolate this figure to those with periodontal disease, we find there are probably very few people

with the disease who are in a position to recognize the need for treatment or be in a position to receive treatment.

Mrs. REID. Thank you.

RESTORATIVE MATERIALS

Mr. MICHEL. Is a gold inlay still a preferred filling for a tooth?

Dr. KRESHOVER. It depends on the nature of the lesion being treated and on the situation of the patient having the lesion. There are situations where so much of the tooth substance has been lost that in order to provide a bulk of strength to resist the thousands of pounds of biting pressure something like a gold restoration in an inlay form would be required.

On the other hand, for an anterior restoration; for the teeth that are visible when one speaks and one smiles, gold probably would be avoided and another material would be used in its stead.

Mr. MICHEL. Is there any research money going into improving or bringing down the cost of dentures for people who lose all of their teeth?

Dr. KRESHOVER. Yes, sir. We have an activity in our intramural research program which is clinically oriented. The activity is one which is primarily targeted toward newer design, and newer mechanisms for fabrication of dentures. Also, through grant support in the course of the last 2 years, for example, in a program identified under the broad heading of "Materials Science," we have been able—not we, but the investigators—to develop a so-called silane-type of material which can bond a porcelain tooth to an acrylic denture without the need for the introduction of pins, which are costly, oftentimes unsightly, and collect foodstuffs in the mouth. This is the kind of advance, to provide just one example, that is being made in the area of prosthodontics.

Other areas that we are emphasizing in our materials science program relate to the development, hopefully at an early date, of a new kind of restorative material that would have bonding qualities which would be adhesive. I could not being to emphasize enough the tremendous loss to our national economy consequent to filling materials which are replaced because they become defective or fall out in other ways.

What we would be hopeful of developing is a restorative material that would bond either inorganically or organically with the natural tooth substance and be lifelong in duration. This is another important effort we are making.

IMPROVING DENTAL HEALTH

Mr. MICHEL. You say to the best of your knowledge 60 percent of our people never see a dentist?

Dr. KRESHOVER. Yes, sir.

Mr. MICHEL. Probably a lot of it is due to economics?

Dr. KRESHOVER. Yes, sir.

Mr. MICHEL. What do you recommended for the 60 percent if you had to do it in a one-shot proposition? You are on national television

and you have a massive audience. You are trying to improve the whole area of dental health. Whether you are talking to the children, middle-aged people, grandma or whomever it is, what would be something you would say that you ought to be doing if you are not doing it today in order to preserve your teeth or improve the dental hygiene of the country as a whole?

Dr. KRESHOVER. It is a challenging question and I would respond by saying that the first thing that would occur to me is to sell our public on the truism that the teeth and the mouth are a part of the body. That disease of the mouth, whether it be a hard tooth structure or the tongue or the gums are part of the total structure of the body and as harm is created in the mouth so harm may be created in the body as a whole. That just as we are striving to make dentistry today a true part of biology and medicine and in the mainstream of biology and medicine, so must our public and our patients see this not as something that they will take care of if they can afford it but rather that they are concerned about it because an infected tooth can cause a septicemia. Dr. Cooper cited this this morning as an example of a serious occurrence.

We have great difficulty in dramatizing oral diseases. This is why people poke fun at it. This is why people give it short shrift, but it is part of the body. If we can sell this concept, people will become more conscious of the need to do something about oral health.

As far as what they should do, the question that you really asked, I would say seek professional attention whether it be in a local clinic, whether it be in a hospital facility which has a dental clinic, whether it be in a dental school, or whether it be a dentist practicing in the community. He is the best man to see and to advise, and I think just as a person who is intelligent would not presume to fail to visit a physician upon the slightest evidence of something that he is really concerned about, so must a patient seek out the dentist so far as oral health is concerned.

Mr. MICHEL. I am sure that a large group of people who do not seek out this professional advice do not do it because they feel all their resources are going for food. Do you think we are pushing to the extent we should be?

Dr. KRESHOVER. It is very difficult to establish priorities in any matters regarding health. At luncheon today we were discussing the kind of question you are asking now. I would recall at this point that the Dean of the School of Medicine at Yale University some years ago became very much interested in the field of dentistry and established a dental program only as a consequence of losing his wife, a fatality, following complications from a diseased tooth. This charged him up sufficiently so that he developed a dental program of graduate study at Yale University.

I believe increasingly we are getting this message across, and I am convinced that the interest Mr. Flood expressed last year and that you further queried me on today regarding what our information office is doing, shows its import, and I think that the message is getting across today.

Mr. SMITH. We are spending millions, as you know, on research on drugs and very, very little on determining what nutrition can do with regard to illness. We do have a very limited number of experiments now.

Are they being set up so that you will retrieve from them information concerning the effect of nutrition upon teeth?

Dr. KRESHOVER. Yes, sir. We must not neglect the matter of nutrition, despite the fact that in the course of some studies over recent years where we provided dental participation in the programs of the Interdepartmental Committee on Nutrition for National Defense, which visited some of the deprived countries of the world and sought to make appropriate recommendations on nutritional needs of the examined populations in connection with dental caries, as an example, and the periodontal diseases, there was no direct relationship to nutritional deprivations of any kind.

Nevertheless, much relates to the nutritional issue and the soft tissues of the mouth that we must come to grips with.

Mr. SMITH. For example, we have an experiment going on in Guatemala?

Dr. KRESHOVER. Yes, sir.

Mr. SMITH. Will you retrieve information from that of value to your institution?

Dr. KRESHOVER. If you are referring, Mr. Smith, to the Institute for Nutrition in Central America and Panama, the so-called INCAP——

Mr. SMITH. Yes.

Dr. KRESHOVER. We have been very much interested in the activities of the INCAP operation in Guatemala.

Mr. SMITH. Is this operation being set up so that you will get information? Have you done what is necessary to find out what the condition of the teeth happens to be for those in the experiment compared to those who are not, so you will be able to get a comparison?

Dr. KRESHOVER. Several years ago, Mr. Smith, we became sufficiently interested in the subject you put on the table now that we sent two of our investigators to Guatemala and they spent some months examining the nutritional status of the natives, various deficiencies in the studies having disclosed that there are indeed oral manifestations that we are particularly interested in. We continue to have an input to INCAP.

Dr. Scrimshaw, a former director of INCAP, is a former member of our Institute's Board of Scientific Counselors. We also are well acquainted with the present Director of INCAP, and we continue to have interest in this operation as well as other operations in South America and Central America.

Mr. SMITH. As this experiment progresses you will also be able to compare the dental results or compare the teeth of those in the experiment with those who are not?

Dr. KRESHOVER. We would hope so.

Mr. FLOOD. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Dental Research

Amounts Available for Obligation

	1969	1970
Appropriation	$29.983,500	$30,062,000
Comparative transfer to "Salaries and Expenses, Office of the Director"	-286,000	.....
Cutback required by P.L. 90-364	-278,000	.....
Total obligations	29,419,500	30,062,000
Disposition of cutback: To be returned to the Treasury	278,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
104	Research		$15,055,000		$15,559,000		+$504,000
	General research support grants		(1,194,000)		(1,215,000)		(+21,000)
	Scientific evaluation grants		(42,000)		(42,000)		(.....)
	Categorical clinical research centers		(400,000)		(400,000)		(.....)
	Dental research institutes		(3,000,000)		(3,400,000)		(+400,000)
110	Fellowships		1,765,000		1,694,000		-71,000
111	Training		5,609,000		5,390,000		-219,000
	Direct operations:						
112	Laboratory and clinical research	217	4,687,000	221	4,947,000	+4	+260,000
115	Collaborative research and development	4	845,000	4	942,000	..	+97,000
116	Biometry, epidemiology and field studies	22	431,000	22	436,000	..	+5,000
117	Review and approval of grants	35	689,000	36	763,000	+1	+74,000
118	Program direction	23	338,500	23	331,000	..	-7,500
	Total obligations	301	29,419,500	306	30,062,000	+5	+642,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions.....	301	306	+5
Full-time equivalent of all other positions	14	14	..
Average number of all employees.....	303	309	+6
Personnel compensation:			
Permanent positions.....	$3,177,000	$3,236,000	+$59,000
Positions other than permanent.....	116,000	116,000	.....
Other personnel compensation.....	22,000	22,000	.....
Total personnel compensation.....	3,315,000	3,374,000	+59,000
Personnel benefits.....	359,000	365,000	+6,000
Travel and transportation of persons.....	141,000	158,000	+17,000
Travel and transportation of things.....	33,000	38,000	+5,000
Rent, communications & utilities.....	101,000	106,000	+5,000
Printing and reproduction.....	42,000	47,000	+5,000
Other services.....	2,347,500	2,661,000	+313,500
Supplies and materials.....	453,000	460,000	+7,000
Equipment.....	202,000	213,000	+11,000
Grants, subsidies & contributions.....	22,429,000	22,643,000	+214,000
Subtotal.....	29,422,500	30,065,000	+642,500
Deduct quarters and subsistence charges...	3,000	3,000	.....
Total obligations by object.....	29,419,500	30,062,000	+642,500

Summary of Changes

1969 estimated obligations	$29,419,500
1970 estimated obligations	30,062,000
Net change	+642,500

Increases	Base Positions	Base Amount	Changes from Base Positions	Changes from Base Amount
A. Built-in				
1. Annualization of 1969 pay increases	...	.....	...	$5,000
B. Program				
1. Research grants	...	$15,055,000	...	504,000
2. Laboratory and clinical research	217	3,629,000	4	210,000
3. Collaborative research and development	4	839,000	...	100,000
4. Review and approval of grants	35	490,000	1	65,000
Total program increases	...	.....	5	879,000
C. Payment to "National Institutes of Health management fund" for centrally furnished services:	...	1,305,000	...	49,000
Total increases	...	.....	5	933,000
Decreases				
A. Program				
1. Fellowships	...	1,765,000	...	71,000
2. Training	...	5,609,000	...	219,000
3. Program direction	23	338,500	...	500
Total program decreases	...	.....	...	290,500
Total net change requested	...	.....	+5	+642,500

Explanation of Changes

Research grants--The increase of $504,000 includes $83,000 for noncompeting requirements of the regular program, $400,000 for noncompeting continuations in the Dental Research Institute program and $21,000 in the general research support grant program.

Fellowships--The decrease of $71,000 represents a reduction of eight fellowship awards to a 1970 level of 113 awards.

Training--The decrease of $219,000 represents a reduction of seven training grants to a 1970 level of 91 awards.

Laboratory and clinical research--The increase of $210,000 and 4 positions will allow for expansion of research in dental caries and oral and related diseases.

Collaborative research and development--The increase of $100,000 will provide funds to support contracts related to the cause and prevention of dental caries.

Review and approval of grants--The increase of $65,000 will provide support for one additional position necessary in the management of the extramural programs.

Program direction--The decrease of $500 represents a loss of support in the Office of the Director in the area of program analysis and review.

Significant Items in House and Senate
Appropriation Committee Reports

Item	Action Taken or to be Taken
1969 House Report	
(1) Encourages the Institute to make more widely known its contributions to dental research and to the whole field of biomedical research. (Page 20)	(1) Information efforts directed at the public have been expanded. Greater use has been made, in particular, of radio and television media. One impact of this greater visibility has been a steady increase in the number of inquiries from the public.
(2) Recent research with hamsters shows that a certain enzyme can dissolve plaque and in doing so remove the harmful bacteria from the teeth. The bacteria and their acids are then washed away by saliva, preventing decay on the surfaces of the teeth. The Committee will be interested in the findings of clinical studies to be initiated in the near future. (Page 21)	(2) Several clinical studies are in progress on the use of the enzyme, dextranase, in the prevention and control of dental caries in humans. The preliminary results of these studies show considerable promise, but, further work is necessary before any conclusive findings can be established.
(3) The Committee feels that the reorganization of the HEW health functions presents an opportunity for developing a more rational arrangement of dental health activities by providing a single focus of leadership for dental research and education at NIH, on the one hand, and the integration of dental service programs with the comprehensive health care activities of the new Health Services and Mental Health Administration, on the other. The Committee will expect the HSMHA to develop clear leadership for both dental service research and general dental service programs. (Page 21)	(3) This matter is being discussed with officials and representatives concerned with dental health activities both inside and outside the Government and is currently under study.

Significant Items in House and Senate Appropriation Committee Reports

Item	Action Taken or to be Taken
1969 Senate Report	
(1) A task force which has been formed to identify promising leads for applied research is exploring the chemical control of bacterial agents responsible for tooth decay, dietary factors and the systemic or genetic susceptibility of individuals. Special attention is also being given to the development of improved oral-facial restorative materials and of new methods of extending the protection of fluoride in communities which do not have the benefit of fluoridated water supplies. (Page 44)	(1) The task force on dental caries has identified several promising avenues for the prevention and control of caries. One of the most promising relates to an enzyme, dextranase, which is now being tested in clinical studies. Another concerns the use of certain antibiotics to control the bacteria which are an essential part of the caries-producing process.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301--Research and Investigation, in general	Indefinite
Title IV, Part C--National Institute of Dental Research	Indefinite

PUBLIC HEALTH SERVICE ACT

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in section 301 of the Public Health Service Act.

The Public Health Service Act, Title IV, National Research Institutes, Part C, National Institute of Dental Research--

"Sec. 421. There is hereby established in the Public Health Service a National Institute of Dental Research (hereafter in this part referred to as the 'Institute').

"Sec. 422. In carrying out the purposes of section 301 with respect to dental diseases and conditions the Surgeon General, through the Institute and in cooperation with the National Advisory Dental Research Council (hereafter in this part referred to as the 'Council'), shall--

(a) conduct, assist and foster researches, investigations, experiments, and studies relating to the cause, prevention, and methods of diagnosis and treatment of dental diseases and conditions;

.....

(c) provide fellowships in the Institute from funds appropriated or donated for the purpose;

.....

(f) provide training and instruction and establish and maintain traineeships, in the Institute and elsewhere in matters relating to the diagnosis, prevention, and treatment of dental diseases and conditions with such stipends and allowances (including travel and subsistence expenses) for trainees as he may deem necessary, the number of persons receiving such training and instruction, and the number of persons holding such traineeships, to be fixed by the Council, and, in addition, provide for such training, instruction and traineeships through grants, upon recommendation of the Council, to public and other nonprofit institutions."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and Expenses, Office of the Director".....	-$286,000	.....	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH Management Fund.

National Institute of Dental Research

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$7,420,000	$9,725,000	$10,164,000	$10,019,000
1961	11,204,000	12,604,000	16,710,000	15,500,000
1962	13,933,000	14,681,000	20,000,000	17,340,000
1963	17,199,000	19,199,000	22,199,000	21,199,000
1964	19,809,000	19,689,000	19,809,000	19,689,000
1965	20,209,000	20,090,000	20,190,000	20,190,000
1966	22,177,000	22,177,000	23,677,000	23,677,000
1967	24,884,000	28,308,000	28,308,000	28,308,000
1968	30,307,000	30,307,000	32,307,000	30,307,000
1969	30,414,000	29,553,000	30,414,000	29,983,500
1970	30,062,000			

Justification

National Institute of Dental Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	301	$3,674,000	306	$3,739,000	+5	+$65,000
Other expenses	...	25,745,500	...	26,323,000	..	+577,500
Total	301	29,419,500	306	30,062,000	+5	+642,500

General Statement

The National Institute of Dental Research conducts and supports basic, clinical, and applied research and research training, in the causes, diagnosis, prevention, and cure of oral diseases and disorders: (1) conducts intramural laboratory, clinical and field research, (2) supports dental and medically-related research and research training by assisting individuals, universities, institutions, and agencies through grants-in-aid for research projects, training, fellowships, and dental research institutes, (3) conducts and supports collaborative and developmental research programs aimed at specific dental problems where major advance seems clearly possible, and (4) disseminates and supports dissemination of research findings and related information. The long-range objective of the Institute is improvement in the oral health of all individuals through the greater understanding of the biological phenomena underlying oral diseases and disorders, and the advancement of capability for the diagnosis, treatment, and prevention of oral disease.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research projects.....	$10,419,000	$10,502,000	+$83,000
Special programs.....	4,636,000	5,057,000	+421,000
Total research grants.....	15,055,000	15,559,000	+504,000

Introduction

A concerted effort is made by the four categorical program areas: (1) Dental Caries and Hard Tissues Program, (2) Periodontal Diseases and Soft Tissues Program, (3) Oral-Facial Growth and Development Program, and (4) Materials Science and Special Clinical Studies Program, to coordinate and in all ways possible support the research that is carried out in the grantee institutions outside NIH. All the categorical areas make use of the regular research grants program, the training grants program, the fellowships program, and collaborative (contract) mechanisms to advance the dental sciences in the nation's dental and medical institutions, universities, and hospitals.

Program plans for 1969 and 1970

Dental Caries and Hard Tissues Program

Evidence now available indicates that dental caries occur only when there is an interplay of host, dietary, and microbiotic factors. Laboratory, clinical, epidemiologic, and applied research on dental caries supported by NIDR can be identified in five specific areas of emphasis:

Host factors --	1. Resistant enamel
	2. Host immunity
Dietary Factors --	3. Cariogenic potential
Microbiologic factors --	4. Plaque control
	5. Antibiotic therapy

These fields of investigation will continue in the next year to strive for the ultimate prevention of caries through a better understanding of the identified contributing factors and the development of methods for interfering with their interplay.

Fluoride is the most significant factor in the development of the resistance of tooth structure to caries. Studies of methods for improving its uptake by enamel will continue. Emphasis will be placed on research directed toward a more precise understanding of the chemical and physical structure of the dental hard tissues, particularly with respect to dissolution by acids. Of importance also is the mechanism of mineralization and remineralization. Studies will be encouraged on host immunity factors and on the role of other elements in the resistance of tooth tissues to caries.

Many facets of the relationship of dietary factors, oral environment and dental caries are worthy of investigation. Of great significance is the influence of diet on the oral flora, and the production of destructive acids. Investigators are seeking a better understanding of the relationship of caries-producing organisms, specific sugars, plaque formation, and acid production. It is important, also, that studies be encouraged which will characterize the cariogenic potential of various foods, identify those with low cariogenic potential, and develop methods for counteracting those that are cariogenic.

A concerted effort is being made as an integral part of the Caries Task Force to capitalize on recent research associating dextran-producing streptococci with the production of smooth surface caries. Investigations will be continued to identify and classify these organisms and to determine their distribution in human populations. Because dextran is responsible for the adhesive properties of plaque, emphasis will be placed on research aimed at the identification of enzymes or agents which will dissolve it, or on methods of substituting dextrans which lack this adhesive property.

The observation that certain antibiotics can suppress the cariogenic flora has not been well exploited. Investigators will be encouraged to identify and test agents which are specific for cariogenic organisms but do not have undesirable side effects.

Evidence continues to accumulate that indicates that caries on smooth surfaces, cementum, and in pits and fissures may be distinct entities requiring differing sets of etiologic circumstances. Research will be encouraged which will delineate the specific etiological factor for each of these entities. Particular emphasis will be given to cemental caries because of its apparently increasing prevalence, frequent pulp involvement, and the difficulty in satisfactorily restoring this type of lesion.

Basic studies on mineralization in human and lower forms of life will continue with emphasis on the understanding of mechanisms and application to problems associated with healing and bone resorption in humans.

Attention also will be given to the need for stimulating research that will add to our understanding of other kinds of lesions affecting hard tooth structure. Prominent among these is root caries, a condition that affects the teeth of individuals who at middle age have suffered gum recession. Tooth abrasion, erosion and surface sensitivity also will be studied.

Periodontal Diseases and Soft Tissues Program

Periodontal diseases are among the most widespread and serious dental disorders existing in the American population today. These disorders are the chief cause of the loss of teeth after age 35. With the increasing life span of the average United States citizen these problems are continuing to grow. At the present time, well over 50 percent of Americans age 40 and over suffer in some degree from these insidious diseases. It is estimated that of this group more than 20 million are in dire need of periodontal therapy.

A number of interacting factors are suspect in the development of the disorders. The individual's general health as well as his diet, age, and oral hygiene determine the health of the periodontium.

Support has and will continue to encompass the concept that a knowledge of the normal structure and function of the periodontium is a base which is necessary for understanding how the disease process develops. Gross anatomy and histology of the periodontium has been well established. Any future programming activities should stress functional aspects in periodontal tissues. It is proposed that special attention be given to an assessment of normal biochemistry, structure, and metabolism of connective tissue (especially collagen); enzymology; the origin, function, and fate of bone cells; the physiology of blood vessels in the periodontium and the factors which regulate their function.

The ultimate goal of research on periodontal disease is to gain knowledge to suppress this prevalent health problem through therapeutic and preventive measures. Research to date has established a relationship between oral hygiene and periodontal disease and has implicated many causal factors. Future research support will stress those programs which are designed to clarify the precise role these factors play in the etiology of periodontal disease. An adequate

program of prophylaxis based upon these findings will necessarily depend on the exploration of new technologies and the conduct of increasingly complex and costly clinical and applied research.

The immunologic aspect of periodontal diseases is an area requiring a great deal of attention for the next several years. A modest increase of support for research in this area will provide some impetus to the ultimate goal of developing immunizing substances to suppress or destroy bacterial agents and bacterial products implicated in periodontal disease.

Oral Ulcerations

Oral ulcerations, which are among the most common and baffling of oral diseases, occur in over 50 percent of the American population and range in severity from an occasional sore to almost constant outbreaks of painful blisters. They include herpes simplex, aphthous stomatitis, erythema multiforme, and pemphigus, all of which have the common characteristics of recurring at intervals during a person's life. Several of these diseases are still of undetermined origin and treatment is given on an empirical basis. In order to determine their causes, knowledge from many specialties must be sought, and relationships established between systemic, psychological, and microbial factors.

Oral Neoplasms

It has been estimated that approximately 7,000 deaths occur annually in this country from oral cancer. A much larger number are severely incapacitated for life. The disease is most frequent in men past the age of 40 but can occur at any age. The psychological impact of oral cancer is very great because those who survive may have lost facial parts in surgery. The tragic toll of oral cancer makes imperative the search for means of early detection and improved diagnosis along with the development of adequate therapeutic measures.

Salivary Gland Disorders

The role of the salivary glands in regulating the oral environment is an important one. The normal integrity of tissue or organ surfaces, both hard and soft, is dependent on a protective flow of salivary fluids. In addition, the microbial ecology of the oral cavity is undoubtedly influenced by the quantity and nature of salivary secretions. When the glands fail to function properly, rampant caries may develop even in elderly people whose teeth previously were fairly free from decay. Research has been initiated and will continue to be supported to determine the causes, pathology, epidemiology, and treatment of specific diseases of the salivary glands, including inflammatory lesions, oral syndromes, and neoplasms, as well as conditions initiated by systemic diseases. Support will also be given to identify the structural and functional components of the glands, to clarify the biochemical events in the metabolism of proteins by salivary glands, and to define the role of the autonomic nervous system in the maintenance of normal structure and function.

Oral-Facial Growth and Development Program

The NIDR program in oral-facial growth and development seeks to improve health through a better understanding of the causative mechanisms of oral-facial malformations and by the determination of the most effective treatment procedures for individuals afflicted with such disfigurement. Through the use of consultants, workshops will be convened to assess the state of knowledge in growth and development relevant to oral-facial malformations. The dissemination of the results of these workshops should serve to stimulate research in the general area of dento-facial abnormalities.

Cleft Lip/Cleft Palate--Clinical Research

Research which will bring about improved rehabilitative procedures is necessary and will be continued. For example, emphasis will be placed on the development and evaluation of surgical repair methods. Techniques ranging from simple flap operations through autotransplants of bone and the insertion of implants, such as teflon, will continue to be developed and evaluated for their potential use in cleft palate cases. Studies also will be supported to develop appropriate diagnostic criteria that will enable the cleft palate team (e.g., plastic surgeon, orthodontist, speech pathologist) to choose the most effective treatment procedure for individual patients. Particular attention will be given to investigations designed to assess various surgical procedures, including evaluation of speech competency. Other studies will include the identification of diagnostic procedures for speech; the role of sensory and motor mechanisms in the pharyngeal, laryngeal and oral area; and factors concerned with the attainment of optimum growth and function of the dento-facial complex.

The support of psychosocial studies which will focus on the social adjustment of the cleft palate individual will also be continued.

Etiology of Cleft Lip/Cleft Palate

High program priority will continue to be given to studies of the etiology of congenital oral-facial malformations, emphasizing the respective roles of genetic and environmental factors. Also receiving attention will be studies of the mode of action of teratogenic drugs which cause cleft palate, particularly from the standpoint of interspecies variability.

Malocclusion

Malocclusion ranges from relatively insignificant deviations to severe and handicapping relationships of the teeth and jaws. Epidemiologic studies will be encouraged for assessing the prevalence and severity of the occlusal anomalies in populations in the United States. Other investigations concerning the normal growth and development patterns of the oral-facial region will be supported. Information from such studies is necessary for the early diagnosis of malocclusion. Projects aimed at evaluating interceptive procedures for the treatment of malocclusion will be continued in an effort to develop simpler and less costly orthodontic procedures.

Materials Science

Since the specialized tissues of the mouth cannot replace themselves when they are lost through disease or accident, various materials must be used for these purposes. The magnitude of the need for improved materials and methods of dental and oral-facial care is indicated by the realization that approximately 50 percent of American adults over 65 years of age have lost all of their natural dentition; that each year, 30,000 new patients sustain aesthetic and functional defects from cancer surgery that require artificial prostheses; and that, the number of congenital oral-facial defects is increasing.

The expanding population and the increasing demands for dental care are placing obligations upon the profession that cannot be met by increasing the number of dentists. It is clear that the success of programs to increase the useful life of materials and to lessen the time and skills required for their application, will expand the capacity of the profession and its auxiliaries more rapidly and more economically than any method other than the complete eradication of the diseases themselves. Therefore, the ultimate objective of the materials science and special clinical studies program is a practical one--to increase the availability of dental care through research and development of new and improved materials and more efficient methods of treatment.

Concerted efforts are being directed toward studies of both synthetic and natural adhesives and other materials which may be of value in the treatment of tooth and bone lesions. In these studies the talents of both physical scientists (engineers, chemists, metallurgists) and biologists are being utilized, and the capacities of industry as well as the facilities of universities are being called upon. As a result, broad studies of the physical and chemical properties of synthetic and biological materials are being carried out, and tests for acceptance of promising materials by tissues are being conducted. The search for new materials is always foremost. For example, it has recently come to light that adhesive secretions by barnacles, mussels, and other common sea animals might serve as an effective seal for dental restorations because they can actually bond to teeth. Studies of such materials are presently underway, and it is hoped that the stage of clinical testing may soon be reached.

In the field of preventive dentistry encouraging results are being obtained in human studies with synthetic adhesives. By application to pits and fissures on the biting surfaces of teeth, it is hoped that such localized areas of high caries susceptibility may be protected. Clinical studies, to date, indicate that certain of these agents provide a high degree of protection for as long as seven months. Continued support of these studies may lead to the development of practical prophylactic measures that may have a strong impact in reducing the number of teeth lost through decay.

Another area of promising effort involves studies on the development of biologically acceptable implants to replace lost or missing teeth. Continuing studies over the past seven years show that plastic implants have been uniquely successful in being maintained in the jaws of subhuman primates in the same functional capacity as are natural teeth. Clinical trials with human subjects will be conducted as soon as the physical and toxicological properties of the plastic implants are determined.

In addition to work on the development of adhesive dental restorative materials and suitable prostheses, an important need is the broader application of biomedical engineering research to improve methods of diagnosis of incipient dental diseases, specifically using advances in telemetry and measurement.

Dental Research Institutes (Centers)

The national purpose of the newly established dental research institute grant support program is to create centers of excellence in the sciences related to oral health. The program is designed to develop broad, interdisciplinary, university-based complexes serving national as well as regional purposes. The program seeks to attract to the dental environment and to the solution of oral health problems the knowledge and skills of personnel in disciplines not heretofore intimately involved in dental research.

Since the dental research institute program represents a unique concept of grant support, specific guidelines have been tailored to its specific requirements. Assessment thus far, has been in terms of attainment of interim objectives, and the orderly development of centers which build on and extend existing institutional research strengths, facilitate the cooperation of a broad range of biological, physical, and social sciences in the study of problems of common interest, and interact with the educational programs of the parent universities.

Although sufficient time has not yet elapsed to expect attainment of all primary objectives, there is encouraging evidence of substantive progress.

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting continuations....	200	$7,718,000	202	$7,801,000	+2	+$83,000
2. Competing projects.	68	2,501,000	68	2,501,000	..	.....
3. Supplementals.....	(15)	200,000	(15)	200,000	..	.....
4. Subtotal regular program.....	268	10,419,000	270	10,502,000	+2	+83,000
5. General research support.....		1,194,000		1,215,000		+21,000
6. Scientific evaluation.....		42,000		42,000		.....
7. Categorical clinical research centers.		400,000		400,000		.....
8. Dental research institutes.....		3,000,000		3,400,000		+400,000
9. Total research grants.....	268	15,055,000	270	15,559,000	+2	+504,000

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Dental caries and hard tissue studies.....	$3,850,000	$3,868,000	+$18,000
Periodontal diseases and soft tissue studies.....	2,752,000	2,786,000	+34,000
Oral neoplasia.....	136,000	138,000	+2,000
Normal and abnormal growth and development including congenital (genetic) and acquired diseases and anomalies.....	2,473,000	2,491,000	+18,000
Materials science.....	1,208,000	1,219,000	+11,000
Subtotal regular program..	10,419,000	10,502,000	+83,000
General research support grants.....	1,194,000	1,215,000	+21,000
Scientific evaluation and planning.....	42,000	42,000	.....
Categorical clinical research centers.....	400,000	400,000	.....
Dental research institutes..	3,000,000	3,400,000	+400,000
Total research grants.....	15,055,000	15,559,000	+504,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Fellowships.....	$1,765,000	$1,694,000	**-$71,000**

Program plans for 1969 and 1970

Predoctoral and postdoctoral fellowships are designed to support the research training of prospective investigators urgently required in science and dental academic institutions in order to advance knowledge that will contribute to the solution of oral health problems.

Funds requested for 1970 will provide for 113 awards, compared to 121 in 1969, a decrease of 8. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	78	$1,219,000	82	$1,312,000	+4	+$93,000
b. Competing.....	6	125,000	2	35,000	-4	-90,000
2. Supplementals.....	(10)	10,000	(7)	9,000	(-3)	-1,000
3. New awards.....	37	411,000	29	338,000	-8	-73,000
4. Total fellowships.....	121	1,765,000	113	1,694,000	-8	-71,000

Fellowships (By type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Predoctoral.....	17	$90,000	17	$90,000	..	.....
2. Postdoctoral.....	35	358,000	33	346,000	-2	-$12,000
3. Special.....	28	406,000	26	405,000	-2	-1,000
4. Development awards.....	37	792,000	33	734,000	-4	-58,000
5. Career awards.....	4	119,000	4	119,000	..	.....
6. Total fellowships.....	121	1,765,000	113	1,694,000	-8	-71,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total training grants.....	$5,609,000	$5,390,000	-$219,000

Program plans for 1969 and 1970

The continued expansion of existing dental schools and the creation of several new dental schools have intensified the search for competent dental research and teaching manpower. Current training grants must supply the greatest share of these young investigator trainees.

Funds requested for 1970 will provide for 91 awards, compared to 98 in 1969, a decrease of 7. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	83	$4,433,000	75	$4,000,000	-8	-$433,000
b. Competing.....	9	450,000	10	712,000	+1	+262,000
2. Supplementals.....	(12)	329,000	(13)	277,000	(+1)	-52,000
3. New grants.....	6	357,000	6	361,000	..	+4,000
4. Scientific evaluation.....	(1)	40,000	(1)	40,000	..	.....
5. Total training grants..	98	5,609,000	91	5,390,000	-7	-219,000

Training Grants (By Type of Program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Graduate training grants:						
1. Basic sciences.....	82	$4,454,000	77	$4,304,000	-5	-$150,000
2. Clinical sciences.....	16	1,115,000	14	1,046,000	-2	-69,000
3. Scientific evaluation..	(1)	40,000	(1)	40,000	..	.....
4. Total training grants..	98	5,609,000	91	5,390,000	-7	-219,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	217	$2,622,000	221	$2,673,000	+4	+$51,000
Other expenses	...	2,065,000	...	2,274,000	..	+209,000
Total	217	4,687,000	221	4,947,000	+4	+260,000

Introduction

The research mission and public health goal of the intramural program continues to be that of ascertainment of new and relevant information regarding the cause of a variety of oro-facial malfunctions, including dental caries, periodontal disease, oral cancer and abnormal oro-facial development. Clearly, successes in this quest would be manifested ultimately as new and efficacious approaches to the alleviation of disease.

Development of each of the abnormal states listed above is most certainly attributable to multiple factors, about which all too little is presently known. As a consequence, the Institute's continuing systematic approach to these problems involves the tripartite commitment of its resources to relevant basic laboratory investigations; to clinical and applied investigations relating to the solution of specific questions which may be formulated as a consequence of progress made at the basic level; and to field studies directed either toward clinical trials of newer therapeutic or preventive concepts, which have evolved from basic and applied studies, or those directed toward further definition of the nature and distribution of oro-facial disease on an epidemiologica or geographic basis.

With specific regard to dental caries, the Institute's intramural policy of a tripartite research approach has, over the past 20 years, led to the acquisition of a substantial body of knowledge concerning the etiology and pathogenesis of the disease. Largely on the basis of this accumulated information, it was determined that a more directed or applied effort toward the eradication of caries as a public health problem could now be undertaken. Consequently, during the past year this Institute established a Caries Task Force involving all relevant scientific capacities within the total Institute. This task force has high priority in the utilization of intramural manpower and resources so as to significantly expand our work in the caries area.

Program plans for 1969 and 1970

Intramural Contribution to NIDR's Caries Task Force

It will be recalled that, largely through the impetus of research from this Institute, community fluoridation of public water supplies now provides the single most effective public health approach to the reduction of dental decay. While in theory fluoridation would appear to be a most efficacious and economical approach to control of dental caries at the public health level, the reality is that nearly 60 percent of the population of this country is not regularly exposed to this preventive measure. Moreover, it should be recognized that the acquisition of fluoride ion by tooth enamel consequent to exposure to fluoridated drinking water, though significantly increasing the intrinsic resistance of the tooth to decay, does little if anything to affect the immediate causative agents of decay, i.e., the oral microflora.

Consequently, the expanded intramural effort in dental caries, now an integral aspect of the Institute's Caries Task Force, is focused upon the attainment of a more thorough understanding of oral bacteria, specifically, those strains of oral streptococci which appear to be integrally involved in the etiology of caries. These organisms are characterized by their ability to adhere tenaciously to the enamel surface, as a component of dental plaque; by preferential utilization of dietary sucrose for their growth and metabolism; and most significantly, by their propensity for producing large amounts of acid as a consequence of sucrose metabolism. It is the latter property, coupled with the close environment relationship to the tooth surface, which presumably render these organisms highly cariogenic. Their cariogenicity has been amply demonstrated in animal experiments. Indeed, organisms of similar properties have been isolated from human mouths.

Recognizing that specific organisms may be the key to the control of dental caries, this Institute's research is now being focused on areas which will serve to define more precisely their absolute role in the caries process; to determine the efficacy of local treatment by antibiotic or by related bactericidal agents; and to test new biological approaches aimed at altering the metabolism of the organisms so as to render them harmless. With regard to the latter approach, Institute scientists are much involved in experiments relating to the possible efficacy of a specific enzyme, dextranase, whose chief effect would be that of preventing the adherence of streptococci to the tooth surface, thereby breaking the vicious circle of events which seems so essential to their role in the genesis of decay.

Finally, and also in concert with the Caries Task Force approach, field trials will be continued to achieve even more effective methods of extending the benefits of fluoride to a wider share of the population, particularly to children. Topical application of fluoride in fitted vinyl mouthpieces, undertaken in the school environment with appropriate professional supervision, has already been shown to exert striking benefits to children of primary school age in areas where water fluoridation is not practiced. These long-term studies are being further expanded to determine whether the benefits of topical application in mouthpieces augment those already extant in areas where community water supplies are fluoridated. Another program of considerable promise relates to an assessment of the long-term benefits which the topical mouthpiece method may provide to pre-school children who have not yet developed their adult dentition.

Periodontal Disease

With the growing concern regarding the role of dental plaque in the etiology of dental caries has developed an increasingly attractive hypothesis that similar adherent masses of bacteria, food debris and gummy materials which comprise the plaque may, over a period of some years, be instrumental in initiating gingival inflammation, and ultimately, frank periodontitis. Research results have already indicated quite clearly that the organism or organisms involved in periodontal disease do not resemble the streptococci which are now being scrutinized with respect to caries. On the other hand, a specific filamentous microorganism has previously been isolated from human diseased gums, and has been shown in experimental animals to elicit a disease state closely resembling periodontal disease. This filamentous organism, Odontomyces viscosus, shares with cariogenic streptococci their capacity for producing large amounts of gummy extracellular material which, as in the case of the streptococci, also tends to hold the organisms in close approximation to the tooth surface at and below gingival margin. Thus, while research continues with respect to the basic characteristics of this organism, increased emphasis is being given to the possibility that its occurrence and its deleterious effects may be facilitated and/or enhanced by pre-existing dental plaque containing cariogenic streptococci. These two aspects of the Institute's research effort, both bearing on dental plaque as the common denominator in caries and periodontal disease, are being carried on in close and effective collaboration.

Basic and clinical studies with respect to the biology of the gums and adjacent tissues continue to provide information which may ultimately contribute to preventive and therapeutic approaches to periodontal disease from the point of view of increasing host resistance to the infectious process. Major support will be given to the ongoing effort to define the nature of those factors, particularly intrinsic enzymes, involved in normal synthesis and breakdown of the major structural proteins of the gums, namely collagen and elastin. These functions are seriously disturbed in periodontal disease.

Oral Cancer

Exploration of the unique properties of the oral mucous membrane appears essential to any ultimate understanding of the relationship between leukoplakia ("white spot") and malignant change. As a consequence, these studies will be continued and expanded with such deliberate speed as funds and manpower will permit.

Growth and Development

Disorders of normal oro-facial growth are manifested as a spectrum of malfunction, ranging from the serious cleft palate to relatively harmless, if aesthetically dissatisfying malocclusions. Significant energy is being devoted to the goal of providing a more rational understanding of the genesis of these conditions. Particular emphasis continues in the area of induced developmental abnormalities of the face and jaws arising from experimental introduction of drugs and other substances into the pregnant animal mother. During 1968 these studies have been extended to non-human primate species, in order to obviate doubts which have arisen as to the applicability of results derived from studies of lower animal forms to man. Of great interest has been the recent demonstration by Institute scientists of drug-induced cleft palate in the baboon. This work will be pursued during 1969.

The increase of $260,000 includes a program increase of $210,000 to support four additional positions for research on dental caries and other related areas defined by the Caries Task Force, $5,000 for annualization of pay increases, and $45,000 for centrally furnished services from the National Institutes of Health management fund.

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	4	$64,000	4	$64,000	..	.....
Other expenses	..	781,000	..	878,000	..	+$97,000
Total	4	845,000	4	942,000	..	+97,000

Program Plans in 1969 and 1970

During 1969 and 1970 program plans will be directed primarily toward the development of adhesive restorative dental materials. This will be accomplished through continued collaboration with other Federal agencies, university research centers and industrial research organizations. Once such a material is available, it will have a far-reaching effect in reducing time and cost related to the treatment of dental caries. Among the various approaches employed in this organized research effort is the study of adhesive properties of barnacle cement, including its structural and chemical characterization, and its synthetic preparation.

High priority is also being given to quick follow-up of promising leads resulting from laboratory and clinical research. For example, laboratory research has demonstrated a highly significant reduction in animal dental caries through the use of the enzyme, dextranase. The efficacy of this enzyme in the prevention and control of dental caries in humans is now being investigated as an integral part of the Caries Task Force.

The net increase of $97,000 reflects $100,000 for program increases related to dental caries and is offset by a decrease of $3,000 for centrally furnished services from the National Institutes of Health management fund.

Biometry, Epidemiology and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	22	$292,000	22	$292,000	..	.....
Other expenses	..	139,000	..	144,000	..	+$5,000
Total	22	431,000	22	436,000	..	+5,000

Program plans for 1969 and 1970

This activity supports the Institute's scientific staff in the design and subsequent analysis of a wide variety of complex experimental investigations, ranging from basic to clinical. Of particular importance is the role of the Institute's biometric arm in the formulation and analysis of field investigations relating both to factors affecting the prevalence of oral disease in the population at large, as well as to the effectiveness of new or improved means, agents, or techniques of diagnosis and/or control of oral disease, as they may be tested on large population groups.

In concert with the Institute's ongoing Caries Task Force effort, program emphasis during the coming year will focus on expanded clinical trials regarding the caries preventive potential of the enzyme, dextranase. Similarly, large scale field studies of children and adults will be implemented with respect to the prevalence of human infection by cariogenic bacteria of the oral streptococcal type. Particular emphasis is to be placed on determining whether a direct correlation can be established between the extent of dental decay and the degree of streptococcal infection.

Continuing efforts will also be made to expand the Institute's current capacity for automated data processing, a now-so-essential tool in the design and analysis of population studies.

The increase of $5,000 is for centrally furnished services from the National Institutes of Health management fund.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	35	$409,000	36	$423,000	+1	+$14,000
Other expenses	..	280,000	..	340,000	..	+60,000
Total	35	689,000	36	763,000	+1	+74,000

This activity provides support for the administration of the Institute's grants programs which include research grants, fellowships, and training grants. The National Advisory Dental Research Council, and staff are responsible for the planning, development, review, and evaluation of the various extramural programs of the Institute. Continuous surveillance of scientific activities and progress is maintained as well as recording and reporting of fiscal and scientific data relevant to all transactions.

Reorganization in 1967 of the extramural programs area along categorical program lines has given this area a significantly increased role in the Institute's total mission during 1968. Particular thought is currently being given to ways and means of expanding the activities which will lead to better determination of the relevance of research work to the immediate goals of the Dental Institute.

The additional position requested would be used to coordinate the state-of-the-art programs carried out in each categorical area. This position is necessary to consolidate findings and recommendations of Institute personnel as well as advisory panels, which provide valuable direction to such organized efforts as the Caries Task Force and work in adhesive restorative materials.

The increase of $74,000 includes one position and $65,000 for program increases and $9,000 for centrally furnished services from the National Institutes of Health management fund.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	23	$287,000	23	$287,000	..	.....
Other expenses	..	51,500	..	44,000	..	-$7,500
Total	23	338,500	23	331,000	..	-7,500

This activity provides support for the Institute Director and his immediate staff who are responsible for the administration and coordination of the varied programs of the Institute. The Institute Director and his immediate staff are responsible for keeping abreast of new developments in the field of dental research in this country as well as elsewhere, and for providing leadership to promising new approaches in scientific investigations.

The decrease of $7,500 includes $500 in the program area and $7,000 in the National Institutes of Health management fund for centrally furnished services.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Laboratory and clinical research			
(2) Chemists	GS-9		$20,308
(2) Dental directors	C.O.		35,134
		(4)	55,442
Review and approval of grants			
Scientist administrator	GS-13		14,409
		(1)	14,409
Total new positions, all activities		(5)	69,851

National Institute of Arthritis and Metabolic Diseases

WITNESSES

DR. G. DONALD WHEDON, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
W. GILBERT BAYLIS, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
DONALD F. CYPHERS, BUDGET OFFICER, NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION

[In thousands of dollars]

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	6,863	7,049	7,216
Positions other than permanent	258	259	266
Other personnel compensation	34	36	36
Total personnel compensation	7,155	7,344	7,518
Personnel benefits: Civilian employees	727	698	714
Travel and transportation of persons	227	249	260
Transportation of things	64	70	74
Rent, communications, and utilities	179	193	195
Printing and reproduction	136	160	160
Other services	11,937	14,623	14,361
Supplies and materials	1,257	1,496	1,580
Equipment	1,074	880	880
Grants, subsidies, and contributions	116,160	114,537	114,244
Subtotal	138,916	140,250	139,986
Quarters and subsistence charges	−18	−18	−18
Total obligations	138,898	140,232	139,968

PERSONNEL SUMMARY

Total number of permanent positions	697	630	647
Full-time equivalent of other positions	36	36	38
Average number of all employees	651	612	623
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING [IN THOUSANDS OF DOLLARS]

Program by activities:			
1. Grants:			
(a) Research	94,203	91,691	92,289
(b) Fellowships	6,574	6,737	6,475
(c) Training	15,383	16,109	15,480
Total grants	116,160	114,537	114,244
2. Direct operations:			
(a) Laboratory and clinical research	13,774	15,891	15,664
(b) Collaborative research and development	4,439	6,498	6,670
(c) Biometry, epidemiology, and field studies	554	706	712
(d) Review and approval of grants	2,101	2,279	2,373
(e) Program direction	253	321	305
Total direct operations	21,121	25,695	25,724
Total program costs, funded [1]	137,281	----------	----------
Change in selected resources [2]	1,617	----------	----------
Total obligations	138,898	140,232	139,968
Financing:			
Comparative transfer to other accounts	423	486	----------
Unobligated balance lapsing	4,633	3,170	----------
Budget authority (appropriation)	143,954	143,888	139,968
Relation of obligations to outlays:			
Obligations incurred, net	139,321	140,718	139,968
Obligated balance, start of year	77,807	72,609	91,608
Obligated balance, end of year	−72,609	−91,608	−97,877
Adjustments in expired accounts	−2,950	----------	----------
Outlays	141,569	121,719	133,699

[1] Includes capital outlay as follows: 1968, $782,000; 1969, $880,000; 1970, $980,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $5,619,000; 1968, $7,236,000; 1969, $7,236,000; 1970, $7,236,000.

Mr. FLOOD. Next is the National Institute of Arthritis and Metabolic Diseases.

We have Dr. G. Donald Whedon, the Director before us.

Doctor, you have been around here how long now?

Dr. WHEDON. This will be my seventh appearance.

Mr. FLOOD. You are no beginner.

Do you have any new people on board with you?

Dr. WHEDON. We have a new budget officer, Mr. Cyphers.

Mr. FLOOD. I think you have a statement, Dr. Whedon? How do you want to proceed?

Dr. WHEDON. I shall be glad to proceed to read my statement, sir, and accept any questions during the statement or at the end, as you wish.

Mr. FLOOD. All right. We will place your biographical sketch in the record, and you may proceed.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name: Dr. G. Donald Whedon.

Position: Director, National Institute of Arthritis and Metabolic Diseases (NIAMD).

Birthplace and date: Geneva, New York, July 4, 1915.

Education: A.B., 1936, Hobart College; M.D., 1941, University of Rochester School of Medicine; Sc. D. (honorary), 1967, Hobart College.

Experience: Director, NIAMD, 1962–present; Assistant Director, NIAMD, 1956–1962; Chief, Metabolic Diseases Branch, NIAMD, NIH, 1952–1965; physician, outpatient department, New York Hospital, 1947–1952; assistant physician, outpatient department, New York Hospital, 1944–1947; assistant professor of medicine, Cornell University Medical College, 1950–1952; instructor of medicine, Cornell University Medical College, 1944–1950; assistant in medicine, university of Rochester School of Medicine, and assistant resident physician in medicine, Strong Memorial Hospital, 1942–1944; interne in medicine, Mary Imogene Bassett Hospital, Cooperstown, N.Y., 1941–1942.

Association memberships: Association of American Physicians; the Endocrine Society (postgraduate committee, 1962–1965); American Rheumatism Association; American Diabetes Association; American Federation for Clinical Research; New York Academy of Sciences; American Association for the Advancement of Science; American Medical Association; American Physiological Society; The Gerontological Society; American Institute of Nutrition; Pan American Medical Association; American Gastroenterological Association.

Special awards, citations, or publications: Certified, American Board of Internal Medicine, 1950; American Board of Nutrition, 1968; assisted DGMS in organizing program of multicategorical clinical research centers in leading American medical institutions, 1959–1961; Subcommittee on Calcium, Committee on Dietary Allowances, Food and Nutrition Board, National Research Council, 1959–1964; Editorial Board, Journal of Clinical Endocrinology and Metabolism, 1960–67; Editorial Board, Calcified Tissue Research, 1967 to present; consultant to Space Medicine Division, Office of Manned Space Flight, NASA, November 1963 to present; Scientific Council of the Maryland Academy of Sciences, March 1965 to present; principal investigator of calcium-nitrogen metabolic balance study on NASA Gemini–VII space flight, December, 1965.

Dr. Whedon is the author of over 50 scientific papers on metabolic and physiologic studies of convalescence, immobilization, paralytic poliomyelitis, diseases of bone particularly including osteoporosis, human energy metabolism, and space medicine.

General Statement

Dr. Whedon. Mr. Chairman and Members of the Committee:

I greatly appreciate this occasion to report on progress by the National Institute of Arthritis and Metabolic Diseases, and to assess briefly our programs and their needs for the fiscal year 1970. As always, I welcome this opportunity to appear before this committee, which has played a vital role in stimulating and supporting biomedical research. I would like to mention some of the research and program highlights of the past year in the areas for which this Institute bears responsibility. These areas include, among others, arthritis and connective tissue diseases, diabetes and other metabolic disorders, diseases of the gastrointestinal tract, and diseases of the blood, bone, liver, kidney and skin. In order to present a broader description, than is possible in this brief presentation, of the background as well as progress and directions of our research, we have prepared detailed Special Reports in a number of major fields.

ARTHRITIS

Experimental evidence continues to suggest that an obscure infectious process may be involved in the causation of rheumatoid arthritis, a chronic, inflammatory connective tissue disease that ranks high among serious health problems. In previous testimony before this committee I had reported that investigators have produced arthritis in monkeys by injecting them with Bedsonia viruses isolated from human patients with Reiter's syndrome, a disease related to rheumatoid arthritis. New studies have shown that Bedsonia viruses infecting the rabbit eye will disseminate to joint tissues, liver, kidney, and spleen, in a manner suggestive of major organ involvement in human rheumatoid arthritis.

Heavy institute research emphasis is also placed on improving therapy of all the various forms of arthritis. A new steroid drug, triamcinolone hexacetonide, has been found to combine the important features of rapid and prolonged action with minimal side effects on long-term repeated use. The response to injections of the drug in 58 patients with rheumatoid arthritis and in eight patients with osteoarthritis was judged excellent. Relief generally lasted for long periods, and side effects from use of the drug appeared to be minimal.

DIABETES

Recent and promising experimental findings in diabetes have evolved from both the laboratory and the clinic. Basic laboratory research has revealed the presence of a heretofore unknown precursor form of insulin, termed "proinsulin," in the human pancreas. This substance has been found to have very little biological insulin activity, and indications are that it may function primarily as a necessary intermediate in the proper assemblage of the active insulin molecule. It is believed that a partial or complete failure of proinsulin conversion to biologically active insulin may account for some form of diabetes.

Concomitantly, insulin has been shown to exist in two distinct forms in man: "little insulin," which is indistinguishable from the hormone produced by the pancreas, and "big insulin," which is a larger molecule and comprises up to 50 percent of the insulin in the circulation. The physiology of insulin secretion is being reexamined in light of these new findings, with emphasis on determining the biological activity of big insulin, its precise relationship to little insulin, and its relationship, if any, to proinsulin.

Clinical studies, meanwhile, have shown that a new oral antidiabetic drug, glycodiazine, significantly reduced elevated blood sugar levels in patients with maturity-onset diabetes and maintained blood sugar concentrations at safe levels as long as the drug was administered. There were no untoward side effects associated with the drug's use and long-term clinical trials are currently underway to evaluate further the safety of this promising new oral antidiabetic agent.

CYSTIC FIBROSIS AND OTHER METABOLIC DISEASES

Significant clinical and fundamental information has been learned this past year about cystic fibrosis, a grave, generalized metabolic disorder of children and young adults. Using special staining techniques to study cultured skin fibroblast cells, a newly discovered difference in staining of such cells has been found between normal persons, patients with cystic fibrosis, and symptom-free carriers of the genetic trait for the disorder. Besides providing a reliable method to identify carriers, the procedure may permit study of the molecular basis for this disease. In the meantime, it has been shown that adult males with cystic fibrosis are infertile, apparently due to the anatomical lack of the vas deferens, the duct which transports spermatozoa from the testes. It thus appears unlikely that the adult male with cysic fibrosis can reproduce, a fact which should be taken into consideration in genetic counseling.

Another new laboratory technique has provided a means to identify children with certain hereditary metabolic disorders prior to birth. The procedure involves studying the activity of an enzyme involved in uric acid metabolism which can be detected in cell cultures grown from cells isolated from the amniotic fluid in which the growing fetus is immersed in utero. Using this method, an as-yet unborn female child has been identified as a symptom-free carrier of the trait for Lesch-Nyhan disease, a tragic disorder marked by brain damage, excessive production of uric acid, and an early death. This new technique of culturing fetal amniotic cells and testing them for suspected biochemical defects (when parents are known carriers of a metabolic disease) should permit the identification of fetuses afflicted with the disease before birth and should lead to more effective genetic counseling in the management of many metabolic disorders.

KIDNEY DISEASE AND TRANSPLANTATION STUDIES

Progress in developing a new compact, highly efficient and disposable artificial kidney has been made under a contract from the Institute's artificial kidney program. The capillary kidney, so-called because it simulates the human kidney's network of blood capillaries, consists of approximately 11,000 hollow, hair-size cellulose fibers packed into a compact case about the size of a large flashlight. This new dialyzer requires no blood pump and requires very little blood to prime it, thus eliminating the need for compensatory blood transfusions (and their attendant hazard of hepatitis). It comes presterilized, ready-to-use, and may be reused several times. Scores of patients with chronic kidney disease have now been maintained for periods of several months using only the capillary kidney. In the meantime, research continues on new special low protein diets for use in chronic kidney failure.

One such study has demonstrated that a 20 gram low-protein diet limited largely to essential amino acids, but unlimited in carbohydrates and fats, can delay the onset of symptoms of uremia and can serve as a temporary life-supporting measure while the patient is considered for either artificial kidney treatment or transplantation. In the latter field, a method has been devised for preserving excised human kidneys as long as 17 hours prior to final transplantation into a patient by using a

transportable organ preservation machine. Other workers have successfully transplanted, for the first time, a thymus gland into a male infant born without this gland, which is believed to be involved in the body's normal antigenantibody reactions and lymphocyte production. The child is now growing normally and is no longer suffering from unusual infections.

GASTROENTEROLOGY AND NUTRITION

The Institute continues its progress in studies relating to gastrointestinal disorders. In recent years I have mentioned to this committee that the stomach hormone gastrin, which stimulates secretion of gastric juices, has been isolated and synthesized. Gastrin has now been shown to reside within particular cells of antral pyloric glands, a finding which should further stimulate research in the peptic ulcer field.

Nutrition research, one of the oldest programs of the Institute, continues to provide strikingly important accomplishments. The major biologically active form of vitamin D has been isolated in pure form. Preliminary tests of its ability to prevent or cure rickets in animals have shown it to be markedly more effective than vitamin D itself, suggesting that the newly discovered active form may be superior to the conventional vitamin in the treatment of rickets and, particularly, in the treatment of conditions heretofore labeled as "vitamin D-resistant."

HEMATOLOGY

Anemias of various types, and clotting disorders such as hemophilia are but a few of the multitude of diseases known to affect the blood and blood forming elements. Aplastic anemia is a grave, and eventually fatal, blood disorder in which the blood marrow fails to produce adequate amounts of essential cellular blood elements. Preliminary trials of oxymetholone, a synthetic derivative of the male hormone testosterone, have now indicated that it has value in treating children with aplastic anemia who do not respond satisfactorily to conventional drug therapy. A new type of usually fatal aplastic anemia following infectious hepatitis has been described. Sixteen cases of the syndrome have been reported last year by a group of grantee investigators. Their studies suggest that the syndrome may result from hepatitis virus-induced chromosomal damage to the bone marrow.

BASIC RESEARCH

Accomplishments in basic research were highlighted this past year by the awarding of a Nobel Prize to Dr. Marshall W. Nirenberg, now of the National Heart Institute but who had reported his celebrated partial cracking of the genetic code while a scientist in this Institute. Institute research in molecular biology is continuing, and several of our investigators are currently collaborating with Dr. Nirenberg in studies of genetic code patterns and of some of the basic control mechanisms in the heredity of living cells.

I will cite merely two of many examples where "basic" research carried out in this Institute has resulted in important new therapeutic applications in clinical medicine. A fundamental development in lab-

oratory synthesis of new custom-made RNA compounds has now permitted their use to induce the production of interferon, the body's natural virus-fighting substance. In other experiments, this interferon stimulation brought about cure, in rabbits, of herpes simplex keratoconjunctivitis, an often fatal viral infection. In another instance, an Institute scientist's synthesis of several precursor forms of a new drug, cytosine arabinoside, made possible use of the drug by other scientists in one type of leukemia where it produced complete remissions in almost half of 40 patients.

SCIENTIFIC COMMUNICATION AND PUBLIC INFORMATION

The past year has also been a particularly productive and rewarding one in the communication of new research ideas and knowledge to our diverse publics. The Institute sponsored or organized many research conferences, notably among these a meeting which brought together a select, international group of experts in the field of bone disease research. Another current-awareness journal, Endocrinology Index, has been developed. This is the latest in a series of well-received specialized, unique periodicals established by the Institute which aim to alert researcher and practitioner alike to the latest research findings from throughout the world.

I am looking forward to another year in which we shall continue the Institute's sound and productive pursuits in health research, and in the support of training of scientists for research.

Mr. Chairman, I am submitting a request for $139,968,000 for 1970, a decrease of $264,000 compared to the 1969 operating level of $140,232,000.

Thank you. I shall be happy to answer any questions.

CYSTIC FIBROSIS RESEARCH

Mr. FLOOD. As you know, this committee has had considerable interest in cystic fibrosis research. Last year we earmarked $2 million for this. What progress are you making?

Dr. WHEDON. Mr. Chairman, I am happy to report to you and to this committee that we have followed, I believe, very carefully the directive of the committee that we intensify our research efforts in this field, and we anticipate that by the end of the fiscal year we will have a program of approximately $2½ million in support of research grant projects in cystic fibrosis.

LIVER TRANSPLANT

Mr. FLOOD. We talked a little last year about liver transplants.

Dr. WHEDON. Yes, sir.

Mr. FLOOD. Do you have anything new to report to us this year on that?

Dr. WHEDON. Yes, sir; I do.

The technique of liver transplantation was begun in July 1966. When I reported to you last year I believe I told you of the results with about five children. The total now, I am informed, is 14 children, four of whom have survived longer than 1 year and three of the four

are still surviving. Two are surviving at 10 and 11 months after transplantation.

What this program is showing is that the transplantation of the liver is basically feasible from a technical point of view at least in very young children. Of course, we still have with this organ as we do with all of the organs the basic problem of tissue immunology, tissue rejection.

KIDNEY TRANSPLANTS

I think what we have learned in the past year, however, particularly in the field of kidney transplantation, is that there are some signs and signals that the body provides which hopefully will be very useful in giving an earlier clue to when a rejection phenomenon will take place; then therapy against rejection can be stepped up.

Mr. FLOOD. I was going to ask you the same question about the kidney transplant.

That is a significant thing, is it not?

Dr. WHEDON. Of course. Kidney transplantation now has progressed to the point where there have been close to 2,000 kidney transplants.

ARTIFICIAL KIDNEY

Mr. FLOOD. What progress have we made with respect to developing a better artificial kidney, especially from the standpoint of size and cost? Is there anything new in that?

Dr. WHEDON. Yes. There are really two developments in that subject.

I think I mentioned one very briefly last year because it was so new just at that time. That is a reduction in size of one type of kidney called the Kiil, named after the man who invented it, in such a way that it takes up much less space and requires a much smaller priming volume of blood. That, of course, is the key development as I hinted briefly in my opening statement. With a reduced amount of blood for priming the instrument, one gets around the need for blood transfusions and thereby avoids the threat of hepatitis which has been such a serious problem.

What I particularly wanted to tell you, Mr. Chairman, with regard to developments during the past year, was the so-called capillary kidney.

This artificial kidney is a quite different design. It is relatively small in shape, as I said, the size of a large flashlight, and consists of several thousand very fine hairlike tubes through which the blood from the patient is passed and around which the wash fluid is passed. This in some ways is a closer simulation of the way the normal human kidney works than the board or coil type kidneys we have been using. This capillary kidney now has been used in two different dialysis centers. Both happen to be on the west coast, and more than 1,000 dialyses have been taken place indicating that this new kidney is effective. The advantages from the point of view of cost are that the capillary kidney can be supplied ready to use, presterilized, and that it can be used several times, seven, eight, or nine times, and then it can be thrown away.

Mr. FLOOD. We have been using these machines of different kinds for several years. Have any problems developed with regard to the health of those who have been treated over a period of years?

Dr. WHEDON. Yes, there have been some rather significant problems which have occurred in conjunction with this treatment and we are not sure whether it is due to the treatment itself or whether it is a relatively natural concomitant to chronic kidney disease. The reason we do not know this is that patients were not kept alive as long as we are able to do now with the artificial kidney.

The principal problems which occur are three in number. There is a peripheral neuropathy; some damage occurs to the nerves, particularly in the legs and arms. There is also anemia which gradually develops, and of particular interest to me, there is a condition known as calcium dystrophy.

May I explain that by indicating that these patients tend to get a thinning of their bones very much like the condition called osteoporosis, and at the same time they tend to get some calcification of their soft tissues. With respect to this latter problem we organized a conference which was held in November of 1968 to examine very closely this problem of calcium dystrophy, and we had present at this 3-day conference, not only experts in artificial kidney treatment, but also people in the field of mineral metabolism who had not been involved in kidney treatment at all, but simply had a tremendous fund of experience in the processes of bone metabolism and calcification.

DIABETES AND ARTHRITIS

Mr. FLOOD. There are two important diseases that you are working on, diabetes and arthritis, regarding which we have been a little disappointed in the advances you have made in the last 5 or 6 years.

Can you give us anything encouraging with regard to these two diseases?

Dr. WHEDON. Mr. Chairman, I think that we do have some encouraging things to say, but I think one has to bear in mind that both of these diseases are very complex and require, for their ultimate solution, a much greater understanding of the basic disease process. Hopefully we will elucidate the exact cause, particularly in the case of arthritis. When we do that we will be much further along the road.

In both of these diseases this year I can give you an example of the sort of progress we are making. We are making progress in that, step by step, we are making little advances toward understanding the basic disease process, and on the other hand we are making little advances each year in providing some form of better treatment, new drugs, for example.

In both arthritis and diabetes in my statement I mentioned the development of a new compound, in both instances, which is effective and has minimal side effects.

I would prefer to stress the gradual, I would say even relentless progress, little step by little step, by which we are learning more and more——

Mr. FLOOD. I like "relentless." That is a good word at the right time.

Dr. WHEDON. May I suggest we submit for the record special reports on arthritis and diabetes which would fill out our testimony?

Mr. FLOOD. Very well.

(Information referred to follows:)

SPECIAL REPORT ON ARTHRITIS

No other disorders cause more prolonged misery to a greater number of people in the United States than do the arthritic and rheumatic diseases. The three most crippling forms of arthritis are rheumatoid arthritis, gout, and to a lesser extent, osteoarthritis. These and other arthritic conditions cause unemployment each year to the equivalent of nearly half a million people, cost the government nearly $200 million annually in lost income taxes, and account for about 12 percent of welfare expenditures through subsistence allowances to arthritics unable to support themselves. The total cost to the individuals involved and to the Government from arthritis and related disorders is estimated at $3.6 billion annually. No price tag, however, can be placed on the untold suffering, pain, invalidism, and mental anguish which these disorders impose on individuals and their families. About 16 million people in the United States afflicted with arthritis look to research for a means to relieve their suffering.

CHANGING RESEARCH EMPHASIS

Because of the immediate need for analgesic and anti-inflammatory agents, scores of beneficial drugs have been developed, ranging from newer forms of the time-proven salicylates, to several types of potent corticosteroids. Some of the new drugs under trial will be mentioned in this report; but while the search for curative or at least palliative drugs continues, considerable emphasis must be and is being placed on finding the underlying causes of arthritis as a key to its more effective treatment and perhaps ultimate prevention.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis, main target of institute research, is a chronic, inflammatory connective tissue disease that ranks high among serious public health problems. In many cases, this disorder, which affects more than 4 million people in the United States, leads to permanent joint deformities and other complications producing disability and chronic invalidism. The majority of its victims are not elderly persons (as is the case in osteoarthritis) but are young and middle-aged adults in their most productive years.

The primary cause of rheumatoid arthritis is still unknown. Two leading theories, supported by considerable evidence, suggest that an obscure infectious process or an autoimmune reaction (characterized by manufacture by the body of antibodies that attack its own tissues) may be involved, or possibly a combination of both processes.

SEARCH FOR INFECTIOUS CAUSE

More research has centered on a possible infectious etiology for rheumatoid arthritis during the past 5 years than during the previous 20, but while specific infectious types of arthritis are known due to invasion of joints by certain microorganisms, no microbial agent has yet been positively identified as a cause of rheumatoid arthritis. At the University of California, Institute grantee investigators demonstrated that Bedsonia viruses isolated from human patients with Reiter's syndrome (a disease with some symptoms resembling rheumatoid arthritis) caused chronic arthritis when injected in monkeys. Now the investigators have extended the finding to rabbits and have demonstrated, further, that Bedsoniae infecting the eye will disseminate to joint tissues, liver, kidney, and spleen, in a manner suggestive of the involvement of major organ systems accompanying rheumatoid arthritis in humans. Control rabbits receiving heat-killed Bedsoniae did not develop arthritis. The rabbit has been shown to be a feasible animal model for the study of Bedsonia arthritis and for evaluation of the mechanisms involved in initiation of joint damage.

If rheumatoid arthritis were produced by a common, easily cultured microorganism multiplying in joint tissues, the cause of the disease might well have

been discovered by Pasteur a hundred years ago. To date, however, attempts to isolate one specific, universally present organism in cultures from joints of patients with rheumatoid arthritis, have been unrewarding. Continuing attempts to demonstrate an infectious basis have from time to time implicated a number of organisms. These include species, mostly large viruses and the mycoplasma, known to cause slowly developing, degenerative diseases of connective tissue in animals. Until recently, the mycoplasma have been impossible to culture so that definitive studies necessary to prove their association with rheumatoid disease could not be made.

DRUG FOR ARTHRITIS SYMPTOMS

In the search for better drugs for treatment of arthritis, attempts are being made to redesign known steroid compounds which have demonstrated salutary antiinflammatory action but which also cause serious side effects on prolonged use. Among other new agents, compounds related to triamcinolone have subject to careful clinical testing. Among these is a new steroid drug triamcinolone hexacetonide, which seems to combine the important features of rapid and prolonged action with minimal side effects on prolonged repeated use. The hexacetonide appears to retain the desirable qualities of the parent compound and to require less frequent administration.

Institute grant-supported investigators at the University of Cincinnati College of Medicine evaluated the effects of intraarticular injections of the drug in 58 patients with rheumatoid arthritis and in 8 with osteoarthritis. Responses to treatment were judged excellent in the great majority of cases, including both forms of arthritis. Relief generally lasted for long periods, and side effects from use of the drug appeared to be minimal. The Institute-supported investigators feel that further experimentation for definitive evaluation of the treatment is warranted.

SYSTEMIC ANTIBIOTIC IN JOINT TREATMENT

More knowledge of transport of antibiotics from the blood into synovial (joint) fluid and surrounding tissues of patients with infectious arthritis is essential. If effective levels of antibiotics could be demonstrated in the synovial fluid of patients receiving *generalized* treatment with the drug through intramuscular or intravenous injection ("systemic therapy"), direct injection of antibiotics into affected joints with its attendant difficulties, such as secondary infection and joint trauma, could be avoided, and treatment could be simplified in cases of multiple joint involvement.

In Institute-supported research at the Northwestern University School of Medicine, systemic antibiotic treatment was shown to result in effective levels of the tested drugs in the synovial fluid of patients with infections arthritis, Fifteen patients with this form of arthritis were treated systemically with antibiotics, and the antibacterial activity was measured in 34 simultaneously obtained samples of serum and synovial fluid. The drugs tested included penicillins, cephaloridine, erythromycin, tetracycline, and lincomycin. The study clearly showed that systemic antibiotic therapy results in effective concentrations of drugs in synovial fluid, avoiding the hazards of secondary infections and drug-induced synovitis that may be associated with local drug injections. Furthermore, determination of bactericidal activity of synovial fluid by the grantee's newly-devised tube dilution method proved to be relatively simple and a practical means of monitoring antibiotic therapy.

PHOSPHOLIPASE C

In examining the mechanisms of infection and immunity at the cellular level, Institute investigators collaborating with colleagues at the National Cancer Institute have found that a bacterial enzyme, phospholipase C, alters the membrane of chick embryo cells so that they will not support reproduction of the nerve-destroying Semliki Forest virus. Although total phospholipid content was reduced 42 percent, cells sustained no damage visible on electron photomicrographs. Attempts will be made to adapt an enzyme of this type for animal trials to determine inhibitory effect against microbes known to be capable of destroying joint (and muscle) sheathing.

SEARCH FOR AN IMMUNOLOGICAL BASIS

Institute grantees at the Albert Einstein College of Medicine, New York City, demonstrated that certain components of human connective tissue and of streptococci are so similar that they cross-react immunologically. Thus it is possible that antibodies formed in the body to combat invading streptococci could mistakenly attack the similar components of connective tissue, initiating an autoimmune reaction with consequent destruction of connective tissues and joints. The finding illustrates that the concepts of an infectious and an autoimmune etiology for rheumatoid arthritis are not mutually exclusive.

INFLAMMATORY LESIONS

Violent immunological reactions within the body involving invading microorganisms, or other foreign substances, and antibodies activated against them, are known to have a potential for causing the type of inflammatory lesions observed in rheumatoid arthritis. Employing radioactive tracers to study the immune reactions and consequent vascular lesions that follow injection of foreign serum which caused serum sickness in rabbits, Institute grantees at the University of Arkansas have shown that permeability of blood vessel walls to immune complexes is an important factor determining the extent of the damaging reactions. Fluid dynamics within the arteries, electromagnetic potentials of particles and vessel walls, and potent naturally occurring body chemicals such as histamine and serotonin, affect the permeability of the blood vessel walls and determine whether the immune complexes can filter into vascular substructures where they have been found to react with greatest force. The mechanisms now being clarified may help explain rheumatoid arthritis, lupus erythematosus, and a number of diseases characterized by localized or systemic inflammatory lesions.

AZATHIOPRINE

At the University of Alabama Medical Center, Institute grantees are giving a number of rheumatoid arthritis patients high doses of azathioprine, a drug which suppresses immune responses and is used widely to prevent rejection of transplanted tissues. The drug was used on the theory that it would also suppress destruction of joint tissues if rheumatoid arthritis is a disease in which defenses of the body erroneously attack its own tissues. In preliminary trials, the investigators observed that most of the 23 patients given azathioprine experienced a reduction in the number of painful and swollen joints and an increase in grip strength and walking speed. More extensive studies now are underway with due consideration for the risks and side effects which can accompany use of this potent drug.

TISSUE BREAKDOWN STUDIES

Central to research on rheumatoid arthritis is an understanding of the breakdown of collagen, the chief protein component of the connective tissue that is vital to structural integrity of major body organs as well as of joints and their sheathing. An enzyme (collagenase) capable of digestive degradation of collagen and, thus, of destroying connective tissue has been recovered from various sites in the body. Recently, collagenase was isolated by an Institute grantee at Massachusetts General Hospital from synovial membranes lining affected joints of patients with rheumatoid arthritis. The importance widely attributed to this area of investigation is evident in the broad collaboration characterizing this work, which is conducted by researchers representing the Massachusetts General Hospital, the National Institute of Arthritis and Metabolic Diseases, the George Washington University Hospital, the Walter Reed Army Medical Center, and the National Institute of Dental Research.

Specimens of synovial membrane taken from 24 patients with active rheumatoid arthritis were compared histologically and in tissue culture with others taken from 8 patients with noninflamatory joint conditions. Within 2 or 3 days a collagen-destroying enzyme appeared in certain of the cell cultures, the amount of enzyme detected being related to numbers of cells and vascularity of the tissues. The specific cells which secrete synovial collagenase have not been identified. There was a strong correlation between severity of the joint inflammation and the amount of collagenase produced by the derived cell cultures. *No* enzyme was detected in cultures of uninflamed joint tissue.

The investigators are inclined to assume that this type of collaganase is not peculiar to rheumatoid arthritis, but is rather a general reaction to inflammation. In any event, future discovery of agents which are capable of inhibiting the activity of the enzyme may lead to improved therapy for inflammatory joint disease.

GENETIC STUDY

Reported observations of aggregation of rheumatoid arthritis in certain families have contributed to the notion that this disease may be caused by some inheritable characteristic predisposing the patient to develop arthritis. In Institute-supported research at the University of Rochester School of Medicine and Dentistry, investigators recently studied 8 sets of identical (monozygotic) twin sisters to identify some genetic factor leading to the disease. In each of the 8 sets, one twin fulfilled the diagnostic criteria of the American Rheumatism Association for classical or definite rheumatoid arthritis, but when the co-twins were examined, none of them showed any evidence of rheumatoid disease. Extensive interviews brought out the fact that there had been extensive psychological stress preceding disease onset in a majority of the affected twins, but no comparable experience of such stress for the unaffected sisters, leaving an impression that the onset of rheumatoid arthritis might be triggered in some manner by periods of emotional stress. In general, these findings provide evidence against hypotheses that heredity is an important factor in rheumatoid arthritis.

GOUTY ARTHRITIS

Although rheumatoid arthritis is essentially an enigma, much is now understood about another major arthritic disease, gout. Classically gout is felt to be an inherited disorder of purine metabolism. Uric acid, a breakdown product of purines, accumulates in the gout patient, forming urate crystals in the joint tissues and resulting in inflammation and pain. Institute scientists, who last year reported that the disorder in purine metabolism in certain patients involves deficiency of an enzyme, hypoxanthine-guanine phosphoribosyltransferase (PRTase), have recently shown that determination of theratio of urinary uric acid to creatinine is useful in screening subjects with PRTase-deficiency disorders, including the Lesch-Nyhan syndrome and gout. The simple screening test permitting early identification of either disorder will allow institution of allopurinol therapy for the prevention of renal (urate stone formation) and other complications.

A few months ago, the investigators found that a unique urate-binding alpha $_{1-2}$-globulin in human blood plasma is present in diminished concentration in some patients with primary gout. Apparently this inherited deficiency of urate-binding protein is, along with the enzyme deficiency, an expression of the gouty trait. Some subjects who produce abnormally high amounts of uric acid do not show symptoms of gout. Theoretically, these individuals might have sufficient urate-binding globulins to avoid clinical expression of the disease while those who produce diminished amounts of these sequestrants develop classical symptoms due to deposition of urate crystals in various tissues and organs.

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (Marie-Strumpell's disease) is characterized by a painful and progressively stiffening spine. The disease attacks the small joints connecting the vertebras including the scroiliac joints. Institute grantees at the University of California recently reported on the results of a 5-year study of use of a nonsteroid, indole-derived drug, indomethacin, in long-term management of patients with ankylosing spondylitis. Indomethacin, which has also been used in treatment of other forms of arthritis, relieved joint pain and inflammation in most of the 28 patients studied, with few side effects from the drug during the extensive period of trial.

OSTEOARTHRITIS

Osteoarthritis occurs primarily with advancing age and is generally thought to be a result of prolonged "wear and tear" on the joints. When inflammation and pain is present, antiarthritic drugs are employed. The new steroid derivative, triamcinolene hexacetonide, mentioned earlier in this report, is an example of a number of drugs under trial in the search for effective chemotherapeutic agents that can be used regularly without development of undesirable side effects.

Simultaneously the components of the synovial fluid and the mechanisms of joint lubrication are under extensive investigation in the hope that means can be found to control the degenerative changes of joint structures typical of osteoarthritis.

In a study of age and weight factors related to osteoarthritis of the hip, Institute grantees at New York Hospital-Cornell University Medical Center, New York, concluded that, contrary to the "wear and tear" theory, body weight did not seem to be an important factor in the development of osteoarthritis of the hip. Also, no relationship was observed between age and development of the disease in both hips rather than in one, suggesting that the disorder is unilateral or bilateral at its inception rather than progressing from one side to the other with time. Studies such as this indicate the complexity of the mechanisms governing the genesis of osteoarthritis.

Outlook

The samples of research in arthritis presented in this report are but a few of the approximately 150 ongoing projects covering the range of these disorders which are being supported by the Institute. The findings reported do not summarize or indicate the total effort, but serve to illustrate the variety of problems associated with research in the arthritides and the broad coverage of the Institute's research and research support efforts. This rsearch attack on arthritis is constantly improving the treatment and control of these diseases, while adding to the base of fundamental biomedical knowledge that is essential to eventual discovery of their causes, to improved management, and to possible prevention of the arthritic diseases.

Special Report on Diabetes

Last year's special report on diabetes reflected a trend toward studies of a more fundamental nature which have yielded information leading toward a better understanding of the underlying causes of diabetes. This trend is continuing, with the most provocative findings having resulted from the continuing search for the precise mechanism of insulin secretion and action, findings which could lead more directly to the understanding of the etiology of the several different forms of diabetes.

A number of notable clinical advances have also been made, including successful preliminary trials of a new oral antidiabetic drug and further clarification of the relationship between obesity and adult-onset diabetes.

According to the best estimates there are, at present, approximately 4 million diabetic people in this country. Moreover, another 5 million of our present population are expected to develop the disease during their lifetime. It is this knowledge which makes continued, intensive, and effective research on diabetes an unceasing obligation on the part of scientists at the National Institute of Arthritis and Metabolic Diseases (NIAMD) and investigators elsewhere who are supported by the NIAMD.

A complicated disease, for which there is no known cure, diabetes ranks seventh on the list of diseases causing death in the United States. Diabetes has been known for some time to be a hereditary disorder. As a result of the body's inability to metabolize carbohydrates normally, the diabetic is unable to convert carbohydrates properly into the stored form, glycogen, or to utilize them for the energy required for normal body functions. The carbohydrates, in the form of glucose, accumulate in the blood and overflow into the urine. As the disease progresses, abnormal carbohydrate metabolism becomes associated with a noticeable derangement in the metabolism of fats and proteins.

In its severe form (occurring more frequently in juvenile diabetes) the untreated disease rapidly progresses to a grave metabolic disorder, ketoacidosis, which may result in coma and death unless controlled by insulin administration and specific supportive therapy. In its less severe form, diabetes patients may suffer from accelerated degeneration or "hardening" of the arteries, and thus, may have a greatly decreased life expectancy. Although the disease can be fatal unless properly treated, in most cases it can be well controlled. Today, with proper treatment, most diabetics can lead a normal life and live almost as long as their fellow human beings. Despite good control of clinical symptoms, however, and the usual ability to hold in check the abnormal blood sugar level, in too many cases the long-term complications of diabetes, primarily those affecting blood vessels, peripheral nerves, kidneys, and the eyes, apparently develop relentlessly.

INSULIN

Many diabetes investigators today believe that determination of the precise mode of action of insulin—how it is produced and released by the pancreas and how it does its vital work in human tissues—is essential to clarifying the cause or causes of diabetes. To this end many skilled scientists are currently devoting their time and efforts. During the past year several revolutionary findings by Institute scientists in Bethesda and Institute-supported investigators elsewhere prompted the president of the International Diabetes Federation to declare that "the next 1 or 2 years promise to be a very exciting period in the field of diabetes."

PROINSULIN

The first of these findings was by a Universtiy of Chicago scientist who has discovered a precursor form of insulin in the human pancreas. The investigator, whose research has long been supported by the Institute, has labeled the substance "proinsulin," and has suggested that a partial or complete failure of proinsulin conversion to insulin may account for some form of diabetes.

Proinsulin was first found by the scientist in a study of insulin biosynthesis by a pancreatic tumor removed from a patient. The substance was later recognized in insulin preparations from several other species, including the cow, pig, and rat, suggesting that it is a normal constituent of all insulin-secreting cells.

Studies have revealed that proinsulin is a larger protein than insulin, and that it contains the ultimate components of the end product, insulin, which can be structurally combined and released by the action of several enzymes. Proinsulin per se was shown to have very little biological insulin activity, and evidence is accumulating to indicate that it may function primarily as a necessary intermediate in the proper assemblage of the insulin molecule. Conversion of proinsulin to biologically active insulin was clearly shown to occur within the insulin-producing cells of the pancreas.

The discovery of proinsulin and clarification of its molecular structure also has important implications for the eventual commercial synthesis of insulin in that it may suggest useful steps in the eventual laboratory synthesis of the hormone.

BIG INSULIN

Coinciding with the discovery of proinsulin was the revelation by an Institute scientist in Bethesda that the insulin which circulates in the bloodstream may exist in two distinct forms in man: "little insulin," indistinguishable from the insulin in the pancreas, and "big insulin," which is a larger molecule and comprises up to 50 percent of the insulin in the circulation. It is believed new findings, particularly in such conditions as obesity and maturity-onset diabetes in obese individuals, which are characterized by glucose intolerance and excessive production of insulin.

The source of both big and little insulin was shown to be the pancreas. In addition, in normal individuals, virtually all plasma insulin was found to be little insulin 15 minutes after glucose ingestion. There was a gradual rise in big insulin over a subsequent 2-hour period, by which time a significant amount of big insulin was found in the plasma. Following a prolonged period of fasting, the percentage of big insulin in the plasma was even greater. Further studies are now underway to determine the biological activity of big insulin, its relationship to little insulin, and its relationship, if any, to proinsulin.

OBESITY AND INSULIN RESISTANCE IN DIABETES

Evidence continues to accumulate rapidly linking onset of the adult form of diabetes to obesity. During the past year an investigator receiving Institute grant support showed that fatty tissue from obese individuals contains unusually large fat cells which are distinctly resistant to the action of insulin in facilitating glucose metabolism. Following weight reduction, and a consequent reduction in the size of these cells, however, both the insulin resistance and the glucose intolerance known to be characteristic of obesity were reversed. Inasmuch as most patients with adult-onset diabetes are obese at first, these findings may shed light on the natural history of this most common type of diabetes. The investigator is presently attempting to determine he precise mechanism or primary tissue defect which underlies the diminished insulin sensitivity in such enlarged fat cells.

In relation to this finding, it was reported 2 years ago that significant small blood vessels disease (the so-called microangiopathy of diabetes) can be demonstrated in genetically prediabetic subjects prior to the onset of metabolic abnormalities. This finding suggested that small blood vessel pathology (primarily a distinct thickening of the capillary basement membrane), generally believed to be characteristic of overt diabetes, may actually represent the primary lesion of diabetes, followed only secondarily by derangement in carbohydrate metabolism. This observation afforded diabetes investigators a new angle of attack.

At an international insulin conference this past year a number of investigators, including an Institute scientist from Bethesda, presented evidence to indicate that the insulin "resistance" encountered in certain tissues of obese and diabetic individuals may result solely from decreased transfer of the hormone across the capillary wall, from the bloodstream to the tissue cells. Conceivably, the abnormal thickening of the basement membrane in capillaries affected by diabetic microangiopathy may constitute a hindrance to hormonal transfer.

Thus, there would appear to be a link between the small blood vessel disease observed in gentically prediabetic subjects and the apparent inability of the capillary wall to transfer insulin normally from the blood stream to the tissue cells. Further studies will be required, however, to determine any possible relationship between small blood vessel disease, tissue resistance to insulin, and an inhibited transfer of the hormone across the capillary wall.

PANCREAS TRANSPLANTATION

This past year, at the University of Minnesota, a surgeon receiving research grant support from the Institute established the feasibility of transplanting a normally functioning pancreas into selected persons suffering from severe diabetes. Three of four patients thus treated were dying from kidney failure, caused by diabetes, at the time of the transplants.

In three of the four patients the transplanted organ produced sufficient insulin to control the blood sugar levels of the person into whom it was transplanted. Although none of the patients survived for more than a few months following the surgical procedure, the study proved that it is technically possible to transplant the pancreas. The Minnesota surgeon has predicted that such a procedure will become more common within the next 5 years, particularly in selected patients with severe pancreatic diseases that are not satisfactorily treated by current methods.

ANTIDIABETIC DRUGS

Four years ago Institute-supported scientists at the Joslin Clinic in Boston reported results of preliminary studies of a new oral antidiabetic drug, acetohexamide. These studies showed acetohexamide to be a safe and effective agent in certain cases of maturity-onset diabetes, and suggested that it had a number of advantages over several antidiabetic drugs now in use.

During the past year the same investigators reported their experience with acetohexamide in the treatment of 290 diabetic patients for periods as long as 6 years. Satisfactory control of blood sugar levels was achieved in 70 percent of the patients, and side effects of the drug were neither frequent nor severe. A satisfactory response was obtained most frequently in persons with adult diabetes of recent onset and in previously untreated patients. Thus, acetohexamide joins the armamentarium of oral antidiabetic drugs which, either singly or in combination, provide control of blood sugar levels in a great majority of patients with adult-onset diabetes, the most common form of the disease.

While the Boston investigators were proving the efficacy of acetohexamide, other grant-supported scientists at the University of Cincinnati were conducting preliminary clinical trials of glycodiazine, a newly discovered oral drug which also is believed to have antidiabetic properties. Seventeen patients with adult-onset diabetes were studies for a period of 27 weeks. Elevated blood sugar levels declined significantly in every patient treated with glycodiazine and remained at safe levels as long as the drug was administered, without any evidence of untoward side effects. The investigators believe that long-term studies are warranted in order to evaluate further the safety of glycodiazine in man.

In the same research area, the Joslin Clinic grantee-scientists recently concluded a postmortem study of diabetic patients who had been treated for

2 years or more during their lifetime with oral antidiabetic drugs of the sulfonylurea type, such as chlorpropamide and tolbutamide. Results were compared with similar studies of closely matched diabetic patients who had been treated either with insulin or exclusively by dietary restriction during their lifetime.

Results of the study showed that the relative frequency of heart disease, cancer, stroke, or severe diabetic complications in patients treated with such compounds is not significantly different from that of patients treated either with insulin or by dietary restriction. On the basis of these findings, it was concluded that administration of sulfonylurea drugs to diabetic patients over a period of several years does not alter in a statistically significant fashion the incidence of the specific complications of diabetes or the pattern of other severe diseases which may affect diabetic patients.

ALCOHOL AND DIABETICS

Diabetic patients are warned constantly of the dangers of excessive use of alcohol, which may impair the patient's judgment and cause him to administer an overdose of insulin or to neglect an injection altogether. An Institute-supported investigator at Harvard University reported during the past year results of a study which showed that alcohol augments the activity of insulin and causes excessive depression of blood sugar levels. Two diabetic patients dependent upon regular insulin injections died without regaining consciousness following an alcoholic binge, while three others suffered severe and permanent brain damage requiring continuous custodial care after being discharged from the hospital.

Because it was impossible to obtain positive proof that these patients had in fact taken insulin and alcohol concomitantly, the investigators tested the effects of simultaneously administered insulin and alcohol in several healthy volunteer subjects. It was found that while both insulin and alcohol, when administered individually, were capable of depressing blood sugar levels as expected, concomitant administration of insulin and alcohol markedly inhibited the subsequent return of the lowered blood sugar levels to normal.

The investigators concluded that the irreversible low blood sugar state induced by the combination of insulin and alcohol predisposes the diabetic patient to multiple complications, and even death, and that diabetic patients receiving any blood sugar lowering agent, including oral antidiabetic drugs, should be warned against excessive use of alcohol.

IDIOPATHIC EDEMA

Two years ago grantee-scientists at the University of Vermont obtained evidence suggesting that idiopathic edema may be a sign or complication of hidden diabetes. Patients with idiopathic edema, which is characterized by localized or generalized swelling associated with fluid retention, were found to have an abnormality of the small blood vessels and impaired carbohydrate tolerance, conditions which are known to precede the onset of clinical diabetes.

Other grantee-scientists at Hahnemann Medical College and Hospital of Philadelphia now have shown that phenformin, an oral antidiabetic drug, when used in conjunction with a diuretic agent, appears to be an effective form of therapy for some patients with idiopathic edema. This therapy was based upon evidence developed by the investigators which indicated that idiopathic edema may be caused by a metabolic abnormality which has been seen in some diabetic and prediabetic subjects. In addition to reducing the characteristic swelling of idiopathic edema, the described therapy also reversed the biochemical abnormalities of carbohydrate metabolism seen in these patients. These findings strengthen the concept that patients with idiopathic edema may be predisposed to diabetes.

EPIDEMIOLOGICAL STUDIES

Continuing epidemiological studies of the Pima Indians of Arizona, who have the highest incidence of diabetes in any population ever reported, are providing information concerning several facets of this complex metabolic disease. Investigators at the Institute's Clinical Field Studies Unit recently compared obesity and diabetes rates among the Pima Indians with those of the Cocopah Indians of

southwestern Arizona. It was found that the frequency of obesity was similar in the two tribes, but the prevalence of diabetes was significantly lower in the Cocopah. The investigators concluded that the frequency of obesity does not account for the difference in the prevalence of diabetes between the Cocopah and the Pima Indians and that obesity per se cannot account for the high incidence of diabetes among the Pimas.

In a subsequent study, the scientists showed that congenital anomalies occur more frequently in the offspring of women who developed diabetes before age 25 than in the offspring of women who developed the disease later in life. Although a genetic mechanism could not be completely excluded, the findings support the theory that diabetes produces fetal anomalies among the Pima Indians by its influence upon the intrauterine environment during early pregnancy.

Outlook

A great deal has been learned about diabetes during the past few years. Only a short time ago, diabetes was believed to be solely a disorder of carbohydrate metabolism characterized by excessive amounts of sugar in the blood and urine. It is now viewed as a hereditary disease complex which produces various syndromes as it progresses through a series of stages, eventually including one marked by loss of carbohydrate tolerance. Although many questions have been answered, many remain, and these are undergoing intensive study. Research findings of the coming years may bring us additional important achievements such as defermet of the onset of diabetes in genetically predisposed individuals, suppression of its severe complications, and, ultimately, its prevention.

REDUCTION IN FUNDS FOR TRAINING GRANTS

Mr. CASEY. We have talked at some length about the problems in connection with the tight budget for research grants and grants in the training area.

Do you have any special problems or do you just fall into the general pattern?

Dr. WHEDON. I am sure that I share with the other Institutes difficulty in funding training grants, but I can speak only to my own problem.

Mr. CASEY. We want to know whether you have special problems or whether your problems are about like the rest of them.

Dr. WHEDON. We find, for example, that as a result of the situation here we are going to be able to provide a significantly fewer number of training grants. What this means is that our supply of investigators for dealing with these diseases is going to be reduced.

We will be able to make 24 fewer awards, for example, of training grants. When you realize that our total level for 1969 was 299 such awards, that is about an 8-percent decrease in our capability.

Mr. SHRIVER. You mentioned investigators in your testimony quite frequently. Are they grantees? Are they otherwise known as the recipients of grants?

Dr. WHEDON. That is correct, Mr. Shriver. When I speak of accomplishments of various investigators, they are either grantees of ours in the universities or else in some instances investigators working in Institute laboratories in Bethesda.

Mr. SHRIVER. That is what I want to know, whether they are regular employees or those people out in the institutions.

Dr. WHEDON. I perhaps did not identify them as clearly as I might have as I went along, which were grantees and which were our employees.

Dr. MARSTON. You might say something about the special relation-

ship of your Institute with departments of medicine in medical schools and centers and in the increased manpower needs for the future.

Dr. WHEDON. Thank you, Dr. Marston. This is indeed of special significance with respect to our Institute. The rather broad scope of categorical diseases and scientific disciplines that this Institute covers means that we are supporting the training of investigators and academicians; that is, teachers of medicine in most of the subdepartments of departments of medicine in medical schools, and we are also responsible for a few of the subspecialties in surgery as well.

Therefore, in this respect, we are of the opinion that our training grants are really the key to providing the manpower needed for investigators in the research laboratories, and also those highly sophisticated individuals who are going to be the teachers in our medical schools.

Mr. CASEY. This reduction in the number of grants, does this mean that you will not be able to initiate that many new ones? You have some that are continuing grants; do you not?

Dr. WHEDON. It means that the total number of our training grants will drop from 299 to an estimated 275. When we wind up with a total of 275, obviously most of those will be continuing grants, but there are always some grants that are either completed, or more usually they do not meet the competition and fail to be renewed, so we will be able to make a small number, but obviously a very small number of new training grants.

I would like to add a point here. We have been so interested in this problem of providing the best quality of clinical investigators for our departments of medicine and other departments of medical schools that some years ago we instituted a new experimental training grant program called experimental training grant for clinical investigation. We felt that if we could devise ways to improve the quality of training in the sophisticated technology required both in the laboratory and at the bedside, we would indeed have more efficient and effective clinical investigators. If we could do more in this direction, this would be a great contribution to the necessary bridging between the developments which come from the laboratory over to the bedside, providing the final and appropriate application of research results to clinical disease.

Mr. CASEY. Mr. Shriver?

ARTHRITIS DRUG

Mr. SHRIVER. The new arthritic drug, triamcinolone hexacetonide, mentioned on page 2 of your statement. That is not on the market yet. When do you think that will be on the market?

Dr. WHEDON. This compound is now on the market. It has been under very broad clinical trial.

CRACKING THE GENETIC CODE

Mr. SHRIVER. You mentioned Dr. Nirenberg's partially cracking the genetic code for which he was awarded a Nobel Prize. What are some of the applications of that evidently great discovery?

(The information is found on p. 456.)

Dr. WHEDON. I think that I can describe for you rather briefly the significance of this work. It means that we are moving into a period where we can actually use enzymes which are really biological catalysts in certain diseases where enzymes are lacking. Actually, we have already been doing something of this sort, but now that we know the exact biochemical procedure by which enzymes and proteins are made, it may be possible for us to administer various substances to patients which will induce, as we say, the body to make the enzymes that have been missing, or intensify the concentration of enzymes which are present, but only present in deficient amounts.

I think it is a bit premature to predict the exact date when we can administer these special materials to stimulate enzyme production, but I am certain that that day will come and that it is not too far off. Also, these techniques can be applied to the synthesis of such compounds. This is actually the particular benefit of another outstanding development this year—the synthesis of the first enzyme, ribonuclease, which is closely related. This was done by two teams, one at Merck and the other at the Rockefeller Institute. The team at the Rockefeller Institute was supported in part by this Institute. Techniques of synthesis of enzymes of this sort will enable us hopefully to apply these similar techniques to synthesize hormones like growth hormones and other important and very useful endocrine agents of that sort.

REDUCING COST OF ARTIFICIAL KIDNEY

Mr. SHRIVER. On page 4 of your statement you talk about a new, compact, highly efficient proposed artificial kidney. How expensive is that one?

Dr. WHEDON. I do not believe that a cost figure can be given at this time, but it is bound to reduce the cost significantly because of the relative ease of its production and the fact that it can be presterilized, can be used for several times, and then thrown away. In other words, the time involved nowadays in manpower preparing and resterilizing the machines most commonly used, is one of the biggest elements in the cost of artificial kidney treatment.

To the extent to which we can make machinery which does not require that sort of manpower-managed upkeep and preparation, we are going to sharply reduce the costs.

Mr. SHRIVER. You are working on other things that would, I hope, lower the costs of such treatment?

Dr. WHEDON. Yes, sir. We are interested in two other particular phases: One is in trying to devise a better system of connecting the artificial kidney machine to the artery and vein of the patient's circulation. At the present time, we rely on a permanently implanted loop or shunt between the artery and vein, in an arm or leg, which can be opened and connected to the artificial kidney, but it has occasional difficulties of infection and plugging, and sooner or later it has to be replaced. We are looking for better materials and equipment for that system. As an example, we are looking for a material that might provide the permanent shunt from the artery to the vein that you need to have, which could be kept underneath the skin and then could be entered with a needle through the skin, just the way a doctor enters

your vein with a needle and syringe when he wants to take a blood sample.

The other aspect that we are working on in an attempt to improve technology is the possibility that we can obtain better artificial kidney membranes than the type we have now, membranes that would be more efficient in removing the specific toxic substances in the patient's blood. At the present time we are using a system which removes toxic materials without a clearly direct relationship to the factors that cause the disease symptoms in the patient.

CRACKING THE GENETIC CODE

Dr. MARSTON. Could I go back just a moment to your question about Dr. Nirenberg?

Mr. SHRIVER. Yes.

Dr. MARSTON. It seems to me that it would be of interest to this committee for us to insert for the record additional information about the significance of this. There are Nobel prizes awarded each year, but I think all would agree that this particular set this year have unusual potentials for all people and I think it might be helpful if we could develop this a little further.

Mr. SHRIVER. That is why I ask the question. Other people besides members of Congress read this report.

Dr. MARSTON. This goes all the way back to giving us an insight into the actual fixation, millions of years ago of the DNA code, all the way up to the types of potentials that Dr. Whedon was suggesting.

(The information follows:)

MEDICAL IMPLICATIONS OF THE DECIPERING OF THE GENETIC CODE

The deciphering of the genetic code is, potentially, the most important medical discovery of the century. As often occurs with fundamental breakthroughs in basic research, it will be years before the full benefits to patients will be realized. Already, however, major effects on many aspects of medical treatment have taken place.

The discovery can be explained as follows. Every cell in the body possesses a control center in its nucleus within which is present all the information necessary to run and reproduce the cell. This control center contains, in coded form, the blue prints for every structural component of the cell together with instructions detailing how these components fit together and function in order to carry out efficiently the thousands of processes which produce the phenomenon of life. All of this information is stored in a master molecule known as deoxyribonucleic acid (DNA). Data for maintaining cell function are dispatched from the DNA in the form of messages (messenger RNA molecules) which travel to designated places within the cell. Any defect which affects the functioning of the cell, such as the synthesis of an abnormal product or the loss of control over the rate of reproduction, is ultimately traceable to information contained in messages dispatched from the DNA. In order to be able to understand and correct abnormal states resulting from messages containing disruptive information it is imperative for us to be able to decode the messages. The magnitude of the problem seems enormous. Each code letter is only 1/50,000,000 inch in diameter. Simply learning what the code letters are was an impressive accomplishment. But to actually "break" this code so that the very language of the cells could be understood is an achievement which is indeed staggering. It meant learning how the code letters form words, how the words form sentences, and how the sentences form the whole language of the cell. This is the discovery which has been made. The uses to which it has been and will now be put in the service of man can hardly be over estimated.

Rather than to attempt to list the many possible benefits, four specific areas will be mentioned to demonstrate how the knowledge of the genetic code is being utilized in health research. The four areas are (1) cancer, (2) hereditary diseases (such as diabetes), (3) viral diseases, and (4) aging.

(1) CANCER

The rate of reproduction of a cell is firmly regulated by information coded in the DNA. If this regulation is lost, the cell may begin to divide rapidly and out of control: it then becomes a cancer cell. The messages that direct the process of division come either from the DNA of the cell, or, in some cases at least, from virus particles arriving from outside the cell. But what is the mechanism by which a cell can no longer control its growth and division? With the ability to decode messages, as well as with the detailed knowledge of the translation machinery of the cell, it might be possible to introduce a corrective message or to counteract the disruptive one. At the very least, specific anti-cancer drugs can be developed which are aimed at the precise step(s) that converts a normal well-controlled cell into a malignantly growing cancer cell.

(2) HEREDITARY DISEASES

Diabetes phenylketonuria (PKU), sickle cell anemia, cystic fibrosis, hypercholesterolemia, gout—all are examples of hereditary diseases (conditions in which the defect is passed on from parents to offspring). The defect in chemical terms is a change in one of the codewords in the DNA which then results in the dispatching of a message which contains an error. In diabetes the error is related to insulin; in PKU it is in the metabolism of the amino acid phenylalanine; in sickle cell anemia it is the structure of the blood protein hemoglobin. In fact, progress has been so rapid in applying the genetic code in this field that the exact codeword change in the disease sickle cell anemia is now known: the middle code letter in the sixth codeword of the hemoglobin chain has changed from an adenine to a uracil. Ways of treating the patient in order to overcome this genetic error are now being sought. Unfortunately, all that can be done at present for children and adults suffering from hereditary diseases is to attempt to alleviate the symptoms: insulin injections for diabetics, low phenylalanine diets for children with PKU, etc. The cure for these diseases, however, is to correct or replace the defective codewords in the DNA and message molecules. A major step in this direction has been taken with the deciphering of the genetic code.

(3) VIRAL DISEASES

Not only certain cancers, but also a whole range of other debilitating diseases are caused by viruses, such as measles, German measles, mumps, chickenpox, smallpox, poliomyelitis, influenza, mononucleosis, and the common cold. Many viruses act as outside messages which, upon entering, force the cell to translate the virus message rather than the cell's own. By understanding the information being carried by these virus messages, their harmful effects might be counteracted. Two important developments have already taken place. First, parts of certain nonpathogenic viruses have been decoded (as a prelude to decoding, under properly safeguarded laboratory conditions, disease-producing viruses). Second, a substance known as "interferon" has been discovered which can selectively prevent the translation of some virus messages while still allowing the cell's own messages to function normally.

(4) AGING

Many workers feel that the process of aging is no more than the accumulation of many small defects within the cells. As these defects accumulate, the cell becomes less able to repair itself, reproduce, or use its energy efficiently. Again, all these functions are mediated by messages from the DNA. It may be possible to detect abnormal messages as cells grow older. Message replacement therapy is even a long-range possibility. In any case, in order to understand the chemical processes whereby an organism grows old, it is necessary to understand normal cell function. Knowledge of the genetic code now allows a more direct approach to this problem.

In conclusion, the deciphering of the genetic code stands as one of the finest accomplishments ever achieved by man. For the first time, a door directly into the control center of the cell has been opened.

ACNE AND PSORIASIS

Mr. SHRIVER. Does your dermatology program include support for the development of anything that would be used in the treatment of acne—or what is the other word for that?

Dr. WHEDON. Acne is the proper term for a condition in which there are multiple infections of the skin. Were you thinking of psoriasis?

Mr. SHRIVER. Yes. I thought they were the same?

Dr. WHEDON. No, they are not. They are quite different. Acne is a very common condition most frequent during the teenage years where there are many pimples, frequently affecting the face and the back, perhaps more than any other part of the body. It is a very difficult problem in itself. We do not have that one solved by any means.

The other skin condition which undoubtedly involves more people and seems to be more traumatic, at least over a longer period of time, is psoriasis in which there is a thickening, scaling, and reddening of the skin, particularly over areas of pressure, such as the elbows and knees, but also may involve other parts of the skin. I believe last year or the year before, I mentioned the beginning use of a compound which has been used in the treatment of certain cancers; a compound known as methotrexate. In initial trials this was somewhat toxic, but recently it has been found that if the doctor administers multiple, minute divided doses throughout the day, this is better tolerated and apparently more effective. So, this new development is now being extended to more patients.

NEW POSITIONS REQUESTED

Mr. SHRIVER. In what areas will the additional 12 positions be used in your in-house research program?

Dr. WHEDON. These positions will in general be used to strengthen our activity as a whole. There are two parts of our activity in Bethesda that we are particularly interested in supporting and which will certainly take some of these positions: one is in arthritis, where we are interested in further work which our Arthritis and Rheumatism Branch is conducting on the possible relationship of mycoplasma infection to the development of rheumatoid arthritis, and the other is in our Pediatric Metabolism Branch, which is particularly interested in cystic fibrosis. A rather ambitious project is envisioned there. I do not know how much of it we will be able to do during the next year with our relatively limited resources, but we hope to expand the study of cultured fibroblasts, a particular development over the past year by one of our grantees at Cornell University Medical College. They showed the rather distinctive character of fibroblast cells in cystic fibrosis patients and provided a hint that cystic fibrosis involves the body quite broadly, and affects many other tissues besides the lung and pancreas with which we have been familiar for some time.

Mr. SHRIVER. Thank you.

CYSTIC FIBROSIS

Dr. WHEDON. In this connection, may I submit for the record a special report on cystic fibrosis?

Mr. SHRIVER. Certainly. We would be glad to have it.

(The information follows:)

SPECIAL REPORT ON CYSTIC FIBROSIS

Cystic fibrosis (CF) is a grave hereditary disease of children. As a cause of death in children under 15 years it outranks many of the better known diseases such as poliomyelitis, rheumatic fever, and diabetes. Although cystic fibrosis has been recognized as a specific disease only since 1938, its increasing frequency throughout the world has made it a public health problem of no mean proportions; estimates of its incidence in the population range as high as 1 in 1,000 live births.

Cystic fibrosis is an inherited generalized metabolic disorder characterized by an abnormality in the products of the body's exocrine glands which secrete fluid to body surfaces, particularly to the skin and to the gastrointestinal and respiratory mucosal linings. Two major types of fluid are normally secreted by the exocrine glands: a watery substance produced primarily by the sweat glands of the skin and a mucous fluid intended to lubricate the gastrointestinal tract and the bronchioles in the lung. The abnormalities which occur in both types of secretions are responsible for the major symptoms and complications in cystic fibrosis.

The basic metabolic disorder of exocrine secretion results in three principal clinical problems. The first of these is the production of sweat with a high salt content. Due to this defect many patients are unable to conserve salt and are in constant danger of developing profound dehydration, or heat exhaustion in the summer months, which may lead to death. With the widespread of use of the sweat test, a technique which measures the unique composition of the sweat in cystic fibrosis patients, a modality is now available for the diagnosis of this disorder.

A second, and considerably more serious facet of the disease, stems from the abnormal functioning of the mucus-secreting glands of the body. In cystic fibrosis, the mucus-producing glands fail to secrete normal, clear, free-flowing fluid. Instead, they produce an abnormally thick, viscous mucus which tends to obstruct the ducts or openings of the glands. When the viscous mucus accumulates in the ducts of the pancreas, it interferes with the ability of this gland to supply digestive enzymes to the intestinal tract thus leading to poor digestion and malabsorption of a number of nutrients. Depending on the severity of this complication, the patient may suffer from malnutrition—one of the major factors resulting in general underdevelopment, poor musculature, and retarded bone growth in children with cystic fibrosis.

The third and most serious complication involves the lungs. Nearly all cystic fibrosis patients develop progressive chronic lung disease. Thick mucus obstructs the smaller air passages in the lung, causing labored breathing and a chronic productive cough. In time, bacteria multiply in the accumulated secretions, and the child may fall victim to chronic bronchitis and frequently pneumonia. The latter infection is the leading cause of death in these patients. Chronic lung changes may increase resistance to pulmonary blood flow and thus may lead to an increased blood pressure in the lung; this can result in chronic right heart strain and eventually in heart failure.

Although in the past cystic fibrosis was thought to be confined to the pediatric age group because of the high mortality in infancy and early childhood, the disease is now recognized with increasing frequency among adolescents and adults.

Recent studies have shown that the course of the disease in these older patients, because of the only partial genetic endowment, is not as serious as full blown cystic fibrosis. The studies have suggested that these various expressions of cystic fibrosis may be responsible for some of the chronic lung and gastrointestinal disorders in adults often attributed to other more common disorders.

RESEARCH DEVELOPMENTS AND TRENDS

At present, no one hypothesis can link all the diverse and often conflicting observations which have been made concerning the widespread malfunction of exocrine glands in cystic fibrosis. In particular, it is not yet possible to give a reasonable explanation of the abnormal behavior of mucous and sweat gland in this disorder. Recent studies, however, have helped to narrow the field for speculation and to clarify some of the mechanisms of the disease.

New straining technique may pinpoint molecular defect

Cystic fibrosis is inherited from parents who carry the genetic trait for the disorder (both parents may be asymptomatic). When both parents carry the trait, the chances are one in four that cystic fibrosis is manifested in the severe and classical form in the offspring. If only one parent carries the trait, although the child may be asymptomatic, the trait may be passed to the offspring, who, in turn, may transmit the disease. Thus, for every overt case, there is a large reservoir of hidden carriers, recently estimated at 2 to 5 percent of the general population. Clearly, since the genetic character of cystic fibrosis makes the disorder particularly pernicious, a method of identifying such carriers would be a major achievement for genetic counseling.

Institute-supported scientists at the Cornell University Medical Center recently have pinpointed a cellular difference between normal persons and those in affected or carrier states of cystic fibrosis. Using a special staining technique, this newly discovered genetic cell marker can be seen in fibroblasts, the flat elongated cells which form fibrous tissue.

Skin biopsy specimens were obtained from seven affected children, 13 parents, 26 healthy individuals, and from 11 patients with a variety of other diseases. Cell cultures of fibroblasts from the healthy group and from the 11 patients with varied other disorders showed only an occasional cell (1 percent) with metachromasia, a condition in which portions of the cell fail to stain uniformly and in the same color as surrounding cell materials. In all seven cultures from children with cystic fibrosis, however, cellular metachromasia appeared in an average of 56 percent of the fibroblasts. A similar staining pattern was seen in 42 percent of cells obtained from parents of children with cystic fibrosis. Thus, the test, though still cumbersome, permits the identification of carriers of the trait for cystic fibrosis in cases where potential parents have requested genetic counseling.

One of the most important implications of this finding will lie in the results of direct investigation into the molecular defect of this metabolic disease. Up to now, clinical and chemical studies have indicated that cystic fibrosis is a generalized exocrine disorder. This new finding hints that the disease is a multicellular disorder also involving the body's connective tissue, and further biochemical analysis of the metachromatic cellular substance may prove to be a step forward in elucidating this theory.

Beyond its value as a research tool, the new test eventually may play a large role in genetic counseling to spot cystic fibrosis carriers, to facilitate studies on genetic linkage, and to determine the frequency of this detrimental gene in the normal population.

Sodium levels and transport

Sodium concentrations in sweat and saliva of patients with cystic fibrosis are known to be elevated. Last year Institute grantees at the University of Wisconsin demonstrated that perfusion of the rat parotid (salivary) gland with sweat and saliva from patients with cystic fibrosis caused a large increase in sodium output of the rat salivary glands. The implication of this finding is significant: The same factor in the sweat and saliva from patients with cystic fibrosis which causes salty saliva in rats may be responsible for the high salt content of the patient's own sweat and saliva. Studies continue to isolate such a factor, which, once isolated, may aid in elucidating the inherited molecular defect which causes cystic fibrosis.

More recently, Institute-supported investigators at the University of North Carolina have described a marked decrease in sodium output from red blood cells of patients with cystic fibrosis, and a similar decrease in the red blood cells of their asymptomatic parents. This defect in sodium transport should be of value in detecting cystic fibrosis carriers, and therefore, should be useful in genetic studies.

Adult infertility

Another development which may aid genetic counseling has been reported by grant-supported investigators at Children's Hospital Medical Center, Boston, who have shown that adult males with cystic fibrosis are infertile due to a failure of the normal development in the vasa deferentia, the tubules which transport spermatozoa from the testes. By contrast, the same study pointed out that 18 women with cystic fibrosis were known to have produced nine apparently normal offspring, and thus the fertility of female patients is apparently unimpaired.

Semen specimens from 25 male patients with cystic fibrosis were studied, and a complete lack of spermatozoa was noted in every specimen. Subsequent studies revealed that while the testes were normal or diminished in size, the epididymides were rudimentary or absent, and spermatogenesis was decreased.

These investigators believe that the anatomical defect (nonpatent or absent vasa deferentia) is developmental in origin, and is characteristic for cystic fibrosis. This belief is supported by another study at Children's Hospital, Los Angeles, which has shown abnormal epididymides and absent vasa deferentia in 10 cystic fibrosis males between 3 days and 25 years of age.

Thus, it appears unlikely that adult males with cystic fibrosis can reproduce. On the other hand, cystic fibrosis does not impair virility or affect the external genitalia.

Lung clearance "jacket"

A grant-supported investigator at Children's Hospital, Boston, has reported, along with other specialists at Monticello Medical Group, Montefiore Hospital and Van Etten Hospital, New York, that a mechanical lung percussion device clears clogging mucus from the respiratory tract of patients with cystic fibrosis six times faster than the conventional physical therapy procedures which involve hand percussion of the chest when the patient is in an inverted position.

Once the jacketlike device is buttoned and the power turned on, six rubber padded disks are forced rhythmically against the chest; when the jacket is reversed, the disks (clappers) apply equal force to the back. Since the clappers are arranged in rows, the patient can operate one row independently of another, and thus, percussion can be adjusted to avoid sensitive areas—such as post-operative sutured regions. With a simple bedside control box, which can be plugged into any household electrical outlet, the patient can adjust the strength and frequency of percussions to suit his needs.

This device has enabled the cystic fibrosis patient to be independent without relying on physical therapists for assistance in postural drainage and chest clapping. Significantly, it has eased the ordeal of eliminating mucus from pulmonary passages with much less strain on the patient.

Drug therapy

A drug that increases the flow and concentration of digestive enzymes from the pancreas in animal models, which may indicate future possibilities in the treatment of cystic fibrosis, has been studied by an Institute grantee at Michigan State University.

The drug, called slaframine, has been isolated and purified from a fungus *Rhizoctonia leguminicola* which grows on clover. Slaframine has been found to stimulate the exocrine glands, especially the salivary glands, and is reported to cause the "slobbering syndrome" in cows that eat forage containing the fungus.

Intraperitoneal injection of 2 milligrams of slaframine doubled pancreatic flow in experimental goats for as long as 5 hours. Digestive enzyme activity was increased about 10 times and remained at that level for 8 hours or more.

Other experiments with animals have demonstrated the drug's capability to stimulate all exocrine glands for prolonged periods. One test revealed its specificity in stimulating exocrine glands without affecting heart rate, respiration, blood pressure, or transmission of nerve impulses.

The exocrine gland-stimulating properties of this drug raise the possibility that in cystic fibrosis patients, slaframine may spur pancreatic activity enough to clear the mucus-obstructed ducts leading to the intestinal tract. The theoretical possibiliy exists that with an increased production of digestive enzymes from the pancreas, the malnutrition commonly observed in young cystic fibrosis patients may be alleviated without resort to therapy with exogenous pancreatic preparations.

Incipient heart disease in cystic fibrosis

Several months ago Institute scientists reported that hypoalbuminemia, an abnormally low albumin content of the blood, in older patients with cystic fibrosis is caused by dilution of a normal albumin mass by an enlarged plasma volume.

Later clinical metabolic studies established that the abnormal increase in volume of circulating plasma in the body (hypervolemia) is secondary to cor pulmonale, an abnormal condition, ultimately leading to right-sided heart failure, brought about by abnormal resistance to pulmonary blood circulation. Since cor pulmonale is difficult to diagnose clinically in patients with cystic fibrosis,

the investigators feel that a low serum albumin concentration may be of value in alerting the clinician to possible hypervolemia secondary to cor pulmonale and incipient heart disease.

OUTLOOK

Cystic fibrosis is a disease of many disguises. Its multifaceted nature has prompted and encouraged many scientists in diverse disciplines to study its metabolic, genetic, and clinical aspects. In recent years, scientists in Bethesda and investigators supported by the Institute have contributed largely to dispelling misconceptions concerning the disease. Two major misconceptions had been that cystic fibrosis is rare and that it is invariably fatal. Neither has been shown to be true. Promising findings in basic research, as well as new methods of diagnosis and treatment, have opened up new avenues for investigating cystic fibrosis, while bringing about a more optimistic outlook for patients with this disorder. Continued progress hopefully will lead to even better means of managing and possibly eventually preventing this grave disease.

TABLE OF OBLIGATIONS

	1966	1967	1968	1969	1970
Cystic fibrosis and related areas:					
Research grants	$950,000	$1,200,000	$1,805,396	$2,600,000	$3,100,000
Intramural research	182,000	185,000	195,000	222,000	221,000
Collaborative studies	20,000				
Total	1,152,000	1,385,000	2,000,396	2,822,000	3,321,000

COST OF ARTIFICIAL KIDNEY TREATMENT

Mrs. REID. Dr. Whedon, as I understand it, the capillary kidney is still in the experimental stage?

Dr. WHEDON. That is correct.

Mrs. REID. You said that you could not estimate the cost but certainly the cost would have to be decreased considerably to be used by the average person, that is, in comparison to the machine now being used. Is that true?

Dr. WHEDON. That is true. I don't know what the end result will be of our efforts. Sometimes we cannot see the end of the road as we start on the road, but we have had great hopes that we could save considerable expense in artificial kidney treatment per year from the current figure of $15,000 by doing more and more dialysis in the home. Certainly for the families that can do this, there is a very significant saving. It is a time-consuming and arduous effort because some member of the family has to go with the patient into the hospital for several weeks to be trained very thoroughly in all of the techniques, preparation of the machines and membranes, and so on, particularly in watching for any accidents that might occur during the course of the procedure. There is a limit, however, to the extent to which we can cut costs by going into home dialysis because many patients do not have the family support which is necessary.

Thus, we are concentrating our efforts now also on more efficient and smaller apparatuses.

Mrs. REID. There is a man who lives in my district who has had kidney failure. I have talked with him and know the tremendous cost and the difficulty he has had to obtain proper treatment. Do you have the up-to-date statistics? If you do I would certainly appreciate your providing them for the record.

Dr. WHEDON. Yes, ma'am.

(The information follows:)

Approximately 55,000 people die each year because of kidney failure. Not all of these patients necessarily suffer from primary kidney disease; many were afflicted by other serious conditions such as high blood pressure, diabetes, or long-standing obstruction of the prostate, which eventually damaged and destroyed their kidneys. An estimated 7,500 of these patients are considered medically suitable patients for permanent maintainance with the aid of artificial kidneys (chronic dialysis). A similar number, and most of these individuals overlap with the first group, are considered suitable candidates for kidney transplantation.

The cost of chronic dialysis, which involves two to three blood cleansing sessions with an artificial kidney in a special hospital dialysis center per week, ranges from $10,000 to $30,000 per year. It now averages between $15,000 and $20,000 if thrice-weekly treatment is used. The cost of dialysis carried out in the home, where a specially trained close relative or sometimes the patient himself conducts the dialysis, ranges from $11,000 to $14,000 during the first year; this includes the expensive in-hospital training period of the patient and his relative, acquisition cost of the artificial kidney, and appropriate alterations in the home. The subsequent yearly cost of home dialysis has been estimated to be between $5,000 and $7,500 exclusive of any serious medical complications with the attendant physician and hospital costs. Unfortunately not every medically suitable candidate for hospital dialysis has the appropriate home conditions, qualified close relative and suitable emotional and intellectual stability which are essential for long-term successful home dialysis.

Mr. FLOOD. This should be a good place to also insert your special report on kidney disease.

(The report follows:)

SPECIAL REPORT ON KIDNEY DISEASE AND THE ARTIFICAL KIDNEY

Today in the United States, an estimated 55,000 individuals die each year of irreversible kidney failure. Medical authorities agree that development of optimal treatment to reach all of these people depends on better knowledge of uremia and on further fundamental improvements in organ transplantation. In addition, more effective understanding of the primary kidney disorders which lead to end-stage uremia is essential for prevention as well as control of most kidney disorders. This past year, scientists supported by the National Institute of Arthritis and Metabolic Diseases have reported on many research findings which shed light on some of the causes and manifestations of chroic renal failure.

THE KIDNEY

The importance of the kidneys can be judged in part by the fact that they receive about one-fifth to one-fourth of the blood volume pumped by the heart. By selective excretion of certain substances and reabsorption of others, the kidneys play an extremely important role in regulating the composition of blood and other body fluids. They continually process blood to eliminate harmful waste products of metabolism. The kidneys help to regulate the chemical environment of the body cells by regulating the concentration and composition of salts and the amount of water in the blood and tissues. They also produce substances which are important in regulating blood pressure and in stimulating the bone marrow to produce blood cells.

The term kidney disease encompasses a number of conditions of varying etiologies. Among the leading causes of kidney disease are—

(1) hypersensitivity diseases in which the kidney tissue is destroyed by an immune reaction initiated by any of a number of causes, including streptococcal infection;

(2) infections in which kidney tissue is attacked and destroyed directly by microorganisms;

(3) circulatory diseases in which the kidney is affected as a result of disease of the blood vessels or of elevated blood pressure;

(4) metabolic diseases in which the kidney is secondarily affected, such as in diabetes or gout;

(5) developmental disorders in which the kidneys fail to develop or develop in an abnormal fashion; and

(6) obstructive conditions in which urine flow is blocked with resultant pressure damage to the kidney and repeated infections.

One characteristic common to most of these diseases is their tendency to eventual progression to a common end-stage—the clinical syndrome of uremia. The term end-stage uremia denotes the total combination of signs, symptoms, and pathology resulting from the loss of the kidney's normal functions of removing wastes from the body and of regulating the internal chemistry of the body.

Patients with uremia may be divided into two groups: those with acute kidney failure, and those with chronic renal insufficiency. In acute kidney failure, the kidneys are damaged by an acute insult and the symptoms of uremia appear and progress rapidly. The damage may be reversible, however, and after a short period the kidneys may heal and regain normal function. On the other hand, chronic kidney insufficiency is brought on by gradually progressive destruction of functioning kidney tissue from which the kidneys do not usually recover. In these cases the kidneys never regain the ability to reverse the trend toward ultimately fatal uremia.

KIDNEY SUBSTITUTES

Two therapeutic substitutes for kidney function have come into use: peritoneal dialysis and hemodialysis (blood purification with the aid of artifical kidneys). Both methods employ the same basic principles of dialysis, the exchange of substances across a semipermeable membrane. Peritoneal dialysis makes use of the membranes of the abdominal cavity as filters and of the abdominal space as a reservoir for "dialysis fluid", a solution meant to wash out metabolic waste products. Waste products of relatively small molecular size which have concentrated in the blood, tissues, and intercellular spaces, pass across tissue membranes into the dilute solution introduced into the peritoneal space and are removed when this dialysate is drained from the abdominal cavity.

For hemodialysis with artificial kidneys, the blood is routed out of the body and through membranous enclosures immersed in large and rapidly replenished volumes of a dilute dialysis fluid. The same mass-transfer principle of substances in more concentrated fluids diffusing spontaneously into the less concentrated medium applies, but here the membrane barrier is not of biological origin as in peritoneal dialysis but consists of cellophane or of a similar artificial material.

TRANSPLANTATION

Kidney transplantation is at present still a developing modality but has shown increasing promise for larger scale application. With continued research, kidney transplantation, supported and made possible by efficient methods of hemodialysis (until the patient is ready for an operation or until a suitable donor kidney is available) should become a more routinely used method of therapy.

The surgical techniques for transplanting kidneys have in large part been developed and are constantly being refined. The body, however, ordinarily defends itself against a "foreign" transplanted organ by making specific antibodies to that graft and by other defensive processes such as thrombosis and phagocytosis. In a series of complex events not at all well defined, the foreign transplanted organ is attacked and ultimately becomes functionless. Treatment with special drugs which suppress the host's immune response to transplanted foreign organs of a different tissue "type" (analogous to the well-known, mutually incompatible blood types) can abort such an attack temporarily. In the long run, however, only organs of identical tissue composition (obtained from an identical twin) or of closely matching antigenic composition bear the promise of prolonged, dependable function in the host.

Thus it has become increasingly apparent that improvement in kidney transplantation and organ transplantation as a whole will depend on additional knowledge of human tissue immunology. Sophisticated methods must be developed for close immunologic matching of donor and recipient tissues. In addition new methodology must be sought for effective long-term preservation of donor organs so that at all times a sufficient number of pre-"typed" (tissue typed) organs with different antigenic composition is available for transplantation into (matching) patients who need them.

Clotting disorder in uremic bleeding

In institute-supported studies of blood clotting abnormalities as the cause of bleeding often encountered in uremic patients, the release time of platelet factor-III has been pinpointed as the failing step in clotting events. Release time returns to normal after dialysis treatment, indicating that an unknown dialysable material is responsible for the delayed platelet factor-III release time. These studies have resulted in a reliable method for quantitating platelet factor-III and have clarified the role of the platelet factor in uremic bleeding.

New disease entity

Grant-supported scientists have described a new clinical entity characterized by a disease pattern clearly distinguishable from regular glomerulonephritis, which it resembles in some aspects. The condition starts insidiously with decreased urine production and progresses to cessation of urine flow, hypertension, edema, nephrotic syndrome and death in from 5 to 27 weeks. It is remarkable for the clearly demonstrated absence of any history of acute streptococcal glomerulonephritis. No clinical, bacteriological or serological evidence of streptococcal infection, concomitant systemic disease, or drug ingestion is encountered. Death results from urema and congestive heart failure.

The newly described condition affects adults, perhaps somewhat more often men, with more servere and rapidly fatal forms appearing in those over 40 years. Although the disease, called RPGN (for rapidly progressing glomerulonephritis), is still of unknown pathogenesis, unusual ultramicroscopic findings provide evidence to warrant search for an immunologic cause of the condition.

Blood glucose utilization

Comparison of insulin and glucose relationships in uremic patients and in normal or diabetic persons have shown the long recognized diabetic-like impaired glucose tolerance of uremia patients to be due to a decreased sensitivity of uremic tissues to insulin action. Initial experiments suggest either the presence of specific insulin antagonists or of intracullular metabolic abnormalities. Additional studies will be carried out on this question since it may uncover new knowledge pertinent to other diseases of carbohydrate metabolism.

Vitamin D3 metabolism

Abnormalities in calcum metabolism in patients with chronic renal failure have been long known. Grantee investigators have been able to show that although absorption of vitamin D3 is normal in uremia, renal failure causes an abnormal twofold increase in the rate of its metabolism, producing an abnormal accumulation of biologically inactive lipid-soluble metabolites and abnormal increases in urinary excretion of both vitamin D3 and biologically inactive metabolites.

Normal vitamin D3 metabolism was found to be restored by renal homotransplantation but not by hemodialysis. Since therapeutic doses of vitamin D3 alone are not helpful in renal osteodystrophy, these metabolic defects in utilization of the vitamin are believed to be acquired with chronic renal failure.

Carbohydrates and kidney stones

Many patients who develop calcium-containing kidney stones have no obvious predisposing factor such as hypercalcemia, urinary obstruction or urinary infection. Although some patients have definite hypercalciuria, others cannot be distinguished from normal subjects inasmuch as their daily total urinary calcium excretion does not exceed the normal range.

It has now been shown by Institute grantees that both urinary calcium concentration and excretion rise sharply in calcium stone-formers and in relatives of stone-formers following sugar ingestion, effects which clearly distinguish these subjects from normal individuals. It is suggested that augmentation of urinary calcium excretion and concentration after meals, or after ingestion of carbohydrate-rich foods or beverages, may be one of a possible number of factors contributing to calcium stone formation in susceptible individuals.

Infection and Ureteral peristalsis

The precise mechanism by which most instances of kidney infection (pyelonephritis) occur is as yet unknown. Grant-supported scientists at Duke University recently have described experiments with animals which suggest that the presence of live or dead bacteria in the ureter, without active infection,

may facilitate subsequent development of pyelonephritis by causing cessation of normal ureteral peristalsis. Whent *E coli* bacteria cultured from urine of patients with pyelonephritis were introduced into the rental pelvis of dogs, ureteral peristaltic activity diminished in most cases by 50 percent and some cases to zero. Endotoxin, a well-known toxic substance in the cell walls of the bacteria, was also shown to influence ureteral motility in vitro. These findings may open new approaches for research on the precise mechanism of infection of the kidney, particularly with organisms derived from the intestinal tract.

Hypercalcemia

Basic studies of mineral metabolism required for better understanding of kidney disease and therapy have produced two beneficial methods of chemical management for patients with hypercalcemia (abnormally high serum calcium levels). This condition occurs both in previously hypocalcemic uremic patients who develop subsequently secondary hyperfunction of the parathyroid glands and in patients with parathyroid gland tumors. Increased amounts of parathormone elaborated by the glands causes mobilization of skeletal mineral which may then be deposited in the soft tissues. Hypercalcemia also occurs in patients with other diseases such as multiple myeloma (a plasma cell malignancy), sarcoidosis, and others.

In the case of hypercalcemia associated with uremic hyperparathyroidism, surgical removal of all but one fourth of one of the four glands was usually found to control the condition so that calcium behavior returned to that usually found in uremic patients. As an unexpected additional reward, this treatment also provided relief from the persistent intolerable itching found in some of these patients.

In the case of multiple myeloma, carefully sheduled phosphate administration was found to restore normal serum calcium levels without causing calcium deposition in the kidney. In this case the new therapy also caused an amelioration of bone pain, and in several cases, complete relief.

Hormonal relationships

Failure of normal red blood cell formation (erythropoiesis) in the bone marrow is believed to be the chief cause of the anemia associated with uremia. Although both bleeding and hemolysis contribute to the anemia, they are generally considered secondary causes, while diminished secretion, by specialized cells in the kidney, of erythropoietin (erythropoiesis stimulating hormone) is viewed as the primary cause of the anemia of uremia. In recent studies, inhibitors of erythropoietin elaborated by kidney cells, have been found in sera from patients with renal disease. According to these studies, secretion of the hormone does not typically diminish. The recent localization of increased inhibitory activity in a cytoplasmic fraction of diseased human kidney has redirected attention to the ery-erythropoietin system in searching for methods for controlling the anemia of kidney failure.

Further work has also been done to elucidate the mechanism of hormonal action in the kidney. The enzyme, adenyl cyclase, which converts adenosine triphosphate (the power source of cellular chemistry) into the cyclic derivative cyclic adeosine monophosphate was found to be stimulated in kidney cells by parathormone and vasopressin. Specifically, parathormone was found to activate this enzyme primarily in the plasma membrane of renal cortex cells, whereas vasopressin stimulates the enzyme in cells from the renal medulla. Understanding of the mechanism of action of parathyroid hormone on calcium and phosphate balance has been advanced by these results.

ADVANCES IN KIDNEY TRANSPLANTATION

At the present time, kidney transplantation is the most frequently executed and successful example of organ grafting, both in the United States and abroad. It owes its success partially to the fact that an affective mechanical substitute organ (the artificial kidney) is available to rehabilitate the patient before surgery, to support the patient and the transplanted organ immediately thereafter and, if needed, to maintain the patient's life permanently (or until a second opportunity for transplantation arises) should the organ be rejected.

In recent years, due to improved immunologic matching of donor and host tissues, the acute rejection of transplanted kidneys has become less of a problem. The 2-year success rate in kidney transplantation from a live blood relative is about 60 percent; that involving well-matched cadaver kidneys is about 40 per-

cent. In most cases the patient must continue taking immunosuppressive drugs in an effort to prevent any belated rejection reactions. The problem of eventual rejection and inactivation of the transplanted organ is far from solved; recent research data indicate that even in the absence of overt acute rejection reactions, a gradual degeneration of the transplanted organ takes place in cases (particularly involving cadaver transplants) where the tissue matching was not of the first order.

Adjuncts to tissue typing

Because transplants, except between identical twins, are often ultimately rejected by the body, the critical problem still is to find methods to reduce and some day to eliminate the immune response to grafts without compromising the body's ability to fight off infection. Lasting success depends on matching the recipient's and donor's cells as closely as possible, and then overcoming any remaining minor incompatibility by inducing immunological tolerance in the recipient's body.

Certain immunosuppressive drugs for use in the prevention or control of the rejection phenomenon are being studied, with special emphasis on those drugs which will be more effective and less toxic than those presently available.

Antilymphocyte serum (ALS), as well as a more purified fraction, ALG (antilymphocyte globulin), have been used to help the body accept a new organ. The globulin tends to suppress the cellular reaction largely responsible for attacking the transplanted organ. Usually prepared in horses or rabbits against pooled human donor lymphocytes, the serum is commonly used in conjunction with other immunosuppressive drugs to combat rejection. It drew considerable attention among U.S. surgeons in late 1966 when a grant-supported Denver surgical team reported its use in the first of a renal transplant series.

In addition to antilymphocyte serum, total and subtotal body irradiation, cytotoxic drugs, and surgical manipulations of the lymphatic system are being used in attempts to reduce or eliminate the lymphocyte population and thus increase tolerance to homografts. These methods, however, also cause undesirable general effects, such as depression of bone marrow and red blood cell formation.

Identification of human protein antigen-antibody complexes

A major immunological technique which may aid tissue typing has been developed by an investigator at the Brooklyn, N.Y., Veterans Administration hospital, whose work is sponsored by a contract from the Institute's artificial kidney program. The technique allows rapid identification of various human proteins by exposing them, in succession to different antisera, to water vapor, and then by evaluating these complexes for their light-scattering ability.

This simple method is based on the knowledge that the ability of a solid to adsorb water is altered if it is first coated with a protein film and then exposed to water vapor. The protein films used in this study were either human plasma, a human fibrinogen-saline solution, a human albumin-saline solution, or a 7S gamma globulin-saline solution.

In all tests the protein film appeared darkest, hence presumably the wettest, where it had been exposed to its matching antiserum. Whenever the test film had been in contact with a nonmatching antiserum it continued to scatter light maximally (that is, it was not wettable) and appeared lighter. Fibrinogen-coated surfaces, which were affected by antifibrinogen serum premixed with serum, did not respond to the same antiserum premixed with plasma. Plasma-coated surfaces were rendered most "wettable" by antiserum to fibrinogen. This water vapor-light scattering method of identifying protein antigen-antibody complexes may prove useful as a simple and rapid procedure in tissue typing.

Short-term preservation of human kidneys prior to transplantation

A transportable organ preservation machine has been developed by Institute grant supported investigators. The machine has maintained human kidneys in a fully usable state for as long as 17 hours and animal kidneys as long as 72 hours prior to transplantation. Human kidneys obtained from cadavers have been transplanted successfully following preservation by the device, which permits transplantation to be a somewhat more elective procedure, rather than an immediate one upon availability if a cadaver kidney. The device provides the necessary time for adequate tissue typing of the organ and proper matching to a suitable waiting recipient.

The unique machine consists basically of a membrane oxygenator, pulsatile pump, perfusion chamber, filter, and heat exchanger. It differs from previous

perfusion devices in that its circulation pulsates, thus obviating the risk of uneven blood circulation within the organ and eventual local tissue damage. In addition, the machine utilizes as a perfusion medium plasma fortified with hormones and other additions, instead of whole blood, avoiding harmful local blood clotting in the perfused organ and breakdown of red blood cells.

While the isolated organ is being perfused, time is gained to allow matching of donor and recipient by tissue typing and to do preparatory surgery. The machines also eliminates the problem of simultaneous surgery and the need for two surgical teams, one to remove the kidney from its original location and the other to transplant it into the new host. Because the unit is easily transportable, perfusion of the isolated kidney can be started immediately upon its removal from the expired donor in one hospital, and continued during transfer to another hospital, even in another city, where the recipient is ready for transplant surgery. Although developed specifically for the preservation of kidneys, studies are now underway to modify the machine for similar preservation of hearts and livers.

ARTIFICIAL KIDNEY PROGRAM

If and when kidney transplantation becomes a routine procedure, the artificial kidney will not be discarded. Many chronically uremic patients are not medically or psychologically suitable candidates for transplantation. Furthermore, patients who are suitable candidates will have to be sustained with an artificial kidney until they are well enough to have a transplantation operation and until a suitable, antigenically matching donor kidney can be found for them. Also they may have to be placed on an artificial kidney after the operation if the donated kidney does not function properly for a time or is rejected.

The problem of perpetual maintenance of patients with artificial kidneys is complicated by the fact that the cost of currently available techniques is too high, both in terms of money and qualified manpower, to permit widespread patient treatment. Also, patients maintained with the aid of artificial kidneys continue to display a number of undesirable symptoms related either to the underlying disease or to the treatment.

The Institute's special artificial kidney program has been created to deal with these problems. An up-to-date report of progress and future plans follows:

Background

In the United States today an estimated 55,000 individuals die each year as a result of irreversible kidney failure. The diseases which originally initiate the chain of events which terminates with advanced kidney failure vary considerably in nature. They may be primary kidney diseases like glomerulonephritis. In other instances progressive kidney damage may be induced by long-standing hypertension or diabetes, or kidney infection, and destruction may be initiated by obstructions such as kidney stones or hypertrophy of the prostate in aged males. Regardless of the original disease, the progressive kidney damage leads to a common final pathway, end-stage kidney disease, followed by fatal irreversible kidney failure.

Although artificial kidneys had been known for many years, until 1960 they could be used only a few times in each individual for lack of a practical method for repeatedly connecting the patient's bloodstream with the artifical kidney machine. In that year a group of Institute grantees at the University of Washington developed permanently indwelling plastic blood vessel connections ("cannulas") which made possible the repeated joining of patients with irreversible kidney failure to artificial kidneys for intermittent maintenance treatment. Subsequently, these investigators proved the feasibility of maintaining life in such patients for a number of years with the aid of artificial kidney treatments ("hemodialysis") given twice or three times each week. With increasing experience with this new treatment modality it soon became evident that existing artificial kidneys and dialysis methods were as yet not optimal, that maintenance treatment with artificial kidneys was extremely expensive and not within the reach of most individuals who needed it, and that rehabilitation of patients on chronic dialysis, using present methods and equipment, was not always optimal. It was estimated, based on recent experience, that about 8,000 patients of the yearly 55,000 individuals with end-stage kidney disease would possess the necessary medical and psychological prerequisites necessary for successful long-term dialysis treatment.

The emergence of this new lifesaving treatment encouraged the Congress, in the summer of 1965, to appropriate funds to this Institute for the pursuit of a planned and centrally directed program of research and development, utilizing predominantly a direct contract approach, aimed at the development of improved and less expensive dialysis hardware and methodologies and at optimal rehabilitation of chronic dialysis patients.

The program

The new artificial kidney program was located in the National Institute of Arthritis and Metabolic Diseases (NIAMD), the Institute which has major responsibility for research in urology and renal diseases.

It was considered important to undertake such a program through the utilization of the best possible consultative talent from both outside and within the National Institutes of Health. Accordingly, 23 outstanding authorities active in the field of chronic uremia and hemodialysis have been appointed as consultants. Among them are physicians who have led programs in artificial kidney centers, renal physiologists, physical chemists and membrane specialists, chemical and electronic engineers, and those rare, talented individuals who combine several of the above qualifications. These consultants are assisting in setting the trend of the program and are reviewing the scientific merit and feasibility of contract proposals.

It was also considered important that the program be undertaken in close cooperation with the activities of the kidney disease control program of the Health Services and Mental Health Administration, HEW (HSHMA). The latter activity is concerned largely with the actual demonstration of chronic dialysis in a community setting—both in specialized dialysis centers and, where feasible, in the homes of selected patients. Staffs of both programs are in close and constant communication and work with a high degree of cooperation. This close cooperation assures a maximum of benefit and prompt application of research and development advances in the artifical kidney field.

Outline of program plans

A thorough study of the state of the art made it apparent that no single specific direction could be followed which would exclude others which might be relevant. Several different types of artificial kidneys are in use at the moment, and different methodologies are being advocated by the various workers in the field. Therefore, at this time, a variety of approaches in artificial kidney development are being supported. Once it becomes evident that one or more approaches show greater promise, efforts will be concentrated in these directions.

Problems of highest priority

The following are outstanding problems in dialysis toward which the Artificial Kidney Program is directing immediate efforts:

1. *Cannulas.*—The life and function of the permanently implanted cannulas are still limiting factors in successful dialysis.

2. *Dialysis membranes.*—Though effective, the cellophane membranes currently in use may not be optimal. The possibility of using other, perhaps more selective membranes, must be explored.

3. *Design of individual dialyzer units.*—Most dialyzers presently in use are cumbersome and costly to assemble and sterilize. A dialyzer exists which utilizes a disposable dialysis-ultrafiltration "cartridge"; this cartridge is expensive for maintenance of chronic patients.

4. *High requirement for professional personnel.*—This requirement is based on the medical nature of dialysis, but aggravated by problems 1, 2, and 3 above.

5. *Lack of effectiveness data.*—No objective information has been obtained through well-controlled studies which permits a meaningful evaluation of the comparative effectiveness of the various dialysis methods and equipment currently in use.

6. *Undesirable symptoms frequently found in patients maintained by repeated dialysis.*—

(*a*) Anemia: On the average, one or more blood transfusions are needed per month per patient maintained in dialysis—with the attendant risk of transfusion hepatitis.

(*b*) A significant incidence of peripheral neurological damage: This may be due to long-term effects of the semi-uremic state in surviving patients on repeated dialysis, or due to the dialysis procedure per se.

(c) Pseudo-gout, secondary hyperparathyroidism, skeletal demineralization, and calcium deposition in joints and in the tissues throughout the body: The most recent findings involve calcium deposition in the cornea of the eye. Simultaneously, there is a tendency to decalcification of bone with resultant fractures produced by minor stresses.

Problems 1 through 4 are primarily responsible for the current high cost of dialysis, which averages $15,000 per year in patients maintained by hospital center dialysis.

Current activities

At present about 60 carefully selected research and development projects are in existence, financed by the program's contract funds. These contracts were placed with universities, nonprofit research laboratories and industrial concerns, and constitute a broad spectrum approach to the problems of highest priority. These projects involve development of improved blood cannulas and filtration membranes; evaluation and development of new polymer surfaces for artificial kidneys, cannulas and membranes which do not induce blood coagulation; design of more efficient, compact, and less costly dialyzer systems; development of a new concept of artificial kidney dialysis ("hollow fiber" or "capillary" kidneys); research on and development of absorption cartridges for blood purification; development of inexpensive disposable dialysis units; improvement and design of new automated dialysate delivery systems; improvement and design of new dialysis units with automated failsafe mechanisms; evaluation of a special protein restricted diet in the maintenance of uremic patients for whom chronic dialysis is deemed not feasible or unobtainable; isolation from dialysates and identification of the as yet unknown compound(s) which is (are) specifically responsible for the toxic symptomatology in uremia, and many other projects related to improved dialysis methodology or apparatus.

Accomplishments

During the past year there have been a number of accomplishments and encouraging developments derived from the ongoing research and development contract program. The new and unique hollow fiber capillary kidney, mentioned briefly in last year's progress report, which is being developed under a contract with the Dow Chemical Co. has progressed to full-scale clinical testing at the Northern California Dialysis Center, San Francisco General Hospital. This low-cost, disposable small dialyzer is being produced at present in a semiautomated facility which has been set up under the contract in order to expand the production of prototype models for clinical testing.

The hollow fiber artificial kidney consists of 11,000 hollow cellulose threads bundled together into a compact plastic cylinder about the size of a quart milk bottle. Blood is passed through these manmade capillaries and they, in turn, are constantly washed on the outside by a blood purifying dialyzing solution. The unique construction of the kidney provides an enormous surface at the cellulosic blood-dialysate solution interphase at which toxic waste products migrate from the blood into the dialysate fluid. This new dialyzer is designed so well that no external blood pump is needed to drive the blood through it. Moreover, its internal blood compartment volume is so small that only about 70 milliliters of the patient's own blood are needed to prime the unit, thus eliminating the need for compensatory blood transfusions (and their attendant hazard of hepatitis) associated with the use of most conventional artificial kidneys. The new compact capillary kidney is easy to use in a hospital or home dialysis setting since it comes pre-sterilized, filled with saline and ready to use. Its cost projections make it more than competitive with conventional disposal coil dialyzers.

The new device has now proven its clinical effectiveness during more than 1,000 dialyses. It is routinely reused three times before it is discarded. It has been established experimentally, however, that it can be reused up to nine times and further studies are planned on this economically import facet. Future larger scale production of the new device is contemplated so that additional clinical trials in a number of dialysis centers throughout the United States can be made. In addition to this particular capillary artificial kidney, other possible designs are being explored by two other contractors of the program, also utilizing the new hollow fiber dialyzer design.

Another contractor who is manufacturing the conventional Kill dialyzer has been successful in the development of a major modification which is considerably

more manageable because of its light weight and different structural arrangement. This new board-type dialyzer substitutes a combination of plastic foam and solid plastic composition for the previous type of construction which is quite heavy and cumbersome. It requires 50 percent less torquing for sealing and has a smaller blood priming volume. It weighs 30 pounds less which permits easier handling in the hospital or home. This new dialyzer already has been introduced into commercial usage.

The same contractor has also developed a considerably smaller and more efficient type of Kiil dialyzer distinguished by a new type of multiple minute, pyramidal membrane supports which increase the effective dialysis area of the membrane in it. Laboratory tests have shown that this new development has increased the dialyzing efficiency of the new modified Kiil-type dialyzer by about 40 percent. A series of the new experimental dialyzer is now being built for clinical testing with patients.

The same group of scientists at the University of Washington, Seattle, which last year devised a technique for storing and re-using artificial kidneys of the Kiil type and of the attached blood tubing (which reduces the cost and simplifies the work involved in performing hemodialysis in the home) has now developed a new type of "quick-connecting" cannula coupler for home use which can be activated by the patient with one hand only. Heretofore, connecting the patient to an artificial kidney machine (by uncoupling his plastic shunt and coupling his permanently implanted plastic cannula to the blood tubing of the artificial kidney) has always required two hands. Since shunts are usually located on the arm of the patient, this meant that one extra person had to be present to connect the patient to his artificial kidney; only in cases where the cannula had been placed in the patient's leg, could the patient effect his own coupling and uncoupling in home dialysis. The newly developed, one-handed cannula coupler has now seen successful initial trial in a small number of patients and will be tested further in preparation for larger-scale manufacture and distribution.

During the past year, the artificial kidney program has striven to encourage clinical studies in the United States of a special diet, and modifications thereof, which has shown in trials in Italy and England that it permits moderate-term survival, cessation of symptoms, and rehabilitation in certain types of patients with chronic renal failure who are otherwise faced with the need for chronic dialysis or kidney transplantation. During a 21-month study period, Institute supported scientists in Los Angeles have indeed demonstrated that a 20-gram, balanced, low-protein diet limited largely to essential amino acids, but unlimited in carbohydrates and fats can ameliorate uremic symptoms in patients with minimial, residual renal function while maintaining a satisfactory body nitrogen balance. The results of dietary treatment, as measured by amount of relief from previous uremic symptoms and total duration of remission, were significant in all patients with a urea nitrogen clearance greater than 1.5 cubic centimeter/minute. Of 27 patients who followed the diet, relief of anorexia, nausea, vomiting, weakeness, fatigue and lethargy was obtained in 23. The results of therapy were felt to be good to excellent in ten patients, with remission of symptoms persisting for 8.3 months in one patient. Serum urea nitrogen decreased in all patients. The resulting remission depends on prevention of acute deterioration of renal function and rigid adherence to the diet by the patient. The program has recently activated investigations to study the efficacy of a maintenance regimen which combines the use of this diet with infrequently administered peritoneal dialysis or hemodialysis.

Similar encouraging results were obtained by another contractor at New York Medical College who has already progressed to maintenance of patients with a combination of this diet and infrequently applied hemodialysis (once every 2 weeks rather than the conventional three times per week).

Future activities of the artificial kidney program

The program will continue all promising current research and development efforts and will pursue any new ideas and approaches which appear feasible. Among these is a new method of detoxification of uremic blood with the aid of special selective adsorbing agents (in contrast to the presently used purification with the aid of membrane dialysis). The complete success of such detoxification-by-adsorption hinges on the successful identification of all toxic substances which accumulate in the bloodstream in kidney failure. The Program is currently fund-

ing a number of studies aimed at the isolation and identification of such unknown toxic factors which may have to be removed from the patients' blood, in addition to metabolic wastes and other substances known to accumulate during kidney failure, such as urea, creatinine, uric acid, potassium, hydrogen ion, and water.

The program intends to follow very closely the clinical and technological developments abroad and, when promising, to enlarge upon them for the benefit of U.S. patients as well. For instance, reports have been received of the preliminary development, in Scotland, of a new miniaturized dialyzer which requires little or no blood priming and of new selective membranes characterized by increased permeability to urea, heat sealability, and improved water flux. Should these new developments prove successful, the program will be interested in fostering larger scale clinical trials and in placement of production of the new membranes and dialyzer in this country.

The program will support further development of special diets (see above) for maintenance of uremic patients, to be used in conjunction with infrequent peritoneal dialysis or hemodialysis. For the latter type of regimen patients would be given surgically constructed, subcutaneous, natural arteriovenous blood vessel shunts (which are adequate for infrequently administered hemodialysis). It is hoped that with the aid of such a special-diet-infrequent-dialysis regimen patients would be maintained without the need for implantation of plastic shunts, and that a larger number of patients with renal failure may be accorded life-saving treatment in this fashion in the face of the great expense of conventional chronic dialysis therapy which is unavailable to most patients with end-stage kidney disease.

Other research and development projects about to be activated by the program include the development of a unique type of dialysis membrane from collagen (a structural portein found in the skin and connective tissues of mammals) and the development of implantable cannulas made from this naturally-occurring tissue protein. Preliminary experiments have given strong indications that a sophisticated laboratory modification of this material can yield a substance which is highly compatible with blood and mammalian tissues. This modified collagen would thus be a welcome substitute for currently used membranes and for implanted plastics (the latter not only in connection with dialysis cannulas but for many other prosthetic purposes). Other future projects deal with the possibility of developing substances which, once ingested, would sequester and trap specific toxicants in the gastrointestinal tract. Such a development could prove to be a helpful adjunct in the maintenance of patients with renal failure by permitting a decrease in the frequency of dialysis.

Conferences, publications, and scientific communication

As a sequel to the previous year's 2-day Conference on Nutritional Aspects of Uremia, the program organized, in October 1968, a timely symposium on the abnormal calcium metabolism and osteodystrophy which characterize chronic renal failure and is found in many patients maintained with the aid of artificial kidneys. The purpose of the conference was to explore and elucidate the serious phenomena such as widespread calcification of soft tissues (including the eyes, joints, blood vessels and the heart), demineralization of the skeleton (leading to frequent fractures), and secondary hyperparathyroidism, which accompany renal failure of long standing and which are seen with increasing frequency in patients whose lives are being maintained with the aid of artifical kidneys or even with kidney transplantation. More than 20 papers were presented concerning various problems related to renal osteodystrophy and disturbed divalent ion metabolism in chronic renal disease and to the possible etiologies and their interactions. This symposium brought together a select group of experts representing several relevant disciplines from France, Switzerland, Canada, Australia, England, and the United States, and the proceedings will be published shortly and will be distributed widely in order to facilitate widespread efforts for dealing with the serious complications of long-term dialysis brought about by the abnormal calcium metabolism of renal failure.

Most of the program's ongoing research and development contracts are systematically structured to yield specific goals according to a built-in time schedule. In many cases the attainment of targeted research and development goals in one contract is essential to the success of projects which are part of other contracts. Thus, close communication of research results between all of the program's contractors is essential for maximum effectiveness of the overall effort. With this in

mind, the program brought together, in January 1968, all of the contractors' senior staff and the program's consultants for a 2-day working conference ("The First Annual Contractors' Conference" of the artificial kidney program). On this occasion each project reported its positive and negative findings to all other active contractors in formal presentations followed by informal general brainstorming discussions. It was felt that this close communication and cross fertilization of ideas from a large number of active contractors and consultants coming from diverse biomedical and technological disciplines was highly productive toward attainment of the common goal of the program—optimal artificial kidney technology, improved clinical methodology and patient rehabilitation—at an early time.

Printed proceedings have now been published and widely distributed to workers in the field and related disciplines. The publication highlights research results, both positive an negative, in four main areas of the artificial kidney program: (1) solute removal, (2) hardware and instrumentation, (3) cannulas and biologically compatible materials, and (4) toxic factors in uremia and dietary management of chronic renal failure. It also contains a body of technical information which was exchanged among the meeting's participants.

The Second Annual Contractors' Conference of the program will take place in January 1969, and again technical proceedings will be made available widely to all scientific workers in the field, in university settings, medical centers, and industry.

A 16-mm. 20-minute color film, "Gift of Life," on the artificial kidney and home dialysis has been produced by the Institute's Information Office to help in public education in kidney disease. Intended for use by television outlets, libraries, universities, civic and voluntary health organizations, as well as professional groups, the film will be distributed by the National Medical Audiovisual Center and the National Kidney Foundation. The new film depicts a man who suffers loss of kidney function following progressive nephritis but who constitutes a productive life with the aid of artificial kidney treatment self-administered in his home.

OUTLOOK FOR KIDNEY DISEASE RESEARCH AND DEVELOPMENT

Research conducted and supported by the National Institute of Arthritis and Metabolic Diseases has added much to the understanding and treatment of chronic kidney disease. Clearly this review of investigation and progress in the broad area of kidney disease, artificial kidneys, and renal transplantation, is not all encompassing. Nonetheless, the variety and fruitfulness of the Institute's efforts and the stimulus to investigation is apparent. Investigations such as those discussed in this report have increased our ability to cope with the problems of kidney failure. Additional new research efforts are called for in order that a more widespread and permanent control of kidney diseases can be achieved. A meaningful program to reduce kidney disease must include all of the various components—research, prevention, treatment, education—available in our armamentarium. Such a total program must be aimed at all the primary kidney diseases as well as at end-stage kidney failure. This combination, led by much-needed research, should yield maximal benefits in the number of lives saved today and the deaths prevented in the years to come.

Mr. Flood. Your special report on organ transplantation is also relevant. We will place it in the record.

(The report follows:)

Special Report on Organ Transplantation

The National Institute of Arthritis and Metabolic Diseases (NIAMD) is charged with research responsibility for the largest spectrum of categorical diseases at the National Institutes of Health. The Institute's support of organ transplantation research reflects this wide range of responsibility and comprises studies related to transplantation of such organs and tissues as kidney, liver, bone, lung, intestine, pancreas, adrenal gland, pituitary gland, thymus, ovary, skin, and salivary glands.

DIRECTIONS OF TRANSPLANTATION RESEARCH

Organ transplantation is a technique whereby a functioning replacement from a living or recently deceased donor is transplanted into a patient whose own organ no longer functions adequately. Although this procedure is at present still in an advanced experimental stage, it shows considerable promise. Surgical tech-

niques for transplanting different organs have been developed to a large extent and are being refined constantly.

The main obstacle to better permanent function of transplanted organs results from the body's determination to destroy any foreign invader, a life-threatening microbe as well as a potentially lifesaving grafted donor organ. Unable to distinguish between helpful and detrimental foreign substances, the body's immunologic humoral and cellular defense mechanisms attack any and all intruders, including a newly implanted organ unless very closely matched immunologically. Transplanted organs, once attacked, will eventually cease to function unless the host's defense response is blunted by special immunosuppressive drugs or sera, irradiation, or surgical manipulation of the lymphatic system.

With presently available methods of immunosuppressive therapy it is often possible to prevent or reverse the initial, acute rejection reaction to an organ transplanted from one genetically nonidentical individual to another. Such immunosuppressive therapy carries with it considerable risk for the patient since it leaves him relatively unprotected against the daily onslaught of a variety of potentially pathogenic micro-organisms which ordinarily are held in check by the individual's normal defensive immune mechanisms. Thus, there is a limit to the extent to which immunosuppressive therapy can be used in any one host, and it is recognized that long-term survival and function of a grafted organ ultimately depends on the best immunologic matching between the source of the graft and its recipient. This is all the more important since recent Institute-supported studies have brought to light evidence of more subtle and chronic forms of immunologic attack upon the transplant that may occur despite long-term immunosuppressive treatment.

The directions of Institute-supported transplantation research reflect the various problems and aspects of transplantation mentioned above: (*a*) mechanical, i.e., the surgical steps of isolating and grafting an organ from a donor organism into a new host organism, (*b*) immunology of organ and tissue transplantation, host: graft compatibility and the bases for rejection reactions comprising the most prominent part of these studies, and (*c*) metabolic and general evaluation studies, with respect to continuing effective structure and function, in patients who have been recipients of transplants. Studies supported in all of these aspects are frequently carried out in experimental animals as an essential step in the potential application of tissue or organ transplantation in human subjects.

ORGAN PRESERVATION OR BANKING

To realize the full potential of transplantation, intensified efforts must be made to develop effective procedures for the preservation of freshly excised cadaver organs pending the selection and preparation for surgery of a matching recipient. To date it has become possible to preserve in viable condition human endeavor kidneys for up to 17 hours; if transplantation is ever to become a successful regular or route procedure, new and improved techniques for the preservation of cadaver organs for considerably longer timespans are essential. The most important single factor which at present limits the extent of kidney transplantation, for instance, is the dearth of living donor organs for which many would-be recipients wait for months. In the case of "single" organs like the liver or pancreas which cannot be donated by a living donor without causing his death, the only practical sources are cadaver organs. Under present techniques these must be transplanted within a very short time after death or they will not be viable. This severely limits the time available for essential immunologic matching to take place between the organ and the recipient. Thus, any large-scale and effective use of transplantation in the future hinges on the preservation of portions of cadavers or cadaver organs in a viable state for many hours and even days to permit adequate matching and efficient distribution of all available organs to a maximal number of suitable waiting recipients.

PROGRESS IN KIDNEY TRANSPLANTATION

At the present time, kidney transplantation is the most frequently executed and successful example of organ grafting, both in the United States and abroad. To a large extent it owes its success to the fact that an effective mechanical substitute organ (the artificial kidney) is available to rehabilitate the patient before surgery, to support the patient and the transplanted organ immediately thereafter and, if needed, to maintain the patient's life permanently (or until

a second opportunity for transplantation arises) should the organ be rejected.

In recent years, due to improved immunologic matching of donor and host tissues, the acute rejection of transplanted kidneys has become less of a problem. The 2-year success rate in kidney transplantation from a live blood relative is about 60 percent; that involving well-matched cadaver kidneys is about 40 percent. In most cases the patient must continue taking immunosuppressive drugs in an effort to prevent any belated rejection reactions. The problem of eventual rejection and inactivation of the transplanted organ is far from solved; recent research data indicate that even in the absence of overt acute rejection reactions, a gradual degeneration of the transplanted kidney takes place in cases (particularly involving cadaver transplants) where the tissue matching was not of the first order.

ADJUNCTS TO TISSUE TYPING

Because transplants, except between identical twins, are often ultimately rejected by the body, the critical problem still is to find methods to reduce, and some day to eliminate, the immune response to grafts without compromising the body's ability to fight off infection. Lasting success depends on matching the recipient's and donor's cells as closely as possible, and then overcoming any remaining minor incompatibility by inducing immunological tolerance in the recipient's body.

Certain immunosuppressive drugs for use in the prevention or control of the rejection phenomenon are being studied with special emphasis on drugs which will be more effective and less toxic than those presently available.

An antilymphocyte serum (ALS) fraction also called ALG (antilymphocyte globulin) has been used to help the body accept a new organ. The globulin tends to suppress the cellular reaction largely responsible for attacking the transplanted organ. Usually prepared in horses or rabbits against pooled human donor lymphocytes, the serum is commonly used in conjunction with other immunosuppressive drugs to combat rejection. It drew considerable attention among U.S. surgeons in late 1966 when an Institute-supported Denver surgical team reported its use in the first of a renal transplant series.

In addition to antilymphocyte serum, total and subtotal body irradiation, cytotoxic drugs and surgical manipulations of the lymphatic system are being used in attempts to reduce or eliminate the lymphocyte population and thus increase tolerance to homografts. These methods, however, also cause undesirable general effects, such as depression of bone marrow and red blood cell formation.

IDENTIFICATION OF HUMAN PROTEIN ANTIGEN-ANTIBODY COMPLEXES

A major immunological technique which may aid tissue typing has been developed by an investigator working with a team at the Brooklyn, N.Y., Veterans' Administration Hospital, sponsored by a contract from the Institute's artificial kidney program. The technique allows rapid identification of various human proteins by exposing them, in succession, to different antisera, to water vapor, and then by evaluating these complexes for their light-scattering ability.

This simple method is based on the knowledge that the ability of a solid to adsorb water is altered if it is first coated with a protein film and then exposed to water vapor. The protein films used in this study were either human plasma, a human fibrinogen-saline solution, and human albumin-saline solution or a 7S gamma globulin-saline solution.

In all tests the protein film appeared darkest, hence presumably the wettest, where it had been exposed to its matching antiserum. Whenever the test-film had been in contact with a nonmatching antiserum, it continued to scatter light maximally (i.e., it was not wettable) and appeared lighter. Fibrinogen-coated surfaces, which were affected by anti-fibrinogen serum premixed with serum. did not respond to the same anti-serum premixed with plasma. Plasma-coated surfaces were rendered most "wettable" by antiserum to fibrinogen.

This water vapor-light scattering method of identifying protein antigen-antibody complexes may prove useful as a simple and rapid procedure in tissue typing.

SHORT-TERM PRESERVATION OF ORGANS PRIOR TO TRANSPLANTATION

A transportable organ preservation machine has been developed by Institute-supported investigators in San Francisco. The machine has maintained human kidneys in a fully viable state for as long as 17 hours and animal kidneys as

long as 72 hours prior to transplantation. Human kidneys obtained from cadavers have been transplanted successfully following preservation by the device, which permits transplantation to be a somewhat more elective procedure, rather than an immediate one upon availability of a cadaver kidney. The device provides the necessary time for adequate tissue typing of the organ and proper matching to a suitable, waiting recipient.

The unique machine consists basically of a membrane oxygenator, pulsatile pump, perfusion chamber, filter and heat exchanger. It differs from previous perfusion devices in that its circulation pulsates, thus obviating the risk of uneven blood circulation within the organ and eventual local tissue damage. In addition, the machine utilizes as a perfusion medium plasma fortified with hormones and other additives, instead of whole blood, thus avoiding harmful local blood clotting in the perfused organ and breakdown of red blood cells.

While the isolated organ is being perfused, time is gained to allow matching of donor and recipient by tissue typing and to do preparatory surgery. The machine also eliminates the problem of simultaneous surgery and the need for two surgical teams, one to remove the kidney from its original location and the other to transplant it into the new host. Because the unit is easily transportable, perfusion of the isolated kidney can be started immediately upon its removal from the expired donor in one hospital, and continued during transfer to another hospital, even in another city, where the recipient is ready for transplant surgery. Although the device was developed specifically for the preservation of kidneys, studies are now underway to modify the machine for preservation of hearts and livers.

SUPPORTIVE BASIC RESEARCH

Paralleling the efforts to develop reagents, tests, and techniques for applying the knowledge already gained are research projects aimed at understanding the more basic immunologic processes of the human body. Intramural projects in Bethesda on immunology focus on such areas as hypersensitivity, mechanisms of the immune response, immunochemistry and induction of delayed hypersensitivity. Many of these studies are closely related to the problems of transplantation.

CLINICAL TRANSPLANTATION PROGRAMS

All major kidney transplantation programs in the United States are being carried out at large university centers where considerable research is continuing in such aspects as organ preservation, immunosuppressive therapy, tissue typing, and data collection and analysis. Some of these programs which are grant-supported by this Institute and form the backbone of clinical transplantation research in the United States are located at the University of California in San Francisco, the University of Colorado Medical Center in Denver, Duke University, University of Minnesota, and the Medical College of Virginia.

OPPORTUNITIES IN TRANSPLANTATION OF ORGANS OTHER THAN KIDNEYS

Strong efforts are now being undertaken to make liver transplantation a practical reality since it would be the answer to thousands of deaths occurring annually either as the result of acute liver failure from overwhelming viral hepatitis and liver poisoning, or as the result of chronic liver disease.

LIVER TRANSPLANTATION ADVANCES

Previous research has demonstrated the surgical and anatomical feasibility of liver transplants. Survival time in these studies has been limited primarily by poor immediate post-operative liver function. Institute-supported scientists at the University of Colorado Medical Center in 1967 reported the first successful liver transplantations in five children. Some of the recipients survived more than 1 year. Earlier hepatic transplantation efforts were successful to a maximum of 23 days. The investigators credited for the newfound success a combination of improved methods of immunosuppression, organ treatment and storage, tissue typing and organ-recipient matching, and operating technique.

To suppress tissue rejection, the investigators placed the patients on a regimen of antilymphocyte globulin (ALG) in combination with azathioprine and prednisone. Two of the donor livers were preserved prior to implantation with a newly devised hyperbaric storage technique combining the use of hypothermia (chilling)

to 4° C., hyperbaric oxygenation at 4 atmospheres pressure, and low flow perfusion with diluted blood. Previous animal experimentation had shown that this type of liver preservation resulted in as good a graft after 8 hours as did immediate transplantation.

Although the long-term prognosis for hepatic transplantation is unknown as yet, the outlook is continually improving. The fact that these recent liver transplants have continued to function long beyond the time limit achieved in earlier transplants holds promise for the future.

SUCCESSFUL THYMUS GLAND TRANSPLANT

A fetal female thymus gland has been successfully grafted into the abdominal muscle of a 7 months old athymic male infant by an Institute grantee at the University of Miami, Fla., and the child has normal immunological reactions 18 months post-operatively. This accomplishment supports the concept that the transplanted thymus is involved in immunological reactions and lymphocyte production.

Born without a thymus gland, the infant suffered from recurrent diarrhea, persistent nasal discharge (rhinorrhea), and diminished growth rate. Lymphocyte counts decreased during the first 6 months of life to well below the normal range. At age 7 months, thymic tissue from a 13-week-old female fetus was implanted into the infant's abdominal rectus muscle. Within 24 hours after implantation the lymphocyte count rose, and has since remained within normal limits. This increase was associated with subsequent cessation of diarrhea and rhinorrhea. To demonstrate a competent cellular immune mechanism, post-operative application of certain chemicals to the patient's skin produced a severe delayed hypersensitive reaction, in contrast to unsuccessful similar attempts to demonstrate delayed hypersensitivity preoperatively.

Prior to the thymic graft, results of several attempts to graft skin tissue (to establish presence or absence of immunological rejection) were equivocal. Four weeks post-operatively, however, the patient accepted an autograft and rejected an allograft, the reaction of normal immunological defense mechanisms. Furthermore, cytological studies showed no XX (female) chromosomes in present lymphocytes, thus indicating the patient's lymphocytes were derived from his own cells and not from the female donor gland. At age 25 months the child is growing normally and, significantly, has had no unusual infections, indicating that the transplanted thymus has successfully enabled the development of an active immunological system.

FIRST PANCREAS TRANSPLANTATION

A University of Minnesota surgeon receiving grant support from this Institute, achieved the first functional pancreas transplants in humans. Using cadaver glands, he established pancreatic transplant feasibility this past year in selected persons suffering from severe diabetes. Three of the four patients were dying from kidney failure caused by diabetes at the time of the transplantation.

The transplanted organ produced sufficient insulin, in three of four patients, to control the blood sugar levels of the person into whom it was transplanted. Although none of the patients survived for more than a few months following the surgical procedure, for reasons unrelated to the transplantation itself, the study proved that it is technically possible to transplant the pancreas. The Minnesota surgeon has predicted that such a procedure will become more common within the next 5 years, particularly in those who have developed severe diabetes in childhood which is not well controlled by insulin treatments. Patients with severe pancreatic disease (such as cancer of the pancreas) which is not amenable to treatment by current methods are also expected to benefit by this treatment.

FUTURE PROGRAM DIRECTION

Despite the relative success with kidney grafts, organ transplantation is still an experimental science. Many unanswered questions remain, such as: What physiogolical mechanisms are involved in the survival of a transplant? Why do failures occur?

It has become increasingly apparent that improvement in success of kidney transplantation, and organ transplantation in general will depend primarily on additional knowledge in the area of human tissue immunology and on the development of effective methods of donor tissue and organ preservation. Multidisci-

plinary studies of the immunologic and thereapeutic means available for achieving permanently successful grafts must continue to be pressed. In addition to a constant refinement of surgical techniques, sophisticated and reliable methods must be developed for immunologic matching of donor and recipient tissues with the same precision now available in blood transfusions. Likewise, new methodology must be sought for preserving and banking donor tissues and organs for the varying and sometimes considerable time periods between their availability and the finding of a suitably matched recipient.

Investigations such as those outlined above have added much to our ability to transplant the various organs of the body. They have indicated, as well, areas for much-needed new research efforts in order that more widespread and more permanent controls of mankind's chronic diseases may be accomplished through organ transplantation.

COST OF ARTIFICIAL KIDNEY TREATMENT

Mrs. REID. At that time this man said that there was only one, dialysis center in that area, and they could only take nine patients, so he was on a waiting list to get to the hospital for I don't know how long. It was costing him over $10,000 a year for these treatments. He said that there was really no State program at all. There was no directive, and he felt that the national program was nil, to use his expression. If this has been improved in the last 2 years, I think it would be good to provide this for the record.

Dr. WHEDON. I shall be very glad to.

(The information follows:)

Unfortunately, little has changed in the last 2 years. Most States have been reluctant to start special programs to aid their victims of kidney failure; neither has there been much initiative on the part of private philanthropy. The overwhelming majority of health insurance companies do not include, at this time, chronic dialysis in their policy coverage. About 3 years ago the Federal Government, through the kidney disease program of the Chronic Disease Division of the Health Services and Mental Health Administration, organized 14 special chronic dialysis hospital centers to serve as demonstration centers which would familiarize the medical profession, hospitals, and local communities with chronic dialysis. Localities chosen for these demonstration centers had to obligate themselves to take over the funding of the centers after the first 3 years of Federal operation. Similarly, 12 centers have been organized with Federal funds to teach suitable patients how to carry out chronic dialysis in their homes.

Dr. WHEDON. If I may add a couple of things, the Federal contribution in this respect has been primarily in the provision of funds for research to learn more about chronic kidney disease, how it comes about and, hopefully, how it can be prevented. This is extremely important to do because this will ultimately cut the number of patients that develop. Federal funds also, of course, have supported artificial kidney development and kidney transplantation.

Mrs. REID. Approximately how many people die from this kind of disease?

Dr. WHEDON. We estimate about 55,000 people a year die from chronic kidney disease of all sorts. Of this number, between 7,000 and 8,000 per year are of the type that lend themselves to artificial kidney treatment. The other facet of our effort has been the artificial kidney program which supports by contract development of improved methodology in this activity. The chronic disease program of the Health Services and Mental Health Administration has been able to support a limited number of dialysis centers for a limited period of time, for community demonstration purposes, usually for 3 years, as an illustration of the practicability of this technique, but funds have not been available beyond that period except through local sources.

I want to complete the picture by saying that we do not believe that the artificial kidney is the final answer in the treatment of chronic kidney disease at all. Kidney transplantation is really the method which will be most effective, at least for larger numbers of people, and I should put in also that even with a very effective transplantation program there will always be a need for the artificial kidney in preparing patients for tranplantation, for carrying patients when a transplant is unsuccessful, until another organ can be found, and so on. Again, more patients will ultimately be handled properly by a very effective kidney transplantation program when we lick the immunology, organ-rejection problem.

KIDNEY TRANSPLANTS

Mrs. REID. Do you have any reason to believe that the rejection factor will be lower in kidney transplants than in heart transplants?

Dr. WHEDON. Well, I think there were some original guesses that there might be less of a problem with the heart, but my understanding is that it is an equal problem with both organs.

Dr. BERLINER. There is one problem that you have in the case of the kidney. The patient can be kept alive on an artificial kidney until you have a kidney that matches that patient, whereas in the heart there is very little choice. You have reached the end of the road. It is then or never.

In addition, so far there has been a little more luck with keeping kidneys suitable for transplantation for longer periods to permit matching with a group of available recipients than the heart. Results with kidneys are better. One additional factor, in a limited number of patients, although this has been decreasing, we have been able to receive kidneys from living donors because everybody has two kidneys and they can get along with one. Therefore, we are able to do this kind of matching related to that and the results are better. Although, as I say, there has been a tendency for that source to diminish.

Mrs. REID. Would the capillary kidney take the place of the kidney transplant?

Dr. WHEDON. No, ma'am. It is another artificial kidney and would have the same uses, and we trust, at least as efficiently if not more so than the other types now available, with certain advantages in utilization and cost. It would not obviate what we predict will be the greater usefulness of truly effective transplantation of natural kidneys.

Mrs. REID. I should think making the public more aware of this problem would be helpful as the iron lung was helpful with polio. Honestly, I was not aware of the dialysis center until I talked with this gentleman in my district.

Dr. MARSTON. Mrs. Reid, I think the point that you make about the iron lung is a very important point to reinforce something Dr. Whedon said earlier. The real answer to polio was not bigger and better iron lungs but it was to understand the disease and to be able to do something about it. The real payoff in terms of chronic renal disease is going to be in preventing it, not in developing gadgets, important as they may be for a short term or on a short-term basis, or even the very expensive utilization not only in dollars but in terms of manpower that is involved in kidney transplantation.

Mrs. REID. I think it might be helpful if the public were made more aware of this disease and the expense involved in the treatments.

Dr. MARSTON. I have two experts here, Dr. Whedon and Dr. Berliner, but I think one of the problems has been the sense of overpromise to patients. I have seen this on the local level. There are patients who just are not suitable for this type of treatment, and it is very hard to have people who are sick to understand that this may not be the answer for their problems.

Then there is the rather overhelming cost factor. And I am not talking just in terms of dollars. I am talking in terms of the utilization of resources which has led to a special study that perhaps Mr. Cardwell will want to comment on—the whole problem of the so-called catastrophic illness, when you have these very high costs in terms of utilization of manpower and facilities that raise the question of whether you are going to do less in other areas in terms of devoting a large proportion of your resources to these areas. That is the type of question that, Mr. Michel, you were raising a couple of days ago of how much of your resources do you put into this versus the problems of young people and children, and so forth.

Mrs. REID. I know it is most difficult to set any priority in this kind for a program.

Dr. MARSTON. Right.

ARTHRITIS

Mrs. REID. It is my impression from your statement and the justifications that research in the field of arthritis is primarily centered on rheumatoid arthritis.

Dr. WHEDON. Yes, ma'am.

Mrs. REID. Are rheumatoid arthritis and other forms of arthritis medically related so that research which is applicable to rheumatoid arthritis applies to other forms of arthritis also?

Dr. WHEDON. They are all related but primarily—

Mrs. REID. In other words, do you have to have separate programs for other forms of arthritis?

Dr. WHEDON. They are related primarily in that they involve the joints and tissues about the joints. Even though the directions of research effort are really quite different for the different kinds of arthritis, we group them together in our intramural operation so that the investigators working on the different kinds of arthritis have their laboratories side by side and see patients together, in anticipation that ideas will be exchanged from one investigator to another. Also, of course, we group them together as we administer our research and training grants. Many of our grantees, for example, are working both on rheumatoid arthritis and on osteoarthritis at the same time. Patients with one or the other of these two main types frequently are seen by the same physician who is knowledgeable over this whole field.

PANCREAS TRANSPLANTS

Mrs. REID. You mentioned in your justifications that in the coming year the Institute expects to give greater attention to pancreas transplants to alleviate diabetes. You don't hear much about pancreas transplants as yet. Have they been successful?

Dr. WHEDON. Very few pancreas transplants have taken place. I think only enough to indicate to the surgeons that such a type of transplantation is probably technically feasible.

Mrs. REID. You cannot tell about the rejection factor as yet?

Dr. WHEDON. There have not been enough of them done as yet, I don't believe, to tell us. The principal point with regard to pancreas transplantation is that we really feel it is rather premature until we are able to learn much more about diabetes. In other words, I think the potential usefulness of pancreas transplantation is not clear in most minds at the present time. You have raised a tricky and fine point.

Mrs. REID. Thank you. That is all.

CYSTIC FIBROSIS

Mr. MICHEL. I am sorry I was not here for all of your testimony and interrogation. I understand the subject of cystic fibrosis has been developed quite thoroughly. You are aware, I am sure, of my personal interest in that. Having cited some quite personal relationships to it in past years, I will not repeat it except to say I think some of the figures that have been spread upon the record in years past show there was a ray of hope that we could move ahead pretty fast in that area. I am glad to see the progress that has been made, and assume that on the record heretofore you have inserted what you have been doing with the additional money we provided.

Dr. WHEDON. Mr. Michel, I am not sure that enough is on the record in this regard. I explained briefly to Mr. Casey off the record what our procedure had been this past year with regard to the management of the directive with regard to research grant funds, and the way in which we used advisors, many of whom came from advisory committees of the National Cystic Fibrosis Research Foundation to meet with us and define cystic fibrosis research and establish a set of guidelines as to what grants should fit or should not fit into this effort. It was on the basis we assigned our grants leading to the summation of approximately $2½ million.

But your question just now speaks more to the more important aspects I think, and that is what are we doing with these dollars. I think I shall try to summarize briefly for you the way I see it.

The principal finding of the past year was the finding of a peculiar staining reaction of fibroblasts taken from the skin of cystic fibrosis patients and then placed in tissue culture. A peculiar color developed on staining which enabled cells from the cystic fibrosis patient to be distinguished from those of other individuals.

It was further found that this same sort of staining, although in different degree, was present in individuals who are carriers of the disease, a relative for example or parents who do not actually have the disease. This new technique of identifying tissues that carry the genetic traits for cystic fibrosis will enable us to intensify our study of the genetic or molecular basis for the disease to find out more about how it is transmitted and what the opportunities truly are for particular offspring to develop the disease itself.

Mr. MICHEL. I think I read in your testimony very hurriedly that

you have come to the preliminary conclusion that males afflicted with cystic fibrosis are sterile.

Dr. WHEDON. That is correct.

Mr. MICHEL. And is it not true that genetically it is passed from the mother on down to the children?

Dr. WHEDON. With respect to the latter part of your question, the trait may be passed by either a male or female, but the presence of the disease depends upon the trait being from both the male side and the female side of the family, as I understand.

With regard to male infertility, Dr. Harry Shwachman at the Children's Hospital in Boston, is the one who has made these studies and what he found apparently is a congenital absence of the vas deferens, which is the tube that leads from the testes up to the seminal vesicles and delivers the sperm. If this duct is truly absent, this clearly indicates a genetic influence which brings about this particular defect. I assume that he and others will look into this more carefully to see whether there may be other influences which could lead to the infertility of the male.

Mr. MICHEL. Please feel free to expand in the record on anything in this area.

ARTHRITIS IN CHILDREN

What about the incidence of arthritis in children? Is this very pronounced? I heard of a case just a short time ago, a 9-year-old child being diagnosed as having arthritis. I was not aware that young children might have it.

Dr. WHEDON. Rheumatoid arthritis can occur at any age. It is much more frequently developed after age 40, but it can occur during the twenties and thirties, and there certainly are cases in which the disease has developed below the age of 10. In that instance, usually the disease seems to be very severe, and it is a very difficult problem to treat.

NUTRITION

Mr. MICHEL. What are you funding in your shop so far as nutrition is concerned?

This is not a new area for you, is it? The thing that is a little bit distressing to some of us is that throughout the budget and in every department they are getting into the act on nutrition. The same would hold true for other popular areas that make the news, and sometimes we ask ourselves whether we have proliferated this thing to such an extent that nobody knows what anybody else is doing. There must be a lot of duplication of effort and waste of money and resources.

What do you have to say?

Dr. WHEDON. Mr. Michel, nutrition research is one of the oldest activities of this institute. One of the very early laboratories in our Institute at NIH, long before there was a National Institute of Arthritis and Metabolic Diseases, was a nutrition research laboratory. The cause of pellagra, for example, was discovered by an NIH investigator in that activity, and much subsequent research on the A, B, and E vitamins has been done at Bethesda by our people.

Mr. MICHEL. Do you know if that word has been disseminated to the extent that all of these other shops that are getting into the act

now are not going to be duplicating the effort. Are they aware of what you have done in the past?

Dr. WHEDON. Mr. Michel, we try.

Dr. BERLINER. I might also point out that Dr. Whedon's two immediate predecessors as directors of the Institute were nutritionists.

Dr. WHEDON. I am the first nonnutrition director and even that might be questioned because I have a particular interests in calcium metabolism, and it is rumored that minerals have something to do with nutrition.

Mr. MICHEL. Put in the record the amount of money that was spent in 1969 in this area, and budgeted for 1970.

Dr. WHEDON. The amount is $7.8 million for 1970. We are the focus of nutrition research in NIH. We support more than half of the research grant activity in nutrition at the National Institutes of Health, and, of course, NIH is the largest supporter of medically oriented nutrition research.

Mr. MICHEL. What is the figure in 1969?

Dr. WHEDON. $7.8 million.

Mr. MICHEL. The year before that?

Dr. WHEDON. $7.7 million.

Mr. MICHEL. Then I have to ask the question: will this go on for 25 years like this, $7 million for research in nutrition? What are we getting for our money?

Dr. WHEDON. I think progress is definitely being made. I think the particular example that we cited this year was the discovery of the biologically active form of vitamin D.

I might say that I am sure you have heard of the surveys that have been conducted initially in foreign countries and now in various parts of this country to detect the degree of malnutrition, particularly among our rural and urban poor. One of the analytical methods used in these surveys, one to detect thiamin deficiency, was developed on a grant supported by this Institute.

We are particularly interested in problems of malnutrition as they relate to mental development. This is of particular interest of course to Child Health Institute. We support it and work with them in the United States-Japan cooperative medical science program.

Mr. MICHEL. In these grants you just spoke of, that are currently alive, how would they break down as to what we doing for own country and what we are doing abroad? Because with all of the attention given to it here at home, you can just imagine up there on the floor some Member raising the question of spending this money trying to find out what the problems are abroad when we have not even figured out what the problem is here at home.

I can foresee that kind of a question being raised. So I raise it to you.

Dr. WHEDON. We do have significant support of nutrition research abroad, but our preponderant effort, of course, is here at home.

In an effort to help you with the answer to that question, I would say that the two efforts are complementary, they help one another. Many of the studies of nutrition that we conduct abroad, we do so because there we can find a greater concentration of cases and of a particular kind and in a particular place, so we can do a more appropriate study. But the results of such a study apply potentially, are clearly applica-

ble, to the problems of nutrition at home. I think it might well be helpful to you to have this special report on nutrition for the record, in which we have attempted to fill out this theme I have just submitted to you.

Mr. MICHEL. I think so far as my own personal desire is concerned, I would like to see it made a part of the record.

We have done something similar to that over in the Agriculture Subcommittee.

You have long been established in this area and I think it would be something well worth while to be placed in the record at this point.

(The report follows:)

SPECIAL REPORT ON NUTRITION

The National Institute of Arthritis and Metabolic Diseases (NIAMD) is responsible for approximately two-thirds of the nutrition research supported by the National Institutes of Health and about three-fifths of all medically oriented nutrition research supported by the Federal Government. In addition to direct research activities in the laboratories and clinics in Bethesda, NIH supports a wide variety of research projects through grants to research centers and medical institutions throughout the United States and abroad. These activities cover the full spectrum of nutrition research from fundamental metabolic and physiologic studies and investigations of dietary requirements of the various nutrients to programs designed to determine how best to alleviate malnutrition and nutritional deficiency diseases both in the United States and abroad.

SCOPE OF THE GRANTS PROGRAM

The grants program may be divided into two groupings, physiology of normal nutrition and nutritional disorders. Projects in the physiologic processes of normal nutrition involve such entities as body composition, digestion and absorption of nutrients in the gastrointestinal tract; appetite regulation and food intake; the biochemistry and physiologic role of nutrients; their fate in the body; quantitative requirements of proteins and amino acids, carbohydrates, fats and fatty acids, minerals, trace elements, vitamins, and fluids and electrolytes; interrelationships between different nutrients and between nutrients and hormones, and nutrients and enzymes; nutrition in infancy; nutrition in old age; and the relationship of the intestinal flora to nutrition.

Research in abnormal nutrition involves discovery and definition of deficiency states, nutrient toxicity, obesity, malabsorption of specific nutrients, and the relationship of diet to specific disease entities (such as the role of saturated versus unsaturated fatty acids in the possible genesis of atherosclerosis and coronary heart disease). Another major subdivision of these research grants relates to nutrition in specific diseases or stress states, such as in diabetes, bone and joint disease, liver disease, gastrointestinal disease, infectious disease, disorders of immunity, anemia, endocrine disorders, gallbladder disease, inborn errors of metabolism, skin disorders, kidney disease and urolithiasis, stress (including surgery, trauma, wound healing and environmental extremes), and reproduction and pregnancy.

In addition to this broad research grants program, the NIAMD finances and administers a substantial and comprehensive program providing research fellowships and graduate research training grants in nutrition.

SPECIAL NUTRITION STUDIES ABROAD

A report on nutrition-related activities of the NIAMD would be imcomplete without mentioning the malnutrition/nutrition portion of NIH's United States-Japan cooperative medical sciences program which is financed by a separate appropriation, carried in the budget of the National Institute of Allergy and Infectious Diseases, but which is administered for programmatic reasons by the NIAMD. The mission of this program is to support research aimed at practical solutions to nutrition and nutrition-related problems of countries in Southeast Asia. This substantial grant and contract program supports research in the

following areas: relationship between malnutrition and mental development, and between malnutrition and infection, nutritional anemias, requirements for essential nutrients, biochemical adaptation to malnutrition, methods for evaluation of nutritional status, development of low-cost protein-rich food (including the enrichment of staple cereals with amino acids and other essential nutrients, the genetic improvement of protein concentration and composition in rice), and investigations into the occurrence and nature of toxic substances in foods.

Another portion of Institute-supported nutrition research overseas is carried out in India, Pakistan, and Egypt with U.S.-owned local currencies under Public Law 480. These studies are concerned with the causes, prevention and treatment of malnutrition and are located in underdeveloped countries because of the ease with which large populations with nutritional deficiencies can be found there. Discovery of pockets of malnutrition among our own population makes those studies of special importance to the welfare of our Nation.

DIET THERAPY IN CHRONIC KIDNEY FAILURE

Another important aspect of nutrition-related studies supported by the NIAMD is pursued in the Institute's artifical kidney-chronic uremia program. This program is a special research and development contract effort aimed at the development of improved and more effective dialysis hardware and methodologies and of methods for optimal rehabilitation of patients in chronic renal failure. A substantial effort is made through this program to develop and expand the use of special diets which permit effective rehabilitation and continued moderate to long-term survival of certain patients otherwise doomed to a rapid demise, without resort to artificial kidneys or kidney transplantation. These diets, originally developed in Italy, are based on the principle of internal reutilization of pathologically accumulating urea (in patients with renal failure) for the daily internal synthesis of new protein. Such diets are particularly useful in patients with chronic irreversible kidney failure who are unable to obtain treatment with artificial kidneys or kidney transplantation.

RESEARCH ACCOMPLISHMENTS

New vitamin D metabolite

Recent findings by Institute grantees at the University of Wisconsin have changed some old concepts of vitamin metabolism. Cholecalciferol (vitamin D_3), for example, has long been considered the active form of vitamin D. It is ingested in small amounts in food or formed from a precursor substance in the skin when the latter is exposed to ultraviolet light or sunlight. Now a new and significantly more active molecule, 25-hydroxycholecalciferol, has been isolated. This compound has already been shown effective in disorders of calcium metabolism which had not responded to the vitamin D preparations previously available. This suggests in such conditions an inability to convert ingested vitamin D to its active form. Apparent inability of the body to use vitamin D in the amounts required by normal individuals is a feature of several well-known disorders: hypoparathyroidism, malabsorption, celiac disease, and chronic renal diseases. Some cases of rickets, the classical vitamin D deficieny disease, also do not respond to holecalciferol in large doses. The new-found compound may provide answers to many basic questions of calcium absorption and physiology, and of bone formation; it may also lead to more effective treatment of disorders previously characterized by an apparent vitamin D resistance.

Diet, alcohol and liver damage

Institute-supported studies have indicated in the past that excessive consumption of alcohol can lead to development of fatty liver—forerunner of cirrhosis—in man despite a concurrent, well-balanced dietary intake, a finding contrary to the conventional hypothesis that a poor diet is the cause of alcoholic liver damage in alcoholic individuals. Institute grantees at Mt. Sinai School of Medicine and at Cornell Medical Division of Bellevue Hospital in New York City now find that, in persons who drink only occasionally, acute exposure to alcohol may lead rapidly (after only 2 days) to fat accumulation in the liver and intracellular microscopic structural changes, regardless of nutritional factors. After 2 days this damage is reversible, but it beomes permanent and cumulative after more prolonged exposures.

According to the investigators, it is clear that alcohol can rapidly produce liver injury when taken in amounts equivalent to those consumed not only by recognized alcoholic persons but by many "social" drinkers as well. The blood alcohol level determinations during the experiments showed that a person need never have been intoxicated to sustain alcohol-induced liver injury.

These findings are significant because they provide insight into the pathogenesis of the alcoholic fatty liver and indicate that, regardless of the high quality of the concurrent diet, alcohol per se in even moderate amounts can lead to the production of a fatty liver.

Malabsorption of vitamin B_{12} in pernicious anemia

Primary pernicious anemia, an ultimately fatal disease unless proper treatment with vitamin B_{12} is instituted, is attributed largely to failure of the gastric mucosa to secrete intrinsic factor, a substance which facilitates normal intestinal absorption of dietary vitamin B_{12}. Secondary intestinal malabsorption of vitamin B_{12} (and of other substances) has now been described by Institute grantees and is believed to be rather common in pernicious anemia. Deficiency of the vitamin causes generalized damage of the intestinal mucosa which then further aggravates vitamin malabsorption even in the presence of therapeutic intrinsic factor, creating a spiraling deterioration of the condition.

Using electron microscopic studies with radioactive vitamin B_{12}, grantees have shown that the vitamin enters the mucosal cells only at certain sites near the tips o fthe villi (fingerlike projections which increase contact area of the intestinal lining). These areas are abnormally flattened in the vitamin B_{12} malabsorption syndrome. The investigators postulate that the growth of the surfact cells of these structures is too slow when vitamin B_{12} cannot be absorbed because of the lack of intrinsic factor. Rapid catabolic processes of the cells therefore continue unchecked, predominate over synthetic processes, and deterioration of the mucosal structures takes place. The vitamin is required in all body cells for the formation of nucleoproteins which form the building blocks of the cell nuclei. Areas where rapid call turnover is necessary for normal function, such as in secretory membranes, the lining of the intestinal tract and sites of erythropoiesis (red blood cell formation) may be the first to react to deficiency of the vitamin, since these areas are constantly producing new cells and, therefore, need adequate amounts of nucleoprotein, which are not formed in the absence of vitamin B_{12}.

Milk intolerance and lactase deficiency

During the past 3 years, Institute-supported researchers have traced the cause of milk intolerance in certain otherwise normal adults and in patients with inflammatory bowel disease to a deficiency in an intestinal enzyme, lactase.

This enzyme, which converts lactose or milk sugar into its simple sugar components, glucose and galactose, is essential to digestion and subsequent absorption of lactose. Subsequently, increasing evidence has been found that intolerance to milk is a relatively common syndrome in adults.

Last year Institute grantees at Johns Hopkins University School of Medicine, Baltimore, demonstrated that milk intolerance based on lactase deficiency is much more common in Negro adults (70 percent in Baltimore and 72 percent in Uganda) than in the adult white population (5 to 10 percent), suggesting that intestinal lactase activity may be genetically controlled. It was also found that lactose-induced symptoms in Negro children and adults increased in frequency with advancing age, suggesting a gradual decrease in lactase activity after weaning. This was not as common in the white subjects studied.

Similar studies also have been carried out by Institute grantees at the University of Oklahoma Medical Center, Norman, Okla. Both the Johns Hopkins and the Oklahoma studies indicate that there is a distinct racial difference in lactase activity, and that a genetically determined intestinal lactase deficiency is responsible for the majority of instances of milk intolerance found in adults.

The same Johns Hopkins investigators now have shown that milk intolerance, presumably due to lactase deficiency, is also very common among adults of oriental ancestry. Thus, a large part of the world's nonwhite population may have a genetically determined intolerance to milk, a situation which would require reevaluation of the importance of milk as a source of nutrition and protein among nonwhite adult population.

These studies have considerable diagnostic and therapeutic significance, particularly for Negro and oriental patients presenting a variety of gastrointestinal symptoms, such as diarrhea, nausea, and abdominal pains, which do not appear to be related to any specifically manifest pathologic lesion. In view of these findings, it becomes necessary to rule out, in such patients, the presence of milk intolerance or lactase deficiency (a presently uncommon diagnosis in adults). Once this diagnosis is confirmed, dietary restriction of milk, milk products, and foods containing milk sugar (lactose) usually leads to cessation of the distressing symptoms.

Deficiency of other sugar-splitting enzymes

Malabsorption of other sugars has been traced to other enzyme deficiencies. Maltose and isomaltose, the major disaccharide end-products of starch and glycogen disgestion by pancreatic secretions, must be broken down by the enzymes maltese and isomaltese. Sucrose (another disaccharide), which is consumed in large quantities in natural as well as combined foods, is broken down by the enzyme invertase. Many cases of deficiency of these enzymes have been found in association with intestinal disorders and malabsorption. Some of these deficiencies are hereditary and others acquired.

Basic findings by several Institute grantees evolving from these enzyme deficiency studies have given new direction to our knowledge of digestion and absorption. Once it was held that disaccharide digestive enzymes are elaborated into the lumen of the intestine from the lining of the digestive tract. Some of them have now been found to exist and act inside the outer "brush border" membranes of the intestinal epithelial cells. Thus, disaccharide sugars (including sucrose), which have long been known to be unabsorbable from the intestine until digested into monosaccharides, do pass into the cells before being hydrolyzed. When the intestinal mucosa is damaged as it is in tenteritis, celiac disease, colitis and other intestinal ailments, disaccharide malabsorption symptoms may arise to aggravate the initial condition. Because sugars are active osmotically they serve to increase the amount of fluid in the intestinal lumen and this increase in bulk may irritate the tissue and speed food elimination before adequate absorption can take place. Another concomitant complication is the overgrowth of certain enteric bacteria which normally are a minority population of the gut flora but, because of their ability to metabolize sugars, grow in abnormal quantities in such conditions. Formation of gas and other irritating byproducts of their flourishing growth adds further insult to the intestinal tract.

Management of fat malabsorption

Dietary supplementation with a semisynthetic fat preparation, medium chain triglycerides, or MCT, has proved its value in managing fat malabsorption disorders of various origins, according to researchers at St. Luke's Hospital Center, New York. MCT has been used to provide additional nutrition both in disorders for which specific therapy exists and in those disorders for which no sepcific therapy is currently available.

Among the former are included gluten induced sprue, an intestinal sensitivity to the protein fraction gluten (found in wheat, rye, oats, and barley), pancreatic and biliary insufficiency, and Whipple's disease; among the latter are included malabsorption following gastrectomy (removal of part of the stomach) and massive resection of the small bowel.

The efficient absorption of MCT in fat malabsorption states has been explained by the finding that medium chain triglycerides are more rapidly hydrolyzed to fatty acids than are most dietary fats, which are composed of long chain triglycerides. In addition, the studies demonstrated that the presence of bile and pancreatic lipase in the intestine is not necessary for the normal absorption of MCT, explaining its importance in hepatobiliary diseases and in pancreatic insufficiency. Further, MCT may be of particular value in therapeutic diet in infancy and childhood, when malabsorptive disorders take more severe forms and tend to impair normal growth.

Sugar-induced calcuria and kidney stone formation

Many patients who develop calcium-containing kidney stones have none of the usual predisposing factors such as high serum calcium levels, urinary obstruction or urinary infection. Although some patients do have definitely high calcium excretion (hypercalcuria), others appear to have normal excretion. Institute-supported investigators have shown that both urinary calcium concentration and

total calcium excretion rise sharply above normal in calcium stone-formers and in relatives of stone-formers following ingestion of high-sugar foods.

Renal clearance was studied in 15 stone-formers and several relatives after ingestion of 100 grams of glucose or sucrose. All of the subjects responded with hypercalcuria and below-normal urinary volume with resulting higher concentrations of calcium in the urine.

The effect of the sugar load was attributed to a decrease in calcium reabsorption in the kidney and diminished urine flow in the kidney tubules, both of which would favor calcium salt precipitation. If the present findings are substantiated by further study, stone-formers may be advised to avoid high sugar intakes, particularly during exertion or in climates favoring dehydration.

Special diet therapy beneficial in chronic kidney failure

During the past year, the Institute's artificial kidney program has striven to encourage clinicial studies in the United States of a special diet, and modifications thereof, which has shown in trials in Italy and England that it permits moderate-term survival, cessation of symptoms, and rehabilitation in certain types of patients with chronic renal failure who are otherwise faced with the need for chronic dialysis or kidney transplantation. During a 21-month study period, Institute supported scientists in Los Angeles have indeed demonstrated that a 20 gram, balanced, low-protein diet limited largely to essential amino acids, but unlimited in carbohydrates and fats can ameliorate uremic symptoms in patients with minimal, residual renal function while maintaining a satisfactory body nitrogen balance. The results of dietary treatment, as measured by amount of relief from previous uremic symptoms and total duration of remission, were significant in all patients with an ability to excrete urea greater than about 2 percent of normal. Of 27 patients who followed the diet, relief of loss of appetite, nausea, vomiting, weakness, fatigue, and lethargy was obtained in 23. The results of therapy were felt to be good to excellent in 10 patients, with remission of symptoms persisting for 8.3 months in one patient. Serum urea nitrogen decreased in all patients. The resulting remission depends on prevention of acute deterioration of renal function and rigid adherence to the diet by the patient. The program has recently activated investigations to study the efficacy of a maintenance regimen which combines the use of this diet with infrequently administered peritioneal dialysis or hemodialysis.

Similar encouraging results were obtained by another contractor at New York Medical College who has already progressed to maintenance of patients with a combination of this diet and infrequently applied hemodialysis (once every 2 weeks rather than the conventional three times per week).

Feasibility of utilization of new types of protein sources

In the face of a worldwide shortage of dietary protein, there have been many suggestions concerning large scale development of food proteins from algae, yeasts, and from bacteria grown on relatively inexpensive petroleum wastes. An Institute grantee has been studying the nutritional consequences to be expected from large-scale dietary use of porteins derived from algae and other microorganisms. One of the imbalances of nutrients found in one-celled organisms is their high content of nucleic acids which are metabolized to urate and uric acid, the metabolites which are abnormally increased in gout. Using a purine-free basal diet varying in protein quantity up to 75 grams and varying in yeast ribonucleic acid up to 8 grams, investigators followed the uric acid levels in urine and plasma in health male volunteers. When 75 grams of protein was consumed, uric acid levels in the plasma were higher than when protein-free diets were taken and levels in the urine were lower. When nucleic acids were fed, the uric acid levels in both plasma and urine rose proportionately in four of five subjects.

The investigators concluded that for practical dietary supplementation of protein-deficient diets, nucleic acid content of microorganisms should not bar their use. These low protein diets, with 10 to 20 grams daily of microbial protein food added could be advantageous and are probably not hazardous with respect to their nucleic acid content. Addition of crude microorganisms to diets containing large amounts of muscle and organ meats however, should be approached with caution since they might precipitate an attack of gout.

Nutritional status of migratory farmers

In a study among migratory agricultural workers in the state of New York, biochemical tests of nutritional status were performed on blood and urine of 104 persons. One-third of the group proved to be deficient in riboflavin and thiamine.

Smaller percentages, particularly among the men, were deficient in ascorbic acid (vitamin C). The diet, prepared in a central camp kitchen, was found to consist almost entirely of beans, rice, luncheon meat sandwiches and potato chips. Wine was consumed with meals to substitute for impalatable high-mineral water, and constituted the largest single food expenditure. Alcoholism was not a problem among the workers, however, and the diet provided important quantities of iron. Fruits and vegetables which were being harvested were not being used in cooking, although amounts which may have been consumed in the field were not recorded. Recommendations were proposed for educating camp leaders of these groups in proper balance of foods.

Nutrition among American Indians

Phase I of a nutrition study directed by the Institute's Epidemiology and Field Studies Branch is now near completion. In this part of the new inquiry into disease patterns among the Pima Indians of Arizona, associations were sought between dietary practices and incidence of diabetes, gallstones, and rheumatic disease. Such knowledge would be expected to contribute significantly to an understanding of the cause of these prevalent ailments. Data from these studies has not yet been evaluated. In previous Institute studies, the Pima Indians have been found to have a prevalence of diabetes 10 to 15 times higher than the average population and a very high prevalence of gallbladder disease.

NUTRITION RESEARCH OVERSEAS

The Institute has traditionally conducted nutrition research in underdeveloped countries overseas because of the ease with which large populations afflicted with nutritional deficiency diseases can be found and studied there. Foremost among such research activities are studies in India, Pakistan, Egypt, and South Africa with particular emphasis on the cause, prevention, and treatment of malnutrition. Considerable contributions to our knowledge of normal nutrition and nutritional deficiencies have resulted from this work which has also yielded concrete benefits to the nutritional status of the local population. The recent pinpointing of pockets of malnutrition and nutritional deficiencies within our own population indicates strongly that these studies are not merely altruistic research exercises, but investigations of utmost importance to the welfare of the United States.

Protein malnutrition studies in India

Illustrative of such comprehensive studies, which also include developmental efforts to increase the world food potential are two interrelated research and development projects administered by the Institute in South India, and funded through Public Law 480 U.S. surplus commodity funds. One is located at the Central Food Technological Research Institute (CFTRI) in Mysore, and the other at the Christian Medical College (CMC), in Vellore. Both projects interdigitate closely in their ultimate aim. They are part of an intensive and comprehensive program to find a practical answer to the problem of protein malnutrition in a typical underdeveloped country setting, while simultaneously studying intermediary metabolism and selected metabolic disturbances in patients hospitalized for kwashiorkor (protein malnutrition). The Mysore project is concerned primarily with the laboratory development of protein-rich food supplements based on indigenous protein sources which are intended to prevent the widespread endemic kwashiorkor prevalent among preschool-age children in India; secondarily, this project involves animal testing and evaluation of such protein supplements, and studies of intermediary metabolism in kwashiorkor. In addition, the Mysore project has become strongly involved in the problem of aflatoxin, a highly toxic substance produced by mold growth in a wide range of foodstuffs all over the world. Aflatoxin is implicated in liver damage and carcinogenesis in animals and man.

The Vellore project encompasses clinical trials of the value of experimental protein blends developed in Mysore in the treatment of patients hospitalized for kwashiorkor, and large scale feeding tests in controlled institutional and village populations of the prophylactic value of these food supplements in the diet of weaning and school age children. In addition, selected metabolic disturbances associated with kwashiorkor are studied in hospitalized patients.

In view of the fact that the scope of the work undertaken is extremely broad and a very large number of individual projects are undertaken, only a very brief summary of recent progress is given in this report.

1. The CFTRI has succeeded in developing a series of protein concentrates and isolates from widely available indigenous plant sources. These include protein concentrates from peanuts, Bengal gram, soy, coconut, sesame and cotton seed. In addition, plain flours (some microatomized) of the above raw materials have been developed as well as solvent-extracted, defatted, and nondefatted fish flours. The preparation of these materials has posed a considerable series of technical difficulties which were overcome in the course of lengthy technological and chemical experimentation.

2. During each of these operations, determinations were made of original vitamin and amino acid content of the raw material and of the resulting refined product. The respective nutritive losses which result from the use of alternate choices of processing methods have been determined, and optimal technology has been developed for preparation of each product. Protein efficiency ratios (PER) and net protein utilization (NPU) were established of the various fractions obtained, and technological choices were made primarily on nutritional considerations, Where PER and NPU values of individual products appeared borderline or low, mixed or amino acid-fortified products were developed.

3. After a large series of animal tests and subsequent formulation of feasible protein food blends for human consumption, feeding experiments were carried out in controlled populations of children in Mysore. These involved many different blends based on the raw materials enumerated above. Significant increases in height, weight, red cell count, and hemoglobin levels were noted in children receiving daily supplements to their usual marginal diet with some of these blends, as compared with control groups receiving isocaloric cereal supplements.

4. A series of feeding trials has established minimal requirements for supplementation of typical, poor, rice diets with lysine, methionine (or dl-methionine hydroxy analogue) and threonine to obtain optimal biological value and net protein utilization in children.

5. A weaning food for infants based primarily on a nutritious mixture of inexpensive vegetable proteins has been developed and has now been accepted for commercial production by the largest Indian manufacturer of infant foods. The product has already seen small-scale animal and clinical testing in Mysore.

6. A Mysore-pioneered mixture of wheat (65 percent), peanut flour (25 percent), and Bengal gram (10 percent) under the brand name of Balahar is presently made by five different food manufacturers for use in the famine in the state of Bihar. The commercial price is 2.5 rupees per kilogram—and thus suitable for prevailing economic conditions in India.

7. Small-scale experiments in Mysore, involving 24 6- to 9-year-old children, have shown that lysine supplementation of a typical marginal sorghum diet can result in a distinct increase in growth and nitrogen retention. Similar experiments are being continued involving other types of local marginal diets.

8. The most important advance in Mysore is the development of a process which destroys aflatoxin in peanut flour. Almost all of the high protein supplements developed in Mysore and tested in Vellore in an effort to provide inexpensive, indigenous protein nutriture to preschool children as a prophylaxis against kwashiorkor are based on peanut flour. Unfortunately, because of the vargaries of the peanut harvest, and the lax methods of harvesting and storage used in India, much of the peanut stores is infested with aspergillus mold and consequently contain the highly toxic factor aflatoxin. Unless a commercially feasible method is found to destroy or remove aflatoxin from peanut flour in India, work with this promising base for any type of local, inexpensive high-protein supplement remains a theoretical exercise. The new process developed in Mysore which is now in the pilot plant stage is capable of destroying aflatoxin without inflicting organoleptic or nutritional damage on the basic raw material. Cost of detoxification is presently reported at 1½ to 2 cents per kilogram, which makes it economically feasible and not prohibitive for a food supplement to be bought by the poorest strata of the population. Animal studies carried out thus far seem to show that the process does not affect the protein efficiency ratio of the peanut protein.

9. A new method has also been developed for the spectrophotometric quantitative determination of aflatoxin. Preliminary results seem to demonstrate that the new method gives faster and more accurate results than the presently used biological tests.

10. In Vellore, a series of clinical trials involved children with kwashiorkor who were fed a variety of fish protein concentrates during convalescence (after recovery had been initiated with feeding of skim milk protein). One of these preparations from CFTRI in Mysore was found satisfactory with respect to clinical progress, nitrogen retention as judged by nitrogen balances, and regeneration of serum albumin. Another showed equivocal results, and suggestions for nitritive improvement of the product were proposed.

11. A very important finding was made during extensive studies on vitamin A metabolism in undernourished preschool children. Contrary to current practice and to previously published reports the group in Vellore has demonstrated unequivocally that the prophylactic injection of a single large lose of vitamin A in oil in children on marginal diets does not have prophylactic value with respect to eventual vitamin A deficiency and its clinical sequellae (which may include xerophthalmia and blindness). On the other hand, the feeding of 1 ounce per day of mixed green vegetables during a 6-month period protects such children from an excessive fall in serum vitamin A levels during the subsequent 6 months on a marginal diet devoid of greens. The Vellore group has now shown quite convincingly that injectable vitamin A in oil is prophylactically inactive in children with frank kwashiorkor. In contrast, the water soluble injectable vitamin A is highly effective. It has also been shown in Vellore that orally administered vitamin A in oil will not improve vitamin A serum levels (or liver storage) in children with kwashiorkor, but will be readily absorbed and will result in improved vitamin A levels once the children have recovered from the acute phase of kwashiorkor. In view of the well-controlled observations concerning the prophylactic failure of the injection of vitamin A in oil, efforts will be made to communicate these findings as broadly as possible, since in many quarters the injection of vitamin A in oil is relied on as a prophylactic measure in threatened child populations. The scientific staff of one of the manufacturers of this material in the United States has been apprised of the lack of efficacy of this material.

A new facet has recently been added to the Vellore project—studies on the fortification of wheat with lysine. Like many vegetable proteins, wheat protein is not of high enough biological quality to support rapid growth in children and to serve as the main source of protein in the human diet. Proteins of high biological value (usually from animal sources, such as milk, eggs, meat, and fish) have a qualitatively and quantitatively more complete complement of amino acid components. The first, most limiting amino acid in the incomplete wheat protein is lysine. There are indications that the addition of inexpensive synthetic lysine to wheat from the United States, which is used for control of undernutrition in India and other underdeveloped countries, might improve the biologic quality of wheat considerably—to the point where lesser quantities of the expensive and unobtainable animal proteins would be needed to attain satisfactory nutrition in the population. Because of the excellent clinical and field-testing facilities already operating in Vellore, a new program of experimental enrichment of wheat (as it is used in its various forms in the local diet) has been started, coupled with laboratory, clinical and field testing of the nutritive efficacy of lysine fortification.

Benefits to United States from overseas nutrition research

The Mysore-developed protein rich products which are evaluated in Vellore and the Vellore-initiated lysine fortification of wheat serve as prototypes for similar efforts in other underdeveloped regions of the world wherever agricultural necessities and economic and social factors preclude large-scale inclusion of animal proteins in the diet.

The scientific findings emanating from this work are enriching the fund of scientific knowledge in the United States. Of particular importance are the contributions concerning intermediary metabolism during protein deprivation and vitamin deficiency which could not have been carried out in the United States adequately because of lack of sufficient patient material concentrated in any one particular locality. Since the majority of these findings are published in American scientific journals they are disseminated to the rest of the world through the medium of the American scientific literature and are thus enhancing the standing and image of American science. These particular studies are also an example of effective and beneficial use of Public Law 480 funds in biomedical studies and demonstrate the value of continued Congressional support of this funding mechanism.

These efforts also contribute specifically to the technological knowhow of the United States food industry. Of particular importance are the contributions to our knowledge concerning aflatoxin. Traces of aflatoxin have been found in U. S.-made peanut butter. There is considerable importation of peanuts (which may be contaminated with aflatoxin) to the United States from abroad, and little is known concerning the presence of aflatoxin in many feeds used in the United States and the potential economic importance of such contamination. The laboratory techniques and technologic achievements in aflatoxin destruction developed in Mysore are of considerable importance in the United States both from the public health standpoint and that of agricultural and food economics.

Projects like those, in addition to the scientific aspects beneficial to the United States, are aimed at helping an underdeveloped country help itself. Rather than letting the host country rely on gifts of expensive protein-rich foods (such as powdered milk) from the United States which this country cannot afford forever, it gives the underdeveloped country the scientific wherewithall to utilize effectively inexpensive proteins which it can produce by itself and with the aid of which it can cope succesfully with the problem of protein malnutrition among its children.

Guide to nutrition terminology

Under the terms of a contract with Vanderbilt University awarded jointly by this Institute and the National Institute of Child Health and Human Development, A guide to the classification of nutrition terminology for indexing and retrieval is being developed. A broadening awareness of the relationships between diet and total health, combined with the rapid increase in world population which demands the most efficient nutritional technology, have created an urgent need for coordinated resources for nutrition data. The guide should help to make such data more readily available and definitive to researchers in the future.

OUTLOOK

Despite the wide reduction of frank nutritional deficiency diseases in this country, the margin of safety is not large. Improved methods of determining nutritional status and revised criteria for normal nutritional status have contributed to a new emphasis on the definition and diagnosis of malnutrition. Through application of new principles and laboratory techniques learned in recent years from studies of intermediary metabolism, many supported by this Institute, the evalution of nutritional status in the absence of overt disease is no longer dependent on ill-defined lesions and symptoms or the subjective judgment of physicians. These advances in knowledge now form the basis for exacting nutrition surveys needed to pinpoint pockets of malnutrition in vulnerable population groups in the United States. They will also be necessary in many developing countries to cope with the world-wide famine and malnutrition predicted for the near future if the runaway disproportion between population increase and agricultural self-sufficiency is not drastically reversed in the near future.

In relation to specific diseases, the discovery of the chemical nature of hereditary molecular diseases and of many physiological consequences of other lesser known diseases of uncertain etiology have contributed effectively to our understanding of the probable roles of required nutrients. Scientists now appear to be near to describing the nutritional participation of individual amino acids and fatty acids as well. The relationship of nutrients to ultramicroscopic physical structures is simultaneously evolving. Of greatest importance, among currently on-going studies, is elucidation of the role which dietary adjustments in lipid intake may play in large scale prophylaxis of atherosclerotic heart disease in the United States.

Once again, the study of nutrition has taken on the vigor which provided its first big advances with the discovery of vitamins 50 years ago. With continued research, investigators in the field of nutrition expect rewards in the near future to be fully as extensive.

Mr. MICHEL. Thank you. I think that is all.

We will stand adjourned until 10 tomorrow.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Metabolic Diseases

Amounts Available for Obligation

	1969	1970
Appropriation	$143,888,000	$139,968,000
Comparative transfer to: "Salaries and Expenses, Office of the Director", NIH	-486,000	0
Cutback required by P.L. 90-364	-3,170,000	0
Total obligations	140,232,000	139,968,000
Disposition of cutback:		
To be returned to the Treasury	3,170,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
133	Research		$91,691,000		$92,289,000		+$598,000
	General research support grants		(9,409,000)		(9,409,000)		(0)
	Scientific evaluation and planning		(20,000)		(20,000)		(0)
	Categorical clinical research centers		(1,500,000)		(1,500,000)		(0)
146	Fellowships		6,737,000		6,475,000		-262,000
148	Training		16,109,000		15,480,000		-629,000
	Direct Operations:						
150	Laboratory and clinical research	487	15,891,000	499	15,664,000	+12	-227,000
157	Collaborative research and development	25	6,498,000	28	6,670,000	+3	+172,000
165	Biometry, epidemiology and field studies	26	706,000	26	712,000		+6,000
166	Review and approval of grants	72	2,279,000	74	2,373,000	+2	+94,000
167	Program direction	20	321,000	20	305,000		-16,000
	Total obligations	630	140,232,000	647	139,968,000	+17	-264,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions.....	630	647	+17
Full-time equivalent of other positions...	36	38	+2
Average number of all employees.....	612	623	+11
Personnel compensation:			
Permanent positions.....	$7,049,000	$7,216,000	$+167,000
Positions other than permanent.....	259,000	266,000	+7,000
Other personnel compensation.....	36,000	36,000	0
Total personnel compensation.....	7,344,000	7,518,000	+174,000
Personnel benefits.....	698,000	714,000	+16,000
Travel and transportation of persons..	249,000	260,000	+11,000
Transportation of things.....	70,000	74,000	+4,000
Rent, communications, and utilities...	193,000	195,000	+2,000
Printing and reproduction.....	160,000	160,000	0
Other services.....	14,623,000	14,361,000	-262,000
Supplies and materials.....	1,496,000	1,580,000	+84,000
Equipment.....	880,000	880,000	0
Grants, subsidies and contributions...	114,537,000	114,244,000	-293,000
Subtotal.....	140,250,000	139,986,000	-264,000
Deduct quarters and subsistance charges...	-18,000	-18,000	0
Total obligations by object.....	140,232,000	139,968,000	-264,000

Summary of Changes

1969 estimated obligations	$140,232,000
1970 estimated obligations	139,968,000
Net change	-264,000

Increases	Base Pos.	Base Amount	Changes from Base Pos.	Changes from Base Amount
A. Built-in				
1. Annualization of 1969 pay costs	...	.....	...	$15,000
Subtotal, built-in increases	...	.....	...	15,000
B. Program				
1. Noncompeting research grants	...	$91,691,000	...	598,000
2. Laboratory and clinical research	487	10,068,000	12	178,000
3. Collaborative research and development contracts	25	6,199,000	3	179,000
4. Review and approval of grants	72	996,000	2	35,000
5. Program direction	...	287,000	...	1,000
Subtotal, program increases	...	.....	17	991,000
Total, increases	...	.....	17	1,006,000
Decreases				
A. Program				
1. Fellowships	...	6,737,000	...	$-262,000
2. Training	...	16,109,000	...	-629,000
Subtotal, program decreases	...	.....	...	891,000
B. Centrally furnished services from the National Institutes of Health management fund:	...	7,191,000	...	-379,000
Total, decreases	...	.....	...	1,270,000
Total, net change	...	.....	+17	-264,000

Explanation of Changes

Research grants--The net increase of $598,000 will support 48 fewer awards than the 2,220 supported in 1969. A total of 2,172 projects will be supported in 1970.

Fellowships--The decrease of $262,000 will fund 57 fewer awards over the 1969 level of 440 or a total of 383.

Training grants--The decrease of $629,000 will fund 24 fewer awards over the 1969 level of 299 or a total of 275.

Laboratory and clinical research--The increase of $178,000 will provide for 12 positions and essential research support costs in the laboratories and clinics.

Collaborative research and development--The increase of $179,000 will support 3 positions and provide for program increases in the Artificial Kidney and Diabetes Hormone Developmental Research Programs.

Review and approval of grants--The $35,000 program increase will support 2 positions and provide other support to strengthen this activity.

Program direction--The increase of $1,000 will assist in strengthening the overall administrative management activities in the office of the Institute Director.

Significant Items in House and Senate Appropriation Committee Reports

Item	1969 House Report	Action Taken or to be Taken
	"The Committee again directs that $2 million of the appropriation be devoted to Cystic Fibrosis research."	The Institute established special review panels and procedures to insure compliance with the directive. It is estimated that research grants on Cystic Fibrosis will exceed $2,500,000 in 1969.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301--Research and Investigation, in general.....	Indefinite
Title IV, Part D--National Institute on Arthritis, Rheumatism and Metabolic Diseases.....	Indefinite

PUBLIC HEALTH SERVICE ACT

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in Section 301 of the Public Health Service Act.

The Public Health Service Act, Title IV, National Research Institutes, Part D, National Institute on Arthritis, Rheumatism, and Metabolic Diseases, National Institute on Neurological Diseases and Blindness, and other Institutes.--

"Sec. 431 (a) The Surgeon General shall establish in the Public Health Service an institute for research on arthritis, rheumatism, and metabolic diseases...."

"Sec. 433 (a) Where an institute has been established under this part, the Surgeon General shall carry out the purposes of section 301 with respect to the conduct and support of research relating to the disease or diseases to which the activities of the institute are directed, through such institute and in cooperation with the national advisory council established or expanded by reason of the establishment of such institute. In addition, the Surgeon General is authorized to provide training and instruction and establish and maintain traineeships and fellowships, in such institute and elsewhere, in matters relating to the diagnosis, prevention, and treatment of such disease or diseases with such stipends and allowances (including travel and subsistence expenses) for trainees and fellows as he may deem necessary, and in addition, provide for such training, instruction, and traineeships and for such fellowships through grants to public and other nonprofit institutions."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and expenses, Office of the Director", National Institutes of Health.....	$486,000	.....	To provide funds covering expenses for the office of the Director which were previously funded through the National Institutes of Health management fund

National Institute of Arthritis and Metabolic Diseases

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	31,215,000	37,799,000	51,200,000	46,862,000
1961	47,541,000	52,841,000	70,760,000	61,200,000
1962	68,740,000	73,661,000	90,000,000	81,831,000
1963	91,921,000	98,721,000	105,721,000	103,388,000
1964	114,717,000	113,679,000	114,717,000	113,679,000
1965	113,369,000	113,344,000	113,544,000	113,344,000
1966	119,203,000	121,203,000	123,203,000	123,203,000
1967	129,908,000	133,687,000	135,687,000	135,687,000
1968	143,954,000	143,954,000	147,204,000	143,954,000
1969	151,718,000	141,287,000	147,287,000	143,388,000
1970	139,968,000			

Justification

National Institute of Arthritis and Metabolic Diseases

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation & benefits.	630	$8,042,000	647	$8,232,000	+17	+$190,000
Other expenses.....	--	132,190,000	--	131,736,000	--	-454,000
Total.....	630	140,232,000	647	139,968,000	+17	-264,000

General Statement

The responsibilities of the National Institute of Arthritis and Metabolic Diseases encompass an unusually diverse area, including the broad spectrum of arthritic, rheumatic, and collagen (connective tissue) diseases, various metabolic disorders such as diabetes, and cystic fibrosis, gastrointestinal diseases such as peptic ulcer, endocrine malfunctions, dermatological conditions such as psoriasis, diseases of blood, bone, liver, and kidney, and research in urology, nutrition and orthopedic surgery.

Established in 1950, the core of NIAMD was NIH laboratories noted for their fundamental studies in experimental biology and medicine, and the Institute was evolved as a center for new knowledge in biochemistry, nutrition, pathology, histochemistry, genetics and numerous other basic disciplines. One of this year's Nobel Prize winners, Dr. Marshall Nirenberg, had performed his pioneering studies of the genetic code in Institute laboratories. The Institute, moreover, maintains a tradition of nutrition research stemming from the classic work by Dr. Joseph Goldberger on pellagra as a vitamin deficiency disease.

The nature and variety of the diseases under its aegis have always provided NIAMD with excellent opportunities for mission-oriented research, quickly bridging the gaps between theory and therapy. At the same time, a primary function of the Institute is to prepare investigators in both basic and clinical fields and to conduct and support the fundamental biomedical research that is absolutely essential to discovery of cause of disease and to disease prevention.

The history of medicine and biomedical research and NIAMD's own experience has repeatedly shown that advances in the treatment and control of a disease usually depend on studies in fundamental knowledge applicable to the disorder. Thus, the Institute has had an important stake in the pursuit or support of research in fundamental sciences associated with its sphere of interests: i.e., biochemistry, enzymology, molecular biology, histology, pathology, pharmacology, toxicology, and genetics.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research projects.....	$80,762,000	$81,360,000	+$598,000
Special programs.....	10,929,000	10,929,000	0
Total research grants.....	91,691,000	92,289,000	+598,000

Introduction

By far the major effort of the National Institute of Arthritis and Metabolic Diseases is carried forward through its program of research grants involving more than 2,000 projects at some 400 institutions throughout the Nation. The expansion and resulting beneficial effects on disease problems of the grant-supported studies over the years has been a result of Congressional interest in and understanding of the principle that results in terms of new and effective treatments developed from extension of studies in many fields and at all levels, fundamental-laboratory and clinical-laboratory as well as at the bedside itself. In certain, selected instances, when opportunities were evident, added Congressional support has enabled the Institute to move forward in special areas and secondarily to extend its research efforts usefully across many fields. As the Institute's spectrum of disease responsibilities has widened, its influence has become an important factor in the Nation's health advances along a broad front.

Arthritis and Related Diseases

The three most crippling and prevalent forms of arthritis, rheumatoid arthritis, gout, and osteoarthritis, provide the primary disease orientation for arthritis grants.

About 16 million people in the United States afflicted with arthritis look to research for a means to relieve their suffering.

Rheumatoid arthritis alone, affects more than 4 million people and leads to permanent joint deformities and other complications producing disability and chronic invalidism. The majority of its victims are not elderly persons (as is the case in osteoarthritis) but are young and middle-aged adults in their most productive years.

The primary cause of rheumatoid arthritis is still unknown. Two leading theories, supported by considerable evidence, suggest that an obscure infectious process or an autoimmune reaction (characterized by manufacture by the body of antibodies that attack its own tissues) may be involved, or possibly a combination of both processes.

Much research has been and will continue to be centered on a possible infectious etiology for rheumatoid arthritis. While specific infectious types of arthritis are known to be due to invasion of joints by certain microorganisms, no microbial agent has yet been positively identified as a cause of rheumatoid

arthritis. Investigators had demonstrated that Bedsonia viruses isolated from human patients with Reiter's syndrome (a disease with some symptoms resembling rheumatoid arthritis) cause chronic arthritis when injected in monkeys. Now the investigators have extended the finding to rabbits and have demonstrated, further, that Bedsoniae infecting the eye will disseminate to joint tissues, liver, kidney, and spleen, in a manner suggestive of the involvement of major organ systems accompanying rheumatoid arthritis in humans.

If rheumatoid arthritis were produced by a common, easily cultured microorganism multiplying in joint tissues, the cause of the disease might well have been discovered by Pasteur a hundred years ago. To date, however, attempts to isolate one specific universally present organism in cultures from joints of patients with rheumatoid arthritis, have been unrewarding. Continuing attempts to demonstrate an infectious basis have implicated a number of organisms from time to time. These include species, mostly large viruses and the mycoplasma, known to cause slowly developing, degenerative diseases of connective tissue in animals. It has been impossible, however, to grow mycoplasma in culture with any regularity so that definitive studies necessary to prove their association with rheumatoid disease have not been able to be made.

A preponderance of future studies will also deal with the immune response as a possible precipitating factor in rheumatoid arthritis, including mainly (1) examinations of the molecular structure of immune proteins and (2) research into the causes of animal diseases that mimic human arthritic and connective tissue disorders. A study is now under way, for example, of the manner in which agents, such as invading microorganisms, antibodies, and active biochemicals, can permeate blood vessel walls and cause inflammation and lesions suggestive of arthritis. In another example of research for an immunological basis for rheumatoid arthritis, it has been demonstrated that certain components of human connective tissue and of streptococci are so similar that they cross-react immunologically. Thus it is possible that antibodies formed in the body to combat invading streptococci could mistakenly attack the similar components of connective tissue, initiating an autoimmune reaction with consequent destruction of connective tissues and joints. The finding illustrates that the concepts of an infectious and an autoimmune etiology for rheumatoid arthritis are not mutually exclusive, and points up the need for further research towards shedding light on this highly provocative area.

In the search for better drugs for treatment of arthritis, attempts will be made to re-design known steroid compounds which have demonstrated salutary anti-inflammatory action but which also cause serious side effects on prolonged use. Among other new agents, compounds related to triamcinolone have been subject to careful clinical testing. Among these is a new steroid drug triamcinolone hexacetonide, which seems to combine the important features of rapid and prolonged action with minimal side effects on prolonged repeated use.

Osteoarthritis occurs primarily with advancing age and has been generally thought to be a result of prolonged "wear and tear" on the joints. When inflammation and pain are present, antiarthritic drugs are employed. The new steroid derivative, triamcinolone hexacetonide, mentioned above, is an example of a number of drugs that will be under trial in the search for effective chemotherapeutic agents that can be used regularly without development of undesirable side-effects. Simultaneously the components of the synovial fluid

and the mechanisms of joint lubrication will be under extensive investigation in the hope that means can be found to control the degenerative changes of joint structures typical of osteoarthritis.

In one study of age and weight factors related to osteoarthritis of the hip, scientists have concluded that, somewhat against the "wear and tear" theory, body weight did not seem to be an important factor in the development of osteoarthritis in this important weight-bearing joint. Also, no relationship was observed between age and development of the disease when it occurred in both hips rather than in one, suggesting that the disorder is unilateral or bilateral at its inception rather than progressing from one side to the other with time. Studies such as this indicate the complexity of the mechanisms governing the genesis of osteoarthritis.

Diabetes

According to the best estimates there are, at present, approximately four million persons suffering from diabetes in this country. Moreover, another five million of our present population are expected to develop the disease during their lifetime. It is this knowledge which makes continued, intensive and effective research on diabetes an unceasing obligation on the part of investigators supported by the NIAMD.

A complicated disease, for which there is no known cure, diabetes ranks seventh on the list of diseases causing death in the United States. Diabetes has been known for some time to be a hereditary disorder. As a result of the body's inability to metabolize carbohydrates normally, the diabetic is unable to convert carbohydrates properly into the stored form, glycogen, or to utilize them for the energy required for normal body functions. The carbohydrates, in the form of glucose, accumulate in the blood and overflow into the urine. As the disease progresses, abnormal carbohydrate metabolism becomes associated with a noticeable derangement in the metabolism of fats and proteins.

Many diabetes investigators today believe that determination of the precise mode of action of insulin - how it is produced and released by the pancreas and how it does its vital work in human tissues - is essential to clarifying the cause or causes of diabetes. To this end many skilled scientists will devote their time and efforts during the next year. For example, studies will continue on a very recent discovery of a precursor form of insulin, labeled "proinsulin", in the human pancreas. It has been suggested that a partial or complete failure of proinsulin conversion to biologically active insulin may account for some form of diabetes. The discovery of proinsulin and further clarification of its molecular structure will have important implications for the eventual commercial synthesis of insulin in that it may suggest useful steps in the eventual laboratory manufacture of the hormone.

Evidence continues to accumulate rapidly clarifying the relationship between onset of the adult form of diabetes and obesity. During the past year an investigator showed that fatty tissue from obese individuals contains unusually large fat cells which are distinctly resistant to the action of insulin in facilitating glucose metabolism. The investigator will now attempt to determine the precise mechanism or primary tissue defect which underlies the diminished insulin sensitivity in such enlarged fat cells.

In relation to this finding, it has been reported that significant small blood vessel disease can be demonstrated in genetically prediabetic subjects prior to the onset of metabolic abnormalities. This finding suggested that small blood vessel pathology (primarily a distinct thickening of the capillary basement membrane), generally believed to be characteristic of overt diabetes, may actually represent the primary lesion of diabetes, followed only secondarily by derangement in carbohydrate metabolism.

A number of investigators have presented evidence to indicate that the insulin "resistance" encountered in certain tissues of obese and diabetic individuals may result solely from decreased transfer of the hormone across the capillary wall, from the blood stream to the tissue cells. Conceivably, the abnormal thickening of the basement membrane in capillaries affected by diabetic microangiopathy may constitute a hindrance to hormonal transfer.

Thus, there would appear to be a link between the small blood vessel disease observed in genetically prediabetic subjects and the apparent inability of the capillary wall to transfer insulin normally from the blood stream to the tissue cells. Further studies will be required during the next year to determine any possible relationship between small blood vessel disease, tissue resistance to insulin, and an inhibited transfer of the hormone across the capillary wall.

In the coming year Institute planning will also focus, for example, on the further feasibility of transplanting a normally functioning pancreas into selected persons suffering from severe diabetes, a procedure already performed in highly experimental trials this past year, and on continuing studies of a new oral hypoglycemic drug, glycodiazine, which has been shown to have promising antidiabetic properties.

Other Inherited Diseases of Metabolism

Although diabetes is the most prevalent and widely known of the inherited metabolic diseases, there are many other such disorders for which the Institute serves as the focus of research support. Among these are cystic fibrosis, phenylketonuria, Wilson's disease, galactosemia, alcaptonuria, histidinemia, homocystinuria, familial Mediterranean fever, the various glycogen storage diseases, congenital nonhemolytic jaundice, and many others.

Cystic fibrosis is a disease characterized, among other symptoms and signs, by an abnormality in the products of glands which secrete fluid to body surfaces. This disorder usually is seen as a grave disease of children, but adults may manifest a partial, less serious form of the disorder, recent studies suggest. Symptoms of chronic lung and gastrointestinal diseases in some older persons may stem from a partial genetic endowment of this error of metabolism.

Cystic fibrosis is inherited from parents who carry the genetic trait for the disorder (both parents may be asymptomatic). When both parents carry the trait, the chances are one in four that cystic fibrosis will be manifested in the severe and classical form in the offspring. If only one parent carries the trait, although the child may be asymptomatic, the trait may be passed to the offspring, who, in turn, may transmit the disease. Thus, for every overt case, there is a large reservoir of hidden carriers, recently estimated at 2 to 5 percent of the general population. Clearly, since the genetic character of cystic fibrosis makes the disorder particularly pernicious, a method of identifying such carriers would be a major achievement for genetic counseling.

In 1970, studies will continue on a highly significant finding which may eventually play a useful role in genetic counseling to spot cystic fibrosis carriers, to facilitate studies on genetic linkage, and to determine the frequency of this detrimental gene in the normal population.

The research finding involves a cellular difference between normal persons and those in affected or carrier states of cystic fibrosis. Using a special staining technique, this newly-discovered genetic cell marker can be seen in fibroblasts, the flat elongated cells which form fibrous tissue.

Skin biopsy specimens were obtained from 7 affected children, 13 parents, 26 healthy individuals, and from 11 patients with a variety of other diseases. Cell cultures of fibroblasts from the healthy group and from the 11 patients with varied other disorders showed only an occasional cell with metachromasia, a condition in which portions of the cell fail to stain uniformly and in the same color as surrounding cell materials. In all 7 cultures from children with cystic fibrosis, however, cellular metachromasia appeared in an average of 56 percent of the fibroblasts. A similar staining pattern was seen in 42 percent of cells obtained from parents of children with cystic fibrosis (carriers of the disease). Thus, the test, though still cumbersome, permits the identification of carriers of the trait for cystic fibrosis in cases where potential parents have requested genetic counseling.

One of the most important implications of this finding will lie in the results of direct investigation into the molecular defect of this metabolic disease. Up to now, clinical and chemical studies have indicated that cystic fibrosis is a generalized exocrine disorder. This new finding hints that the disease may be a multicellular disorder also involving the body's connective tissue, and further biochemical analysis of the metachromatic cellular substance may prove to be a step forward in elucidating this theory.

In the coming year research support in cystic fibrosis will also stress investigations to improve methods of treatment, such as a jacket-like device which has been developed through Institute support. It enables a patient to clear mucus from his respiratory tract through percussion by rubber padded disks operating rhythmically in the jacket. The method is significantly more effective than conventional physical therapy.

Institute grantees will continue to identify specific biochemical abnormalities at the root of other inborn errors of metabolism such as histidinemia and L-glyceric aciduria. The list of such disorders that can now be traced to specific inherited impairments in metabolism is steadily increasing. The Institute will support basic studies designed to advance existing knowledge of intracellular processes of metabolism, including protein synthesis and enzyme regulation and their genetic control.

Metabolic and Endocrine Disorders (Unrelated to Genetics)

Endocrinology concerns itself with the endocrine glands (pituitary, thyroid, adrenal, ovary, testic and others), with their secretions and with the effect of hormones on the chemical and physical processes of life. A wide spectrum of problems is involved, since the endocrine system, in close cooperation with the nervous system, controls almost all the metabolic growth and reproductive functions of higher animals and man.

Endocrinology is one of the cornerstones of modern clinical and biomedical research. NIAMD bears responsibility for the classic endocrine disorders, such as hypo- and hyperthyroidism, hypo- and hyperpituitarism, adrenal disorders, hypo- and hyperparathyroidism, and certain hormonal aspects of fertility and sterility.

In recent years, great strides have been made in our knowledge of the hormones and in the laboratory synthesis of specific hormones; yet, lack of fundamental knowledge of the precise mechanism by which hormones influence metabolism, and how hormones react with each other, hinders greater progress.

Osteoporosis, a disorder with mixed metabolic and endocrine background, afflicts a large percentage of women over 50 years of age, and many older men. Causing a gradual decrease in both the amount and strength of bone tissue, osteoporosis is often the real cause of the numerous broken hips which hospitalize so many older people, and in many cases, start their physical decline. This disease is one of the major causes of physical disability in old age, especially in women. In the following year, studies will continue on the involvement of nutritional, hormonal and genetic factors in the disease.

There has been a considerable upsurge in research activity concerning thyrocalcitonin, a recently discovered hypocalcemic substance secreted by the thyroid gland. Several laboratories will be engaged in extracting and purifying this hormone. Intensive efforts are underway to develop sensitive radio-immunoassay techniques for measuring the low levels of this hormone which occur in circulating blood. The development of more sensitive assay methods would greatly facilitate efforts to understand the mode of action of this substance which is apparently a new hormone. In addition, several laboratories have isolated purified parathyroid hormone, and research is underway to ascertain its mode of action. Efforts will be made to develop more sensitive methods of assaying parathyroid hormone circulating in the blood so that better diagnostic measurements can be made in humans. Further research on these two hormones can be expected to lead to a better understanding of the problems of calcium homeostasis, which in turn may make possible improvements in the diagnosis and therapy of diseases of abnormal mineral and skeletal metabolism.

This past year high levels of thyroid-stimulating hormone have been found in the serum and thyroid tissue of patients with thyroid cancer. This suggests that prolonged overstimulation by this hormone may be a causative factor in this disease, a hypothesis that now will be investigated more fully in the coming year. Elsewhere, grantees have been able to localize tiny tumors of the adrenal gland by measuring in adrenal vein blood the levels of aldosterone these tumors produce. The need for exploratory surgery and/or surgical removal of both glands in equivocal cases now is obviated through the new procedure.

Gastroenterology and Liver Disease

Gastroinestinal ailments are among the most common serious illnesses in this country. They rank second only to diseases of the heart and circulation in the number requiring attendance by a physician. Peptic ulcer alone, it has been estimated, strikes more than 10 percent of all adults in the United States at some time in their lives. Diseases of the stomach and intestines may strike persons of any age, but usually affect those in the middle-age groups at the

peak of their most vigorous and productive periods, often causing prolonged and expensive hospitalization and countless social and emotional problems.

The causes of many of these disorders, such as peptic ulcers, ulcerative colitis, regional ileitis, among others, seem to lie in highly complex interactions of a variety of factors. In a few disorders, the results of various investigative approaches are disparate, and potential gains must be discussed with reference to ultimate objectives.

In recent years grant-supported investigators reported that the chemical nature and structure of gastrin, the hormone which stimulates secretion of gastric juices, was elucidated and the hormone subsequently synthesized. This last year it was shown that gastrin resides within particular cells of antral pyloric glands, a finding which should further stimulate research this next year in the peptic ulcer field.

Research will be followed on the effects of alcohol intake on the liver, as well as on milk intolerance and deficiency of the enzyme lactase. During the last year it was determined that discernible liver damage can result even from occasional weekend social drinking, despite a well-balanced diet. Continuing studies of milk intolerance in adults, traced by grantees to a deficiency of the intestinal enzyme lactase, essential to digestion of lactose (milk sugar), have shown that the deficiency is common in adults and considerably more common among Negroes than among whites. More recently, it has been found to be very common among adults of Oriental extraction. Thus, a large part of the world's non-white adult population may be intolerant to milk, a situation which would require re-evaluation of the importance of milk as a source of nutrition and protein among non-white adult populations.

Other recent achievements to be followed next year in gastroenterology include a new treatment for malabsorption in intestinal scleroderma; a new diagnostic technique to detect patients with ulcerogenic tumors of the pancreas; and the successful use of exchange transfusions in moribund patients with hepatitis.

Studies in acute liver failure will also be aimed at developing extracorporeal treatment systems to "carry" patients until their livers heal sufficiently to resume normal function. Experiments will continue, for example, on a method of circulating a patient's blood through the isolated liver of a large experimental animal until the human liver recovers and regains its ability to function.

Institute-supported investigators have achieved significant advances in the very difficult procedure of liver transplantation in patients with end-stage disease, through use of advanced surgical techniques, the judicious use of a serum that modifies rejection mechanisms of the body (antilymphocyte serum), improved organ storage, and meticulous tissue typing. Prognosis for liver transplants is continuing to improve, with a few young recipients surviving up to a year or more. The antilymphocyte serum (ALS) fraction, employed by Institute grantees is commonly used with immunosuppressive drugs to combat rejection not only of liver and kidney transplants but of other organ transplants as well.

Kidney and Urologic Disease

Today in the United States, an estimated 55,000 individuals die each year of irreversible kidney failure. Medical authorities agree that development of optimal treatment to reach all of these people depends on better knowledge of uremia and on further fundamental improvements in organ transplantation. Even more important is effective understanding of the primary kidney disorders which lead to end-stage uremia. Such understanding would ultimately be more effective in dealing with the kidney diseases since it would lead to prevention as well as better control.

The importance of the kidneys can be judged in part by the fact that they receive about one-fifth to one-fourth of the blood volume pumped by the heart. By selective excretion of certain substances and reabsorption of others, the kidneys play an extremely important role in regulating the composition of blood and other body fluids. They continually process blood to eliminate harmful waste products of metabolism. The kidneys help to regulate the chemical environment of the body cells by regulating the concentration and composition of salts and the amount of water in the blood and tissues. They also produce substances which are important in regulating blood pressure and in stimulating the bone marrow to produce cells.

The term kidney disease encompasses a number of conditions of varying etiologies. One characteristic common to most of these diseases is their tendency to eventual progression to a common end-stage - the clinical syndrome of uremia. The term end-stage uremia denotes the total combination of signs, symptoms and pathology resulting from the loss of the kidney's normal functions of removing wastes from the body and of regulating the internal chemistry of the body.

Patients with uremia may be divided into two groups: those with acute kidney failure, and those with chronic renal insufficiency. In acute kidney failure, the kidneys are damaged by an acute insult and the symptoms of uremia appear and progress rapidly. The damage may be reversible, however, and after a short period the kidneys may heal and regain normal function. On the other hand, chronic kidney insufficiency is brought on by gradually progressive destruction of functioning kidney tissue from which the kidneys do not usually recover. In these cases the kidneys never regain the ability to reverse the trend toward ultimately fatal uremia.

Research support planned by this Institute in the coming year in kidney and urologic disease will continue to develop basic, clinically useful information on diseases of the genitourinary tract, as well as on the ultimately fatal uremic syndrome of end-stage kidney failure, dialysis therapy and kidney transplantation.

Two therapeutic modalities have come into use in recent years to help patients in end-stage kidney failure. One of these, hemodialysis (blood purification with the aid of artificial kidneys) has been known for the last two decades but had been limited prior to 1960 to supportive use, for a temporary period of time, in cases of acute kidney failure or dysfunction. Prior to 1960, connecting the patient with failing renal function to the artificial kidney was dependent on surgical procedures which could only be applied for a limited number of times in each patient. Since then, however, a grantee of the NIAMD

had developed a system of permanently implanting plastic vessel connectors in patients who require artificial kidney treatment. This development has ushered in the era of repeated dialysis in the same patient ("chronic intermittent dialysis") a mode of treatment which permits long-term maintenance of the life of the patient who has permanently lost the function of his kidneys.

The second therapeutic modality of relatively recent origin is kidney transplantation, the development and refinement of which has been and is being strongly supported by NIAMD research grants. At present, transplantation is still in a development stage but has seen increasing application and demonstrated significant promise for larger-scale usage. With continued research, improved kidney transplantation made possible by currently developed effective methods of hemodialysis (before transplantation, until the patient is ready for a transplant and a suitable donor kidney has been found, and after transplantation in those cases where the procedure was not permanently effective) should become a more widely and routinely used method of therapy.

The surgical techniques for transplanting kidneys have in large part been developed and are constantly being refined. The body, however, ordinarily defends itself against a "foreign" transplanted organ by making specific antibodies to that graft and by other defensive processes such as thrombosis (clotting of the blood supply) and phagocytosis (engulfing of tissue particles by white cells). In a series of complex events not at all well defined, the foreign transplanted organ is attacked and ultimately becomes functionless. Treatment with special drugs which suppress the host's immune response to transplanted foreign organs of a different tissue "type" (analogous to the well-known, mutually-incompatible blood types) can abort such an attack temporarily. In the long run, however, only organs of identical tissue composition (obtained from an identical twin) or of closely matching antigenic composition bear the promise of prolonged, dependable function in the host.

Thus it has become increasingly apparent that improvement in kidney transplantation and organ transplantation as a whole will depend on additional knowledge of human tissue immunology. Sophisticated methods must be developed for close immunologic matching of donor and recipient tissues. In addition new methodology must be sought for effective long-term preservation of donor organs so that at all times a sufficient number of pre- "typed" (tissue typed) organs with different antigenic composition is available for transplantation into (matching) patients who need them.

Further studies are expected in 1970 on a transportable organ preservation machine which has been developed by Institute grant-supported investigators. The machine has maintained human kidneys in a fully usable state for as long as 17 hours and animal kidneys as long as 72 hours prior to transplantation. Human kidneys obtained from cadavers have been transplanted successfully following preservation by the device, which permits transplantation to be a somewhat more elective procedure, rather than an immediate one upon availability of a cadaver kidney. The device provides the necessary time for adequate tissue typing of the organ and proper matching to a suitable waiting recipient.

Other highly significant advances this past year which warrant further study and continued support in the coming year were, for example, elucidation of a clotting disorder in uremic bleeding.

In this study of blood clotting abnormalities as the cause of bleeding often encountered in uremic patients, the release time of platelet factor-III has been pinpointed as the failing step in clotting events. Release time

returned to normal after dialysis treatment, indicating that an unknown material removed during the cleaning process is involved. A reliable method for quantitating platelet factor-III has been developed that will help to clarify the role of this factor in uremic bleeding.

Another finding concerns kidney stones. Many patients who develop calcium-containing kidney stones have no obvious predisposing factor such as high blood calcium, urinary obstruction or urinary infection. Although some patients have a definite increase in the calcium in the urine, others cannot be distinuished from normal subjects inasmuch as their daily total urinary calcium excretion does not exceed the normal range.

It has now been shown by Institute grantees that both urinary calcium concentration and excretion rise sharply in calcium stone-formers and in relatives of stone-formers following sugar ingestion, effects which clearly distinguish these subjects from normal individuals. It is suggested that augmentation of urinary calcium excretion and concentration after meals, or after ingestion of carbohydrate-rich foods or beverages, may be one of a possible number of factors contributing to calcium stone formation in susceptible individuals.

A finding which may open new approaches for research on the mechanism of infection of the kidney, particularly with organisms derived from the intestinal tract, has also been reported. The precise mechanism by which most instances of kidney infection (pyelonephritis) occur is as yet unknown. Scientists have described experiments with animals which suggest that the presence of live or dead bacteria in the ureter, without active infection, may facilitate subsequent development of pyelonephritis by causing cessation of normal ureteral peristalsis. When E coli bacteria cultured from urine of patients with pyelonephritis were introduced into the renal pelvis of dogs, ureteral peristaltic activity diminished in most cases by 50 percent and in some cases to zero. Endotoxin, a well-known substance in the cell walls of the bacteria, was also shown to influence adversely ureteral motility in vitro.

Clinically important areas in urology that will receive increased Institute research support include studies of problems of painful urination, urinary stone formation, obstructions of the urinary tract, diseases of the prostate and, endocrine relationship to prostatic hypertrophy. Other Institute support will involve the congenital abnormalities of the lower genitourinary tract in children and the related development of kidney disease in later life. Such research, it is expected, will lead to improved means of detection, treatment and management.

Hematology

Research in hematology is directed toward understanding the blood and its components, anemias, immunological aspects of transplantation, other immunology reactions, blood coagulation, drug reactions, and hemoglobin synthesis. Specific areas of research include studies in the genetic transmission of hemophilia, sickle cell anemia and other hereditary blood diseases; Rh incompatibility; blood clotting; immunologic aspects of the coagulation disorders; and investigations of the composition, structure and characteristics of serum proteins and fibrinogen, thrombin and hemoglobin.

Antihemophilic factor (AHF), widely accepted as an effective form of therapy for the tendency toward uncontrollable bleeding characteristic of this disease, is now being produced in abundant quantities as a result of research by grantees of this Institute and the National Heart Institute. Perfusion of isolated pig spleen with human hemophilic blood has been found to stimulate splenic production of AHF by a hitherto unknown substance in the hemophilic patient's blood. In other work under Institute support, investigators have shown that oxymetholone, a synthetic derivative of testosterone, is a potent bone marrow stimulant and thus is of value in the therapy of aplastic anemia. These findings are typical of those being made across a broad front in hematology.

Dermatology

The focus of interest of more investigators in the field of dermatology will be upon growth, structure, and function of the cellular elements of skin since such studies will lead to a better understanding of the skin under normal and disease conditions.

An increasing number of research projects involve study of biosynthetic pathways of the skin and the process of epidermal keratinization. This research will eventually shed new light on age-old problems such as psoriasis and ichthyosis. New insight into the possible mechanism of certain bullous (where blisters are a prominent part) skin diseases has been gained by immunologic studies leading to a better understanding of the nature of pemphigus as well as certain other skin diseases.

A Symposium on the Biology of the Skin is supported annually by this Institute. In these conferences emphasis is upon those biological phenomena that are most directly applicable to man--hair, growth, pigmentation, aging, carcinogenesis. The symposia have been a major contribution to progress in dermatological research and teaching for several years and have been valuable as a means of stimulating research and generating a great deal of constructive interest in dermatology, a field to which normally only few research workers tend to gravitate.

Particular attention will be paid to the alterations of human skin as a result of chronic exposure to sunlight. Recent dermatologic interest has been focused upon the aspect of photobiology that deals with the adverse effect of ultraviolet light on the skin of certain individuals who have applied topically or ingested specific chemicals or medicaments. Because of the great health and economic problems caused by these processes, the Institute will explore means by which research into the underlying mechanisms involved in such photodermatoses can be stimulated.

One example of a promising study in psoriasis which warrants further support concerns a new dosage schedule for the drug, methotrexate. Many cases of psoriasis, a chronic inflammatory skin disorder, resist all forms of therapy. Now grantee scientists have produced excellent clinical results in eight of 14 patients with recalcitrant psoriasis. The patients whose psoriasis resisted larger doses of methotrexate (or who reacted poorly to large doses) responded favorably to administration of the same drug, in multiple, minute, divided doses given throughout the day. It is believed that further study of this therapeutic procedure should be followed in a large number of psoriatic patients.

Nutrition

At the National Institutes of Health, the National Institute of Arthritis and Metabolic Diseases is the major focus of research support in nutrition providing almost two thirds of all extramural NIH support in this area. A variety of investigations on the biologic and physiologic properties of nutrients are supported. Specific dietary components including vitamins such as B_{12}, thiamine, pyridoxine, and vitamin E; minerals, notably manganese, selenium, vanadium, and zinc; and the amino acids are being studied from the standpoint of their absorption from the gastrointestinal tract and their subsequent metabolism in health and disease.

Partial control of a number of metabolic diseases has been achieved through alterations in diet. Obesity is a particular concern in the United States, and a number of investigations continue to seek means for control of this widespread disorder. Much future work will be devoted to elucidation of appetite regulation and its abnormalities and to possible metabolic derangements which, in addition to simple overeating, might predispose specific individuals to obesity.

Institute support for research in nutrition in the coming year will continue to stress studies on the interrelationship between carbohydrate, fat, and protein metabolism, and expanded studies on the effects of qualitative and quantitative variations in the diet on body composition, appetite regulation and food intake.

A strikingly important accomplishment this past year which will be further elucidated in 1970 was the isolation in pure form of the biologically active form of vitamin D. Preliminary tests of its ability to prevent or cure rickets in animals have shown it to be markedly more effective than vitamin D itself, suggesting that the newly discovered active form may be superior to the conventional vitamin in the treatment of rickets and, particularly, in the treatment of conditions heretofore labeled as "vitamin D-resistant."

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
1. Arthritis	$ 7,013,000	$ 7,061,000	+$ 48,000
2. Dermatology	1,858,000	1,871,000	+13,000
3. Diabetes	5,007,000	5,044,000	+37,000
4. Endocrinology	12,357,000	12,448,000	+91,000
5. Gastroenterology	9,442,000	9,512,000	+70,000
6. Hematology	6,065,000	6,110,000	+45,000
7. Metabolism	21,764,000	21,921,000	+157,000
8. Nutrition	6,166,000	6,209,000	+43,000
9. Orthopedics	3,358,000	3,383,000	+25,000
10. Urology and kidney diseases	6,057,000	6,102,000	+45,000
11. Other or interrelated areas	3,175,000	3,199,000	+24,000
12. Subtotal 1/	82,262,000	82,860,000	+598,000
13. General research support grants	9,409,000	9,409,000	0
14. Scientific evaluation and planning	20,000	20,000	0
15. Total obligations	91,691,000	92,289,000	+598,000

1/ Includes $1,500,000 in 1969 and $1,500,000 in 1970 budgeted for Categorical Clinical Research Centers.

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting continuations	1,619	$56,000,000	1,571	$56,598,000	-48	+598,000
2. Competing projects	336	13,470,000	336	13,470,000	0	0
3. New	265	9,492,000	265	9,492,000	0	0
4. Supplementals	(194)	1,800,000	(194)	1,800,000	0	0
5. Subtotal regular program	2,220	80,762,000	2,172	81,360,000	-48	+598,000
6. General research support grants		9,409,000		9,409,000		0
7. Scientific evaluations		20,000		20,000		0
8. Categorical clinical research centers		1,500,000		1,500,000		0
9. Total research grants	2,220	91,691,000	2,172	92,289,000	-48	+598,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Fellowships.....	$6,737,000	$6,475,000	-$262,000

A critical requirement in the scientific inquiry into arthritis, diabetes, endocrinology, metabolism, gastroenterology, hematology, in short, the biomedical research responsibilities with which the Institute is charged, is a sufficiently large and highly trained pool of scientific manpower. The fellowship program is designed to increase the number and improve the quality of individuals in research and closely related academic efforts in the Institute's biomedical disciplines and clinical research areas. Through this program fellowships are awarded to highly motivated scientists preparing for careers in research, to support part of the cost of the necessary academic training and research experience. In the coming year, the Institute anticipates an increase in urology and renal disease fellowships, and hopes to stimulate fellowship activity in the area of arthritis and gastroenterology.

For the Ph.D., postdoctoral or special fellowships provide postdoctoral training, which may be in a clinical or basic science department. In addition, extended periods of training in basic science departments are available to the considerable number of research-oriented physicians who require them and are financed through special fellowships.

The Postdoctoral Fellowship program is designed to increase the number of individuals trained for research and teaching by providing support directly to selected individuals (rather than indirectly through trainers in the case of training grants). Training may be taken at any institution in the United States to provide necessary facilities and direction. One of the special advantages of this type of award is that it may be unique in character or content and thus can be a contributing first step in evolving an important future research field.

The Research Development Award is designed to aid and encourage the further training and development of outstanding young scientists who have demonstrated research ability in their post-doctoral training period and who are believed ready to embark on careers of independent research in the health related sciences. Full salary support is provided through the sponsoring Institute for a limited number of years to assist these developing investigators in realizing their professional potential in research and teaching.

Funds requested for 1970 will provide for 383 awards, compared to 440 in 1969, a decrease of 57. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting	226	$4,102,000	220	$4,180,000	-6	+$ 78,000
b. Competing	22	215,000	20	354,000	-2	+139,000
2. Supplementals	(10)	15,000	(14)	20,000	(+4)	+5,000
3. New	192	2,405,000	143	1,921,000	-49	-484,000
4. Total fellowships	440	6,737,000	383	6,475,000	-57	-262,000

Fellowships (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral	185	$1,630,000	150	$1,420,000	-35	-$210,000
2. Special	108	1,400,000	86	1,217,000	-22	-183,000
3. Research career:						
a. Career	29	825,000	29	854,000	0	+29,000
b. Developmental	118	2,882,000	118	2,984,000	0	+102,000
4. Total fellowships	440	6,737,000	383	6,475,000	-57	-262,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Training Grants.....	$16,109,000	$15,480,000	-$629,000

The primary locus of training grants supported by the Institute is in the clinical departments of various medical schools, and almost all of the trainees, with the exception of about 5 percent, are physicians. As a result of its responsibilities for the largest number and greatest variety of diseases, this Institute is the principal focus at NIH of support for training related to disease problems.

In the coming year, the Institute will direct itself, as before, towards solving a basic problem, the inadequate number of independent clinical research investigators and teachers having the necessary competence required for research training and effective biomedical research. The situation applies to the well established fields of research interest, such as arthritis, diabetes and endocrinology, and in even greater degree to emerging or resurgent areas of research, such as dermatology, orthopedics, urology and gastroenterology.

Also in the coming year there will be attempts to assess the impact of past programs and to use this as the basis of deciding programs for the future. For example, a pioneer contribution towards a fresh approach of training program yield and of the relevance to emerging need has been made by the Gastroenterology Training Committee in a cumulative review completed last year, based on an analysis of present activities of the various trainees in gastroenterology supported over a ten-year period. More recently the Orthopedics Training Committee has embarked on a survey of the five-year experience, just completed, with NIH training support. Other assessments of training programs will also be made during FY 1970.

Funds requested for 1970 will provide for 275 awards, compared to 299 in 1969, a decrease of 24. This decrease reflects the Department priorities in the 1970 President's Budget related to national health programs, which gives emphasis to the development of health services personnel.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	234	$12,363,000	225	$12,432,000	-9	+$69,000
b. Competing.....	44	2,705,000	34	2,206,000	-10	-499,000
2. Supplementals.....	(2)	25,000	(3)	30,000	(+1)	+5,000
3. New.....	21	956,000	16	752,000	-5	-204,000
4. Scientific evaluation...	(1)	60,000	(1)	60,000	0	0
5. Total training grants...	299	16,109,000	275	15,480,000	-24	-629,000

Training Grants (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Graduate.....	299	$16,049,000	275	$15,420,000	-24	-$629,000
2. Scientific evaluation...	(1)	60,000	(1)	60,000	0	0
3. Total training grants...	299	16,109,000	275	15,480,000	-24	-629,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	487	$6,509,000	496	$6,637,000	+12	$+128,000
Other expenses		9,382,000		9,027,000		-355,000
Total	487	15,891,000	496	15,664,000	+12	-227,000

Introduction

The Institute bears responsibility for a broad array of chronic disabling diseases--a wider, more diversified range of illnesses than any of the other Institutes of the National Institutes of Health. Research activities, in addition to studies of the various arthritic, rheumatic and collagen diseases, include study of a broad spectrum of metabolic diseases, such as diabetes, inborn errors of metabolism such as cystic fibrosis, gastroenterology, hematology, nutrition, endocrine disorders, mineral metabolism, and subjects related to the above. Underlying these clinical and laboratory studies in disease areas is extensive fundamental research in biochemistry, pathology, histochemistry, chemistry, physical, chemical and molecular biology, pharmacology, and toxicology.

The major objectives of the Institute's intramural program are to develop more complete information about fundamental chemical and physiological mechanisms on a cellular level as well as in the organism as a whole, and to employ such knowledge to discover the mechanism by which diseases develop. Of equal importance are studies to discover better methods of therapy and prevention of disease. About one-fifth of the intramural research manpower is involved in studies directly concerned with patients in the Clinical Center and their disease problems.

Arthritis and Rheumatism

Arthritis and rheumatism are broad terms applied to a large number of disease conditions. A main target of Institute research is the form known as rheumatoid arthritis, a chronic, inflammatory connective tissue disease that ranks high among serious public health problems. Rheumatoid arthritis not uncommonly leads to permanent joint deformities and other complications producing disability and chronic invalidism. The majority of its victims are not elderly persons (as is the case in osteoarthritis) but are young and middle-aged adults in their most productive years. While the search for curative or at least palliative drugs continues, considerable emphasis now is being placed on finding the underlying causes of rheumatoid arthritis and other little-understood forms, as a key to more effective treatment and perhaps ultimate prevention.

The hypothesis that an obscure infection or abnormal immune response may trigger rheumatoid arthritis is being examined. In exploring this hypothesis at the cellular level, Institute investigators collaborating with colleagues at the National Cancer Institute have discovered an enzyme action which may be useful in protecting against such obscure infections. They have found that a bacterial enzyme, phospholipase C, alters the membrane of chick embryo cells so that they will not support reproduction of the nerve-destroying Semliki Forest virus. Although total phospholipid content was reduced 42 percent, cells sustained no

damage visible on electron photomicrographs. Future attempts will be made to adapt an enzyme of this type for animal trials to determine inhibitory effect against microorganisms known capable of destroying joint (and muscle) sheathing.

Although rheumatoid arthritis is essentially an enigma, much is now understood about another major arthritic disease, gout. Classically, gout is felt to be an inherited disorder of purine metabolism. Uric acid, a breakdown product of purines which is also synthesized de novo in the body, accumulates in the gout patient, forming urate crystals in joint tissues and resulting in inflammation and pain. Institute scientists, who last year reported that known disorders in purine metabolism involve deficiency of an enzyme, hypoxanthine-guanine phosphoribosyltransferase (PRTase), have recently shown that determination of the ratio of urinary uric acid to creatinine is useful in screening subjects with PRTase-deficiency disorders, including Lesch-Nyhan syndrome and gout. The simple screening test permitting early identification of either disorder will allow institution of allopurinol therapy for the prevention of renal (urate stone formation) and other complications. A few months ago, the investigators found that a unique urate-binding alpha 1-2globulin in human blood plasma is present in diminished concentrations in some patients with primary gout. Apparently this inherited deficiency of urate-binding protein is, along with the enzyme deficiency, an expression of the gouty trait and may prove useful in detection of such individuals.

Future studies in arthritic and rheumatic diseases will continue to range from purely molecular phenomena to the natural history of human disease or animal models of human disease.

Diabetes and Other Metabolic Diseases

Diabetes, which afflicts about four million Americans, ranks seventh as a cause of death and third as a cause of blindness. Moreover, based on current knowledge of the genetics of the disease, about five million other persons living today in the United States are likely to become diabetic patients with increasing age.

After development several years ago of (blood-sugar-lowering) drugs that can be administered orally where insulin injections are not indicated, research began to focus primarily on the mechanisms of this complex disease. One fundamental defect is a flaw in normal conversion of starches and sugars into energy, a process which is impaired in the absence of insulin. During the past year Institute scientists have found that circulating insulin may exist in two distinct forms in man, characterized as "big" and "little" insulin. "Little" insulin is indistinguishable from the hormone as it comes from its source, the pancreas, a gland located near the stomach. In the circulating blood plasma, however, up to 50 percent of insulin is "big" insulin. Investigators long have been puzzled by the finding that many diabetics seem to have sufficient insulin circulating in their blood, but that it does not perform its task of facilitating transport of sugar into body cells. The new discovery will turn attention to the quality of insulin in terms of the structure and biological activity of the two different forms. This work by Institute scientist Dr. Jesse Roth won for him the 1968 Distinguished Young Scientist Award, presented by the Maryland Academy of Sciences to a scientist not yet 35 who makes an outstanding contribution. Further studies are underway by Dr. Roth to determine the biological activity of "big insulin," its relationship to "little insulin," and its possible relationship to "proinsulin," reported previously in this narrative in the research grants section.

Institute accomplishments in the past have included the identification of a number of other inborn errors of metabolism. For example, Institute scientists had demonstrated that the specific biochemical defect in galactosemia resides in a specific enzyme deficiency, and that another grave metabolic disease, alcaptonuria is caused by the absence or ineffectiveness of a single enzyme. Similarly, Institute scientists pinpointed the enzymatic defects in other disorders, such as homocystinuria, and phenylketonuria, or PKU, which can produce mental retardation in newborn infants if not discovered and treated. More recently, Institute scientists have identified the exact enzymatic defect in two hereditary metabolic diseases, an absence of sulfate oxidase in a previously undescribed disease accompanied by mental retardation and death in childhood, and an absence of the previously-mentioned PRTase in the Lesch-Nyhan syndrome, a tragic hereditary disorder marked by brain damage, a compulsion to chew away lips and fingers, and an early death.

This past year Institute scientists identified in utero an as yet unborn female child as a carrier of the trait for Lesch-Nyhan disease, a landmark finding which should lead to more satisfactory counseling in the management of pregnancies likely to produce babies with severe defects.

The complete picture of Lesch-Nyhan disease is only found in males. Female children who have inherited the genetic trait merely serve as carriers who, in turn, can transmit the disease to their male offspring. Results of the Institute study indicate that male children with the full-blown disease also can be identified prior to birth. The findings provide a more dynamic and selective aspect to genetic counseling of prospective parents of such children, and suggest that victims of other hereditary metabolic disorders might be identified in a similar manner before they are born.

Institute scientists Dr. J. E. Seegmiller and his associates examined cells isolated from the amniotic fluid of a known carrier of the Lesch-Nyhan trait who was in her fourth month of pregnancy. It was found that some cells lacked PRTase activity, while other cells did not, a pattern known to be characteristic of carriers of the disease trait. The studies also indicated that the fetus was a female. Thus, the investigators concluded that the unborn female child is a carrier of the trait for Lesch-Nyhan disease.

Methods heretofore in use for the study of amniotic fluid cells for diagnostic purposes did not permit differentiation between normal male and affected male children. The Institute technique, however, now extends the diagnostic capabilities to permit the identification and differentiation before birth between carriers of the disease trait, victims of Lesch-Nyhan disease, and normal children.

In 1968, Dr. Seegmiller won the coveted Gairdner Foundation annual achievement award in acknowledgement of his outstanding work in revealing the metabolic defects of Lesch-Nyhan disease. It is expected that further efforts by his Laboratory this following year will provide more insight into the mechanisms of gout and Lesch-Nyhan disease.

Prenatal examination by Institute scientists of amniotic fluid and the fetal cells it contains has also permitted intrauterine diagnosis of two other hereditary metabolic disorders, the Hurler and Hunter syndromes. These disorders of mucopolysaccharide metabolism, although transmitted by different modes of inheritance, are both characterized clinically by skeletal deformities, mental retardation and early death.

Amniotic fluid cells from a 28-year-old mother of a child with the Hurler syndrome during the 25th week of pregnancy, and from a 23-year-old mother of a child with the Hunter syndrome during the 14th week of pregnancy displayed two distinguishing chemical characteristics of the Hurler and Hunter syndromes - a distinctive kinetic pattern of sulfate incorporation into mucopolysaccharide, and metachromatic staining with toluidine blue. These characteristics were also exhibited by cultured skin fibroblasts derived from affected siblings. The 28-year-old subject subsequently delivered a female infant with clinical and chemical evidence of the Hurler syndrome, while the 23-year-old subject elected therapeutic abortion in view of the prenatal diagnosis.

These findings have demonstrated the feasibility of intrauterine diagnosis of the Hurler and Hunter syndromes by using cultured amniotic fluid cells. It is obvious that this type of approach is applicable to any metabolic disorder which is expressed in such cells and for which a reliable assay can be developed. Appropriate therapy could then be initiated for an affected fetus or, if no such therapy exists, the parents could be given the option of having the pregnancy terminated.

In the meantime, studies will continue in Institute laboratories of both syndromes during the coming year. Scientists, for example, will attempt to learn more about the abnormal, excessive accumulation of mucopolysaccharide in the tissues of patients with Hurler's syndrome.

As mentioned in the research grants portion of this document, cystic fibrosis is a disease of many disguises. Its multifaceted nature has prompted and encouraged many scientists in diverse disciplines to study its metabolic, genetic, and clinical aspects. In recent years, scientists in Bethesda have contributed promising findings in basic research and have opened up new avenues for investigating cystic fibrosis.

Several months ago Institute scientists reported that hypoalbuminemia, an abnormally low albumin content of the blood, in older patients with cystic fibrosis is caused by dilution of a normal albumin mass by an enlarged plasma volume.

Later clinical metabolic studies established that the abnormal increase in volume of circulating plasma in the body (hypervolemia) is secondary to cor pulmonale, an abnormal condition involving high blood pressure in the pulmonary artery and ultimately leading to right-sided heart failure, which is brought about by abnormal resistance to pulmonary blood circulation. Since cor pulmonale is difficult to diagnose clinically in patients with cystic fibrosis, the investigators feel that a low serum albumin concentration may be of value in alerting the clinician to possible hypervolemia secondary to cor pulmonale and potential right-sided heart failure.

Continuing fundamental studies of cystic fibrosis during the following year will center around the biochemical, immunologic and physiologic aspects of submaxillary glands. For example, Institute scientists, in collaboration with scientists from the National Institute of Dental Research, have obtained evidence that excess calcium in the salivary glands of cystic fibrosis patients combines with a certain type of protein in the saliva to form an insoluble compound. It is possible that this abnormal precipitate is the same which gives rise to the widespread obstruction of various organ ducts seen in cystic fibrosis and which may eventually lead to many of the pathological and clinical findings in this disorder.

Endocrinology

The field of endocrinology embraces broad studies of the internally secreting glands of the human body, such as the pituitary, thyroid, parathyroid and adrenal glands, their respective hormones, and the roles they play in the normal and abnormal physiology of the body. Hormones, specialized chemical messenger substances produced in the various endocrine glands, are capable in some instances of modifying specific metabolic or physiologic reactions and in other instances of modulating the over-all rate of metabolic processes. Additionally, hormones are primarily responsible for and control sexual differentiation of an individual before birth; later they control and modulate growth, intellectual development, vigor, reproduction and senescence. Thus, hormones regulate a broad spectrum of organ and body activities; abnormalities in hormonal action are the basis for a multitude of serious diseases.

Institute investigators recently have shown, for example, that while parathyroid hormone and vasopressin both activate enzymes that control urinary excretion of biologically active chemicals, these hormones act at anatomically separate sites in the kidney, parathormone in the cortex and vasopressin in the medulla. In similar manner, a step-by-step mapping of pathways of action of numerous hormone byproducts, is being accomplished that will undoubtedly lead to understanding of biochemical detours and roadblocks expressed in the form of various diseases.

Institute researchers are pursuing broad, intensive studies designed to elucidate precisely how hormones influence metabolism and other body functions and how they crossreact with one another, as well as to clarify their molecular structure. Research projects also are under way which seek to develop feasible methods for chemical synthesis of hormones, especially the pituitary human growth hormone, and to modify other mammalian growth hormones so as to obtain fractions biologically active in man.

Research accomplishments concerning thyrocalcitonin, a thyroid hormone that lowers blood levels of calcium, have enabled the awarding this past year of an important scientific prize to Institute scientist Dr. Gerald D. Aurbach. Sharing the Prix Andre-Lichtwitz, a newly established French award for outstanding biological research in the area of phosphorus-calcium metabolism, with Dr. Aurbach was Dr. John T. Potts of the National Heart Institute.

The two investigators have been in close collaboration on problems of parathyroid physiology since 1962 at the National Institutes of Health. Drs. Aurbach and Potts operated as a team to develop and apply to clinical use knowledge in the area of the chemistry, physiology, regulation of secretion and mechanism of action of parathyroid hormone and thyrocalcitonin.

Within the past year this work has culminated in elucidation of much of the composition and structure (amino acid sequence) of the biologically important region of the parathyroid hormone, determination of the important factors regulating its secretion and discovery of the biochemical action of parathyroid hormone, elucidation of the complete composition and structure (amino acid sequence) of thyrocalcitonin leading to synthesis of the active molecule, development of a radioimmunoassay for thyrocalcitonin, and application of this assay to show that thyrocalcitonin is indeed secreted in response to a physiologic demand, thus suggesting that this active agent is in fact a hormone.

Gastroenterology

Disorders of the gastrointestinal system which may range from stomach upset to

peptic ulcer and ulcerative colitis, are among the most frequent ills to which man is heir. The momentum of gastroenterological research, however, has been increased by the growth of biochemistry, development of new technics and the expanding availability of new mechanical and electronic devices. Since progress in research in this field is inseparable from clinical advances, large numbers of patients who suffer from peptic ulcers, inflammatory enteritis, biliary colic, cirrhosis, pancreatitis, or even simple constipation, among other disorders, have benefited.

The primary focus of Institute studies at Bethesda is a group of disorders characterized by improper absorption by the intestine of various ingested substances. Emphasis is placed on clinical-laboratory investigations of Whipple's intestinal lipodystrophy, celiac disease, and on malabsorption syndromes that appear to be inherited. A form of Whipple's disease that seems to be related to infection and is susceptible to therapy with antibiotic drugs also is under study as a project in continuing attempts to understand, classify, and treat or prevent various forms of intestinal malabsorption.

Hematology

Hematological research is assuming an increasingly important role in the activities of the Institute. Anemias of various types, and clotting disorders like hemophilia are but a few of the large number of diseases known to affect the blood and blood forming elements. Considerable progress is being made at the Institute in discovering the basic mechanisms that are operating in some of these disorders. As in all scientific work, however, each new finding poses additional questions.

Studies are being conducted on the biochemistry of blood coagulation with particular reference to the development of better forms of therapy for various congenital and acquired hemorrhagic diseases. Included will be investigations of hemophilia, von Willebrand's disease, circulating anticoagulants, afibrinogenemia, fibrinolysis, as well as on obscure undiagnosed bleeding disorders. Circulating anticoagulant associated with lupus erythematosus is of particular interest. Immunological aspects of thrombocytopenia, anemia, and granulocytopenia will also be under investigation. Sera of patients with suspected drug sensitivity will be tested.

In studies of neonatal purpura, maternal-fetal incompatibility of platelet and leukocyte types can now be determined, and methods are being developed, through antibody tests of mothers who have had thrombocytopenic or leukopenic infants, to establish the diagnosis or to predict likelihood of recurrence in subsequent pregnancies.

Differences in the structures of carbohydrates which occur on the surface of red blood cells, responsible for differences in the well-known A, B, AB, and O blood types that distinguish humans, is another area of continuing research interest. These complex carbohydrates, also present in secretions such as saliva and milk are formed by the linking together of simple sugars in a stepwise fashion by enzymes called transferases. Last year, it was found that the presence or absence of specific transferases in individuals is genetically controlled and that it determines the structure of the complex carbohydrates on the surface of red blood cells and hence the blood type of the individual.

Sickle cell anemia is another blood disease which will be under investigation during the following year. The hereditary disorder, striking Negroes almost

exclusively, is the result of an abnormal hemoglobin, the oxygen-carrying element in red blood cells. Upon deoxygenation these cells which normally have a round, doughnut shape, assume an abnormal, flattened-pointed "sickle" shape and clog up small blood vessels, blocking circulation. The subsequent local lack of oxygen may cause pain and dysfunction, severe pain in the joints, infections, and may damage vital organs eventually leading to jaundice and heart or kidney failure. Affected individuals are subject to recurring crises requiring hospitalization and may usually die before age forty. This next year it is expected that a three dimensional scale model of the human hemoglobin molecule built by an Institute scientist will illuminate further the molecular mechanism of "sickling" in sickle cell anemia disease.

Basic Research

The importance of stimulating and supporting basic research is best illustrated by some exciting advances made possible by new fundamental knowledge. For example, Institute scientist Dr. Maxine Singer's arduous experimentation utilizing a specific enzyme led ultimately to the easy, and previously impossible preparation of synthetic, double-stranded ribonucleic acids (RNA) of predetermined composition. Subsequently, it was found by other investigators that a combination of two of these, called PI:C in biochemical shorthand, can induce interferon production in animal cells. Interferon, the body's natural virus-fighting substance, has long been known for its ability to prevent viral diseases. A scientist from the National Institute of Allergy and Infectious Diseases now has provided solid evidence that interferon stimulation with PI:C can cure an acute and often fatal viral infection, herpes simplex keratonconjunctivitis, in rabbits. The use of these RNAs, which stimulate the body's interferon system, now has opened possible new therapeutic approaches to a host of other viral infections. Thus, a research effort best characterized as "basic research" again has made available new materials of great potential usefulness in clinical medicine.

Another example of basic research resulting in handsome dividends came when National Cancer Institute scientists reported that a drug called cytosine arabinoside, or Ara-C, has produced complete remissions in 19 of 40 patients with acute myelocytic leukemia, a form of cancer against which little progress has been made to date. This clinical accomplishment stemmed directly from earlier basic laboratory research conducted by a scientist of this Institute, Dr. C. Glaudemans, who devised a wholly new method for synthesizing several precursor forms of Ara-C. Other investigators subsequently extended his methods to permit the synthesis of a variety of related agents, including Ara-C. Were it not for the basic research by Dr. Glaudemans, such drugs as Ara-C would not be available for clinical studies and commercial production at the present time.

The net decrease of $227,000 is attributed to a decrease of $420,000 for centrally furnished services to the National Institutes of Health management fund offset by increases of $178,000 to provide for 12 positions and essential research support costs in new and continuing laboratory and clinical investigations and $15,000 for annualization of the 1969 pay raise costs.

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	25	$ 310,000	28	347,000	+3	+37,000
Other expenses	..	6,188,000	..	6,323,000	..	+135,000
Total	25	6,498,000	28	6,670,000	+3	+172,000

Introduction

The mission of the Institute and the versatile role it must play in pursuit of its goals has evolved other programmatic modes of approach to problems which fall within the Institute's province of responsibility. When the need becomes evident for a major new development, such as new organ preservation techniques or new, effective drugs to counteract the body's rejection barrier, it is usually impractical and inefficient to reassign to new directions intramural scientists engaged in an ongoing orderly and productive research program. It is likewise seldom that competent and high caliber outside scientists will be willing to drop whatever studies they are engaged in, in favor of a new problem for which there would be a possibility of Institute support. In attempting to meet special needs, then, where the kind and content of the work required is clear, direct collaboration is sought with specific scientific talent or resources, usually already engaged and competent in closely related efforts and techniques, to further the accomplishment of the specific goal. Thus a third type of Institute activity has evolved through the years which encompasses features borrowed both from the extramural and intramural research approach, which is financed by direct operations funds of the Institute in contrast to extramural funds, and which makes use of the contract mechanism to finance its activities; this is the "collaborative" approach to attainment of Institute goals.

An excellent example of a program which is best served through the "collaborative" approach is the improvement of repeated hemodialysis for patients with permanently impaired kidney function once this life-saving therapeutic modality was proven applicable and useful. Other examples, in smaller scope, are the important area of scientific communications, which includes the publication of current-awareness journals, the preparation of films and other communications media, and the organization, when needed, of specific scientific working conferences.

Artificial Kidney Program

In the United States today an estimated 55,000 individuals die each year as a result of irreversible kidney failure. The diseases which originally initiate the chain of events which terminates with advanced kidney failure vary considerably in nature. They may be primary kidney diseases like glomerulonephritis. In other instances progressive kidney damage may be induced by longstanding hypertension or

diabetes, or kidney infection, and destruction may be initiated by obstructions such as kidney stones or hypertrophy of the prostate in aged males. Regardless of the original disease, the progressive kidney damage leads to a common final pathway, end-stage kidney disease, followed by fatal irreversible kidney failure.

Two therapeutic substitutes for kidney function have come into use: peritoneal dialysis and hemodialysis (blood purification with the aid of artificial kidneys). Both methods employ the same basic principle of dialysis, the exchange of substances across a semi-permeable membrane. Peritoneal dialysis makes use of the membranes of the abdominal cavity as filters and of the abdominal space as a reservoir for "dialysis fluid" a solution meant to wash out metabolic waste products. Waste products of relatively small molecular size which have concentrated in the blood, tissues, and intercellular spaces, pass across tissue membranes into the dilute solution introduced into the peritoneal space and are removed when this dialysate is drained from the abdominal cavity.

For hemodialysis with artificial kidneys, the blood is routed out of the body and through membranous enclosures immersed in large and rapidly replenished volumes of a dilute dialysis fluid. The same mass-transfer principle of substances in more concentrated fluids diffusing spontaneously into the less concentrated medium applies, but here the membrane barrier is not of biological origin as in peritoneal dialysis but consists of cellophane or of a similar artificial material.

Another, more complete approach to provision of substitute kidney function is represented by kidney transplantation. Kidney transplantation is at present still a developing modality but has shown increasing promise for larger scale application. With continued research, kidney transplantation, supported and made possible by efficient methods of hemodialysis (until the patient is ready for an operation or until a suitable donor kidney is available) should become a more routinely used method of therapy.

If and when kidney transplantation becomes a routine procedure, the artificial kidney will not be discarded. Many chronically uremic patients are not medically or psychologically suitable candidates for transplantation. Furthermore, patients who are suitable candidates will have to be sustained with an artificial kidney until they are well enough to have a transplantation operation and until a suitable, antigenically matching donor kidney can be found for them. Also they may have to be placed on an artificial kidney after the operation if the donated kidney does not function properly for a time or is rejected.

The problem of perpetual maintenance of patients with artificial kidneys is complicated by the fact that the cost of currently available techniques is too high, both in terms of money and qualified manpower, to permit widespread patient treatment. Also, patients maintained with the aid of artificial kidneys continue to display a number of undesirable symptoms related either to the underlying disease or to the treatment.

The Institute's special Artificial Kidney Program has been created to deal with these problems. An up-to-date report of progress and future plans follows:

Problems of Highest Priority: The following are outstanding problems in dialysis toward which the Artificial Kidney Program is directing immediate efforts:

1. Cannulas. The life and function of the permanently implanted cannulas are still limiting factors in successful dialysis.

2. Dialysis membranes. Though effective, the cellophane membranes currently in use may not be optimal. The possibility of using other, perhaps more selective membranes, must be explored.

3. Design of individual dialyzer units. Most dialyzers presently in use are cumbersome and costly to assemble and sterilize. A dialyzer exists which utilizes a disposable dialysis-ultrafiltration "cartridge"; this cartridge is expensive for maintenance of chronic patients.

4. High requirement for professional personnel. This requirement is based on the medical nature of dialysis, but aggravated by problems 1, 2, and 3 above.

5. Lack of effectiveness data. No objective information has been obtained through well-controlled studies which permits a meaningful evaluation of the comparative effectiveness of the various dialysis methods and equipment currently in use.

6. Undesirable symptoms frequently found in patients maintained by repeated dialysis.

   a) Anemia. On the average, one or more blood transfusions are needed per month per patient maintained in dialysis -- with the attendant risk of transfusion hepatitis.

   b) A significant incidence of peripheral neurological damage. This may be due to long-term effects of the semi-uremic state in surviving patients on repeated dialysis, or due to the dialysis procedure per se.

   c) Pseudo-gout, secondary hyperparathyroidism, skeletal demineralization, and calcium deposition in joints and in the tissues throughout the body. The most recent findings involve calcium deposition in the cornea of the eye. Simultaneously, there is a tendency to decalcification of bone with resultant fractures produced by minor stresses.

Problems 1 through 4 are primarily responsible for the current high cost of dialysis, which averages $15,000 per year in patients maintained by hospital center dialysis.

Current Activities: At present about sixty carefully selected research and development projects are in existence, financed by the Program's contract funds. These contracts were placed with universities, nonprofit research laboratories and industrial concerns, and constitute a broad spectrum approach to the problems of highest priority. These projects involve development of improved blood cannulas and filtration membranes; evaluation and development of new polymer surfaces for artificial kidneys, cannulas and membranes which do not induce blood coagulation; design of more efficient, compact, and less costly dialyzer systems; development of a new concept of artificial kidney dialysis ("hollow fiber" or "capillary" kidneys); research on and development of absorption cartridges for blood purification; development of inexpensive disposable dialysis units; improvement and design of new automated dialysate delivery systems; improvement and design of new dialysis units with automated failsafe mechanisms; evaluation of a special protein restricted diet in the maintenance of uremic patients for whom chronic dialysis is deemed not feasible or unobtainable; isolation from dialysates and identification of the as yet unknown compound(s) which is (are) specifically responsible for the toxic symptomatology in uremia, and many other projects related to improved dialysis methodology or apparatus.

Accomplishments: During the past year there have been a number of accomplishments and encouraging developments derived from the ongoing research and development contract program. The new and unique hollow fiber capillary kidney which is being developed under a contract with the Dow Chemical Company has progressed to full-scale clinical testing at the Northern California Dialysis Center, San Francisco General Hospital. This low cost, disposable small dialyzer is being produced at present in a semiautomated facility which has been set up under the contract in order to expand the production of prototype models for clinical testing.

The hollow fiber artificial kidney consists of 11,000 hollow cellulose threads bundled together into a compact plastic cylinder about the size of a quart milk bottle. Blood is passed through these manmade capillaries and they, in turn, are constantly washed on the outside by a blood purifying dialyzing solution. The unique construction of the kidney provides an enormous surface at the cellulosic blood-dialysate solution interphase at which toxic waste products migrate from the blood into the dialysate fluid. This new dialyzer is designed so well that no external blood pump is needed to drive the blood through it. Moreover, its internal blood compartment volume is so small that only about 70 milliliters of the patient's own blood are needed to prime the unit, thus eliminating the need for compensatory blood transfusions (and their attendant hazard of hepatitis) associated with the use of most conventional artificial kidneys. The new compact capillary kidney is easy to use in a hospital or home dialysis setting since it comes pre-sterilized, filled with saline and ready to operate. Its cost projections make it more than competitive with conventional disposable coil dialyzers.

The new device has now proven its clinical effectiveness during more than 1000 dialyses. It is routinely re-used three times before it is discarded. It has been established experimentally, however, that it can be re-used up to nine times and further studies are planned on this economically important facet. Future larger scale production of the new device is contemplated so that additional clinical trials in a number of dialysis centers throughout the United States can be made. In addition to this particular capillary artificial kidney, other possible designs are being explored by two other contractors of the Program, also utilizing the new hollow fiber dialyzer design.

Another contractor who is manufacturing the conventional Kiil dialyzer has been successful in the development of a major modification which is considerably more manageable because of its light weight and different structural arrangement. This new broad-type dialyzer substitutes a combination of plastic foam and solid plastic composition for the previous type of construction which is quite heavy and cumbersome. It requires 50 percent less torquing for sealing and has smaller blood priming volume. It weighs 30 pounds less which permits easier handling in the hospital or home. This new dialyzer already has been introduced into commercial usage.

The same contractor has also developed a considerably smaller and more efficient type of Kiil dialyzer distinguished by a new type of multiple minute, pyramidal membrane supports which increase the effective dialysis area of the membrane in it. Laboratory tests have shown that this new development has increased the dialyzing efficiency of the new modified Kiil-type dialyzer by about 40 percent. A series of the new experimental dialyzer is now being built for clinical testing with patients.

29-867 O—69—pt. 4——34

The same group of scientists at the University of Washington, Seattle, which last year devised a technique for storing and re-using artificial kidneys of the Kiil type and of the attached blood tubing (which reduces the cost and simplifies the work involved in performing hemodialysis in the home) has now developed a new type of "Quick-Connecting" cannula coupler for home use which can be activated by the patient with one hand only. Heretofore, connecting the patient to an artificial kidney machine (by uncoupling his plastic shunt and coupling his permanently implanted plastic cannula to the blood tubing of the artificial kidney) has always required two hands. Since shunts are usually located on the arm of the patient, this meant that one extra person had to be present to connect the patient to his artificial kidney; only in cases where the cannula had been placed in the patient's leg, could the patient effect his own coupling and uncoupling in home dialysis. The newly developed, one-handed cannula coupler has now seen successful initial trial in a small number of patients and will be tested further in preparation for larger-scale manufacture and distribution.

During the past year, the Artificial Kidney Program has striven to encourage clinical studies in the United States of a special diet, and modifications thereof, which has shown in trials in Italy and England that it permits moderate-term survival, cessation of symptoms, and rehabilitation in certain types of patients with chronic renal failure who are otherwise faced with the need for chronic dialysis or kidney transplantation. During a 21-month study period, Institute supported scientists in Los Angeles have indeed demonstrated that a 20 gram, balanced, low-protein diet limited largely to <u>essential</u> amino acids, but unlimited in carbohydrates and fats can ameliorate uremic symptoms in patients with minimal, residual renal function while maintaining a satisfactory body nitrogen balance. The results of dietary treatment, as measured by amount of relief from previous uremic symptoms and total duration of remission, were significant in all patients with a urea nitrogen clearance greater than 1.5 cc/min. Of 27 patients who followed the diet, relief of anorexia, nausea, vomiting, weakness, fatigue and lethargy was obtained in 23. The results of therapy were felt to be good to excellent in ten patients, with remission of symptoms persisting for 8.3 months in one patient. Serum urea nitrogen decreased in all patients. The resulting remission depends on prevention of acute deterioration of residual renal function and rigid adherence to the diet by the patient. The Program has recently activated investigations to study the efficacy of a maintenance regimen which combines the use of this diet with <u>infrequently</u> administered peritoneal dialysis or hemodialysis.

Similar encouraging results were obtained by another contractor at New York Medical College who has already progressed to maintenance of patients with a combination of this diet and infrequently applied hemodialysis (once every two weeks rather than the conventional three times per week).

<u>Future Activities of the Artificial Kidney Program</u>: The Program will continue all promising current research and development efforts and will pursue any new ideas and approaches which appear feasible. Among these is a new method of detoxification of uremic blood with the aid of special selective adsorbing agents (in contrast to the presently used purification with the aid of membrane dialysis). The success of such detoxification-by-adsorption hinges on the successful identification of <u>all</u> toxic substances which accumulate in the bloodstream in kidney failure. The Program is currently funding a number of studies aimed at the isolation and identification of such unknown toxic factors which may have to be removed from

the patients' blood, in addition to metabolic wastes and other substances known tc accumulate during kidney failure, such as urea, creatinine, uric acid, potassium, hydrogen ion, and water.

The Program intends to follow very closely the clinical and technological developments abroad and, when promising, to enlarge upon them for the benefit of U. S. patients as well. For instance, reports have been received of the preliminary development, in Scotland, of a new miniaturized dialyzer which requires little or no blood priming and of new selective membranes characterized by increased permeability to urea, heat sealability, and improved water flux. Should these new developments prove successful, the Program will be interested in fostering larger scale clinical trials and in placement of production of the new membranes and dialyzer in this country.

The Program will support further development of special diets (see above) for maintenance of uremic patients, to be used in conjunction with infrequent peritoneal dialysis or hemodialysis. For the latter type of regimen patients would be given surgically constructed, subcutaneous, natural arterio-venous blood vessel shunts (which are adequate for infrequently administered hemodialysis). It is hoped that with the aid of such a special-diet-infrequent-dialysis regimen patients would be maintained without the need for implantation of plastic shunts, and that a larger number of patients with renal failure may be accorded life-saving treatment in this fashion in the face of the great expense of conventional chronic dialysis therapy which is unavailable to most patients with end-stage kidney disease.

Other research and development projects about to be activated by the Program include the development of a unique type of dialysis membrane from collagen (a structural protein found in the skin and connective tissues of mammals) and the development of implantable cannulas made from this naturally-occurring tissue protein. Preliminary experiments have given strong indications that a sophisticated laboratory modification of this material can yield a substance which is highly compatible with blood and mammalian tissues. This modified collagen would thus be a welcome substitute for currently used membranes and for implanted plastics (the latter not only in connection with dialysis cannulas but for many other prosthetic purposes). Other future projects deal with the possibility of developing substances which, once ingested, would sequester and trap specific toxicants in the gastrointestinal tract. Such a development could prove to be a helpful adjunct in the maintenance of patients with renal failure by permitting a decrease in the frequency of dialysis.

Conferences, Publications, and Scientific Communication: As a sequel to the previous year's two-day Conference on Nutritional Aspects of Uremia, the Program organized, in October 1968, a timely symposium on the abnormal calcium metabolism and osteodystrophy which characterize chronic renal failure and is found in many patients maintained with the aid of artificial kidneys. The purpose of the conference was to explore and elucidate the serious phenomena such as widespread calcification of soft tissues (including the eyes, joints, blood vessels and the heart), demineralization of the skeleton (leading to frequent fractures), and secondary hyperparathyroidism, which accompany renal failure of long standing and which are seen with increasing frequency in patients whose lives are being maintained with the aid of artificial kidneys or even with kidney transplantation. More than 20 papers were presented concerning various problems related to renal osteodystrophy and disturbed divalent ion metabolism in chronic renal disease and to the possible etiologies and their interactions. This symposium brought together a select group of experts representing several relevant disciplines from France,

Switzerland, Canada, Australia, England, and the United States, and the proceedings will be published shortly and will be distributed widely in order to facilitate widespread efforts for dealing with the serious complications of long-term dialysis brought about by the abnormal calcium metabolism of renal failure.

Most of the Program's ongoing research and development contracts are systematically structured to yield specific goals according to a built-in time schedule. In many cases the attainment of targeted research and development goals in one contract is essential to the success of projects which are part of other contracts. Thus, close communication of research results between all of the Program's contractors is essential for maximum effectiveness of the overall effort. With this in mind, the Program brought together, in January 1968, all of the contractors' senior staff and the Program's consultants for a two-day working conference ("The First Annual Contractors' Conference" of the Artificial Kidney Program). On this occasion each project reported its positive and negative findings to all other active contractors in formal presentations followed by informal general brainstorming discussions. It was felt that this close communication and cross fertilization of ideas from a large number of active contractors and consultants coming from diverse biomedical and technological disciplines was highly productive toward attainment of the common goal of the Program - optimal artificial kidney technology, improved clinical methodology and patient rehabilitation - at an early time.

Printed proceedings have now been published and widely distributed to workers in the field and related disciplines. The publication highlights research results, and a body of technical information which should contribute significantly to the state of knowledge in this field.

Scientific Communications

A continuing problem confronting individual physicians and research scientists today is the difficulty of keeping up with rapidly developing fields of knowledge directly related to their work or at a tangent to it. The Institute, through its Office of Scientific Communications, provides current-awareness ("alerting") publications and other materials in areas within its purview, conducts retrospective literature studies, initiates conferences and workshops to disseminate knowledge in pertinent fields, and concerns itself with other activities related to scientific communication, such as the production of a limited number of specialized motion pictures and development of thesauri.

The latest publication in the series of well-received and unique current awareness periodicals established by NIAMD since 1964 is the bi-monthly "Endocrinology Index" initiated last year. It contains an organized listing of reference to recently published endocrinology-related articles from throughout the world and provides a key-word abstract of each citation. Other regular publications in the series are "Arthritis and Rheumatic Diseases Abstracts", "Diabetes Literature Index", "Gastroenterology Abstracts and Citations", and "Artificial Kidney Bibliography".

The Institute, in collaboration with the National Institute of Child Health and Human Development, is engaged in facilitating the development of another alerting journal to fill the existing communications gap in the field of nutrition through the development of a guide to nutrition terminology (essential for any orderly attempt at automated retrieval of specific literature from computer storage). NIAMD also supports by contract a retrospective literature search on the Nutritional Requriements of Vertebrates Other Than Man; Publication of results is undertaken by the National Academy of Sciences.

Scientific conferences on bone mineral measurement, and other topics have been sponsored during the past year, among a variety of continuing activities of the Institute's Office of Scientific Communication.

National Pituitary Agency

Human growth hormone is secreted by the pituitary gland, the so-called master gland of the body which produces a number of vital hormones. Insufficient secretion of human growth hormone (HGH) results in a condition called hypopituitary dwarfism which can be treated by administration of HGH.

The main problem currently facing fundamental and clinical research related to HGH is the scarcity of the hormone. At present the only source of HGH is the pituitary gland of the deceased, and research has shown that one human pituitary gland provides only enough hormone for about five day's treatment of a hypopituitary child. Extracts of growth hormone from animal pituitary glands are not active in man.

In an effort to alleviate this problem, the Institute had contracted for the operation of the National Pituitary Agency, originally affiliated with Johns Hopkins University but now with the University of Maryland School of Medicine, to increase and improve the collection of human pituitary glands and to provide for the distribution of purified HGH to qualified research scientists. Clinical studies are aimed at determining HGH's metabolic effects and mechanism of action and at determining its possible usefulness in other endocrine-metabolic disorders. Biochemical research emphasis is on an analysis of the detailed molecular structure of HGH in order to make possible its laboratory synthesis and eventual commercial manufacture and thus to eliminate reliance on the hard-to-obtain natural human hormone.

At present, HGH can only be administered to patients in conjunction with research studies because it is impossible to collect enough human pituitary glands to obtain sufficient HGH for treatment of the estimated 5,000 to 10,000 children suffering from hypopituitary dwarfism in the United States. Hence the Medical Advisory Board of the National Pituitary Agency reviews applications submitted by research endocrinologists and determines the scientific merit of the proposals and the amount of hormone each investigator is to receive based on the requirements of the proposed study and on the available supply. As part of this research, about 400 children around the country with various problems of growth will be given HGH in clinical research studies.

The net increase of $172,000 will provide additional funds for the Artificial Kidney/Chronic Uremia and Endocrine and Diabetes Hormone Developmental Research Programs, including provisions for 3 additional positions to assist in the management of these programs. There is a $7,000 reduction in centrally furnished services from the National Institutes of Health management fund.

Biometry, Epidemiology, and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	26	$238,000	26	$239,000	0	+$1,000
Other expenses	..	468,000	..	473,000	..	+5,000
Total	26	706,000	26	712,000	0	+6,000

One of the most useful tools for learning the causes of diseases is the science of epidemiology, which deals with the relationships of the various factors which determine the frequencies or distributions of a disease. For example, determining why a certain population in a given geographic area has a high frequency of a disease may help investigators to understand more about the factors favoring on causing that disorder.

The Institute maintains a Clinical Field Studies Unit in Phoenix, Arizona which has demonstrated in a comparatively short period of time the value and importance of epidemiological research. In recent years, studies by Unit investigators have indicated that rheumatoid arthritis is little influenced either by climatic or by genetic factors. More recently, the Unit showed that the Pima Indians of Arizona have the highest prevalence of diabetes ever recorded in a circumscribed, apparently normal population group, a rate 10 to 15 times that of the U.S. population as a whole. The finding represents a unique opportunity to explore the precipitating factors in diabetes, the progress of the disease and its complications, the role of diet and other environmental factors, and possibly the effects of various therapeutic measures.

In diabetes studies this past year, Unit investigators compared obesity and diabetes rates among the Pima Indians with those of the neighboring Cocopah tribe. It was found that the frequency of obesity was similar in the two tribes, but the prevalence of diabetes was significantly lower in the Cocopah. The investigators concluded that the frequency of obesity does not account for the differences in the prevalence of diabetes between the Cocopah and the Pima Indians. In another study, the scientists showed that congenital anomalies occur more frequently in the offspring of Pima women who developed diabetes before age 25 than in the offspring of women who developed the disease later in life.

In addition to arthritis and diabetes, the Unit has initiated a long-term program to study gallbladder disease among the Pima Indians who also display a higher-than-normal prevalence of this disorder. Various conditions and factors, including hereditary, environmental, dietary, and anthropological aspects, that may have a bearing on the frequency and severity of these diseases will be investigated. Findings will be contrasted with similar studies performed on other populations with different characteristics or environment. The Clinical Field Studies Unit, along with other components of the Institute, is also looking forward to future opportunities to collaborate with the Indian Health Service in a collaboratively planned research wing in the latter's new Phoenix Medical Center.

The $6,000 increase is for centrally furnished services from the National Institutes of Health management fund.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	72	$758,000	74	$781,000	+2	+$23,000
Other expenses	..	1,521,000	..	1,592,000	..	+71,000
Total	72	2,279,000	74	2,373,000	+2	+94,000

Introduction

This activity involves professional and supporting personnel who are responsible for the administration of the Institute's several grants activities. They assist in the planning and development of programs in research, training, and fellowships that will best serve to accomplish the desired results in the areas of disease interest for which this Institute is responsible; review and evaluation of research and training grant applications for presentation to the National Advisory Arthritis Council; required Council staff assistance; liaison with applicants, grantees, other components of NIH and the Department, advisory bodies, and interested organizations; continuous surveillance of scientific activities and progress; and recording and reporting of fiscal and scientific information relevant to all transactions.

The increase of $94,000 includes $35,000 to provide for additional computerized processing costs and for the support of 2 additional grants management and professional staff needed to administer the complex problems presented by the large number of competitive grant applications. The remaining $59,000 is for an increase in centrally furnished services from the National Institutes of Health management fund.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	20	$227,000	20	$228,000	0	+$1,000
Other expenses	..	94,000	..	77,000	..	-17,000
Total	20	321,000	20	305,000	0	-16,000

This activity is comprised of the Institute Director, his immediate staff and administrative management and service personnel who are responsible for the general direction, coordination and administration of the total Institute activities.

The decrease of $16,000 is attributed to a decrease of $17,000 for centrally furnished services from the National Institutes of Health management fund, offset by a $1,000 increase for strengthening administrative management services.

New Positions Requested Fiscal Year 1970

	Grade	Annual Salary
Laboratory and Clinical Research		
(2) Medical Officer	GS-14	$39,542
(1) Medical Officer	GS-13	18,249
(2) Scientist	GS-13	28,818
(2) Scientist	GS-12	24,348
(2) Research technician	GS-6	12,642
(2) Secretary	GS-5	11,464
(1) Clerk-typist	GS-4	5,145
	(12)	140,208
Collaborative Research and Development		
(1) Medical Officer	GS-14	19,771
(1) Secretary	GS-6	6,321
(1) Clerk-steno	GS-4	5,145
	(3)	31,237
Review and Approval		
(1) Grants Management Specialist	GS-9	8,462
(1) Grants Management Specialist Assistant	GS-7	6,981
	(2)	15,443
Total, new positions, all activities	(17)	186,888

FRIDAY, MARCH 28, 1969.

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

WITNESSES

DR. EDWARD F. MacNICHOL, JR., DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ELDON L. EAGLES, ASSISTANT DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ECKART WIPF, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ROBERT L. SITHENS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	6,105	6,837	7,315
Positions other than permanent	292	331	343
Other personnel compensation	91	113	120
Total personnel compensation	6,488	7,281	7,778
Personnel benefits: Civilian employees	686	713	753
Travel and transportation of persons	335	372	372
Transportation of things	75	83	83
Rent, communications, and utilities	200	222	225
Printing and reproduction	106	119	139
Other services	14,071	14,491	14,519
Supplies and materials	1,142	1,270	1,270
Equipment	645	710	710
Grants, subsidies, and contributions	76,435	78,006	77,638
Quarters and subsistence charges	−2	−2	−2
Total obligations	100,181	103,265	103,485

PERSONNEL SUMMARY

Total number of permanent positions	732	685	690
Full-time equivalent of other positions	45	55	45
Average number of all employees	712	660	713
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

See footnotes at end of table.

PROGRAM AND FINANCING (In thousands of dollars)

	1969 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	50,524	59,134	59,506
(b) Fellowships	2,694	3,213	3,085
(c) Training	11,130	15,659	15,047
Total, grants	64,348	78,006	77,638
2. Direct operations:			
(a) Laboratory and clinical research	8,488	9,879	10,100
(b) Collaborative research and development	9,651	9,742	10,092
(c) Biometry, epidemiology and field studies	2,790	3,016	3,028
(d) Training activities	66	74	72
(e) Review and approval of grants	1,894	2,058	2,114
(f) Program direction	579	490	441
Total, direct operations	23,468	25,259	25,847
Total program costs, funded [1]	87,816	103,265	103,485
Change in selected resources [2]	12,365		
Total obligations	100,181	103,265	103,485
Financing:			
Comparative transfers to other accounts	21,798	22,918	
Unobligated balance lapsing	4,977	2,748	
Budget authority	126,956	128,931	103,485
Budget authority:			
Appropriation	128,633	128,934	103,485
Transferred to other accounts	−1,677	−3	
Appropriation (adjusted)	126,956	128,931	103,485
Relation of obligations to outlays:			
Obligations incurred, net	121,979	126,183	103,485
Obligated balance, start of year	71,244	69,776	89,652
Obligated balance, end of year	−69,776	−89,652	−82,508
Adjustments in expired accounts	−4,098		
Outlays	119,349	106,307	110,629

[1] Includes capital outlay as follows: 1968, $789,000; 1969, $710,000; 1970, $710,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $2,799,000; 1968, $15,164,000; 1969, $15,164,000; 1970, $15,164,000.

Mr. NATCHER. The committee will come to order.

We have before the committee at this time Dr. Edward F. MacNichol, Jr., Director of the National Institute of Neurological Diseases and Stroke.

Dr. MacNichol, I believe you have with you, in addition to Dr. Marston, the Director of the National Institutes of Health, certain other members of your staff whom you might want to present to the committee at this time.

Dr. MACNICHOL. I believe they have all been here many times before. This is Mr. Wipf, our Executive Officer, Mr. Sithens, our Financial Management Officer, and Dr. Eagles, the Assistant Director of the National Institute of Neurological Diseases and Stroke.

Mr. NATCHER. We are glad to have all you gentlemen appear at this time.

Dr. MacNichol, this is your first appearance before this committee?

Dr. MACNICHOL. Yes, sir.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Mr. NATCHER. And we have your biographical sketch which we shall insert at this point in the record.

(The sketch follows:)

Name: Edward F. MacNichol, Jr.; Position: Director, National Institute of Neurological Diseases and Stroke; and Acting Director, National Eye Institute: Birthplace and date: Toledo, Ohio, Oct. 24, 1918; Education: A.B., Princeton University (physics), June 1941; Ph.D., The Johns Hopkins University (biophysics), June 1952.

Experience: September 1968, Director, National Institute of Neurological Diseases and Stroke; and Acting Director, National Eye Institute; 1952–68, The Johns Hopkins University, Department of Biophysics (from instructor to professor); 1957, visiting professor, Venezuelan Institute of Scientific Research (IVIC); 1941–1946, staff member, radiation laboratory, Massachusetts Institute of Technology.

Association memberships: member, Board of Scientific Counselors, National Institute of Neurological Diseases and Blindness, 1964–68; chairman, 1967–68; member, Visual Sciences Study Section, National Institutes of Health, 1962–66; member, Committee on Photobiology, National Academy of Sciences, National Research Council, 1965; member, Committee for Pure and Applied Biophysics, National Academy of Sciences, National Research Council, 1964–65; fellow, Institute of Electrical and Electronic Engineers, Inc., 1964; editor, Transactions on Biomedical Engineering, Institute of Electrical and Electronics Engineers, Inc., 1962–64; member, editorial board, Proceedings of the Institute of Electrical and Electronics Engineers, Inc., 1966.

Special awards, citations, or publications: Army-Navy Certificate of Appreciation for work done at MIT Radiation Laboratory, 1948. Morlock Award of the Institute of Electrical and Electronics Engineers, Inc. (IEEE), 1965. Publications: Over 30 scientific and technical publications on the electrophysiology of vertebrate and invertebrate eyes and on the measurement of pigment in single vertebrate photoreceptors.

Mr. NATCHER. I see you were born in Toledo, Ohio. That is a good State, Doctor.

Now, we shall be glad to hear from you.

GENERAL STATEMENT

Dr. MACNICHOL. With your permission, sir, I will read the opening statement.

Mr. NATCHER. Go right ahead.

Dr. MACNICHOL. Mr. Chairman and members of the committee. It is my privilege to appear before you in behalf of the National Institute of Neurological Diseases and Stroke.

Areas of urgent need trouble all who have visited friends or family members in a chronic disease hospital or rehabilitation center. They see the challenges which this Institute faces. Our responsibility, with your help, is to find the cause, means of prevention, and effective treatments for the many major chronic neurological, sensory, and muscular disorders. Also we have a responsibility to train gifted investigators to make continuing progress in the fight against these diseases.

High on our list of most urgent problems is a safe and effective method to diagnose impending strokes before these devasting accidents occur. Priority has also been given to immediate and effective treatment for the thousands afflicted each year with brain and spinal cord injury. Other major needs relate to epilepsy, multiple sclerosis, cerebral palsy, muscular dystrophy, and deafness.

Such an order seems formidable even when many scientists are seeking the answers. Yet, with the support provided by Congress, we are finding some of the answers which we believe will help thousands.

L-DOPA TREATMENT OF PARKINSON'S DISEASE

Perhaps the most exciting research progress in the neurological field in the past year is the effective use of L-Dopa in the treatment of Parkinson's disease. Many of the 350 patients who have been treated at four medical centers have benefited substantially.

May I put in a short paragraph here to update this?

Mr. NATCHER. Certainly you may.

Dr. MACNICHOL. An NINDS-initiated analysis of the data provided by these four centers has just been completed. It indicates that L-Dopa is effective in the majority of cases and that the adverse effects of the drug range from mild to severe. Two drug companies have initiated trials of their L-Dopa products in approximately 30 hospitals throughout the country to obtain data for new drug applications. A meeting with the participants has indicated that Institute help, for purposes of FDA clearance, is unnecessary, and we will therefore focus our attention on questions which the industry trials will not answer.

As a basic research scientist, I would like to call your attention to L-Dopa as an example of the payoff of basic research. Some years ago, physiologists and biochemists began to study synaptic transmitter substances. These are released in nerve endings that excite or inhibit the next nerve in the pathway. The first of these substances, acetylcholine, was discovered many years ago. Understanding its role, and that of the enzymes that destroy it, has made possible partially effective treatment for such diseases as myasthenia gravis. A more recently discovered synaptic transmitter is dopamine, normally present in large quantities in a particular region of the brain. In Parkinson's patients, however, it is largely lacking. An obvious thought was to administer dopamine to these patients. Unfortunately, dopamine will not pass easily from the blood to the brain; but its precursor, L-Dopa, will, although it must be given in large quantities and has unpleasant side effects.

Fortunately, by building up the dose gradually, Dr. George Cotzias of the Brookhaven National Laboratory, and several Institute grantees, including Dr. Melvin Yahr of Columbia, Dr. Fletcher McDowell of Cornell, and Dr. Benjamin Boshes of Northwestern, have managed to produce marked improvements in about 75 percent of their patients and dramatic results in some of them.

L-DOPA probably will not be the ultimate drug of choice for parkinsonism because its side effects are too severe. Nevertheless, L-DOPA has opened the door to a great new area of study which we hope will evenually lead to a more effective treatment and the discovery of the causes and methods of prevention of Parkinson's disease.

It is indeed gratifying to be able to report that the funds that have been authorized by this committee have aided in achieving what now appears to be a major breakthrough.

DRUG THERAPY FOR EPILEPSY

Drug therapy for epilepsy—in more effective forms—is greatly needed. Since 1960, no new anticonvulsant drug has been marketed in the United States. This is true in spite of the fact that physicians are

presently unable to control convulsions completely in 25 to 30 percent of epilepsy patients. Why does this situation exist? First, there is little financial incentive for companies to invest in drug studies where the market is relatively small; and second, it is difficult for these companies to obtain adequate patient studies once a decision has been made to attempt to market a drug.

The Institute is aware of eight new anticonvulsant drugs for which pharmaceutical companies have arranged trials with patients. Unfortunately, some of these trials have been in this stage for more than ten years. In an effort to move this program forward, the Institute has begun a 5-year program to offer support for laboratory and clinical studies of new anticonvulsant drugs. This could open the way for thousands more to study or work, free from seizures.

Rapid progress is also being made in the study of virus diseases of the nervous system. In addition to the previously announced discovery that kuru is a virus disease, a much more prevalent disease, Jakob-Creutzfeldt's has been successfully transmitted to chimpanzees. Also, an acute brain disease, subacute sclerosing panencephalitis has recently been shown to be caused by a virus closely related to measles.

STROKE

A national stroke program is attacking cerebrovascular disease, a major national cause of death and disability. The stroke program of this Institute, in collaboration with the National Heart Institute, has three major objectives: first, to discover the specific causes; second, to prevent worsening of the early symptoms; and third, to develop and evaluate improved methods of diagnosis and treatment. To pursue these objectives, 19 stroke clinical research centers are now active.

This program can be expanded into every region of the country. In addition, in laboratories and training centers throughout the Nation, stroke research projects and training programs have been initiated and basic research and skilled manpower have been mobilized. This coordinated national program has kindled hope in an area which only 5 years ago was often considered a hopeless medical catastrophe.

BRAIN AND SPINAL CORD INJURY

Brain and spinal cord injury too often dooms the victim and overwhelms his family. Brain damage may cause death or prolonged coma or may leave persistent mental confusion. Spinal cord damage often causes severe paralysis. To solve these problems, the Institute has launched a pilot program of multidisciplinary centers for clinical research on head and spinal cord injury. We expect that these centers will provide the required blueprint for a national brain and spinal cord injury program.

EFFECT OF MOTHER'S HEALTH ON CHILD'S MENTALITY

The possible influence of the health of the mother on her child's mentality was recommended last year by the committee for special attention. The Institute's collaborative perinatal project's decade of

vigorous data collection has made it possible to present some definitive findings on this critical problem.

We have found that the physical health of pregnant women is strongly related not only to the intellect but to the very survival of their children. Diabetes and high blood pressure are conditions associated with a high perinantal mortality rate. Increasing evidence indicates that such disorders in pregnant women contribute heavily to neurological and mental damage in those children who do survive.

In addition to these illnesses, other diseases during pregnancy seem to produce neurological abnormalities particularly in small or premature children. Our evidence points to the central factor of poor maternal health, reflected in underweight, poor weight gain in pregnancy, and acetonuria as an indicator of poor nutrition.

The finding regarding acetonuria (not a disease but an indicator of faulty metabolism or acute starvation) is an apt illustration of the anticipated value of the project's large data base. From initial observations that the offspring of diabetics often have lower IQ's as compared with those of nondiabetics, it was found that this outcome was confined not only to diabetic women who also had acetonuria in pregnancy, but also to acetonuric women who had no diabetes at all. This last finding is particularly meaningful. Although only about one percent of all women of childbearing age have diabetes, acetonuria may occur in about 5 percent due to other causes.

NEUROMUSCULAR DISEASES

The neuromuscular diseases affect primarily America's greatest asset—her children and young adults. Estimates of the number of people affected by the disorders of muscle weakness, wasting, or paralysis range between 250,000 and 1 million. The two most prevalent nueromuscular ailments are muscular dystrophy (MD) and myasthenia gravis, the former affecting mostly children and the latter young adults.

Research on the neuromuscular diseases conducted and supported by the National Institute of Neurological Diseases and Stroke is concentrated in three main areas: genetic research, cell biology and chemistry, and drug treatment. Over $4 million has been spent this year on research conducted both in the Institute's Medical Neurology Branch and on over 100 research projects at medical institutions throughout the country.

Many basic research studies are designed to elucidate the precise biochemical or metabolic defects causing each neuromuscular disorder. Other studies are concerned with the fundamental physiological and chemical characteristics of both normal and diseased muscle cells. As these studies provide us with greater knowledge of what is normal in muscle cells, we will be better able to understand, identify, and correct disease processes. Some therapeutic trials are being conducted.

HEARING LANGUAGE AND SPEECH

Hearing, language, and speech problems of preschool children affect their school progress. In many instances, if these problems are identified by age 3 and properly treated, the child can have a normal

school life by 5 or 6. However, if not identified until school age or later, many children must be put in special education classes and some never catch up.

The needs in the communicative field, of course, are not confined to the very young. Any or several of the communicative mechanisms can lose some of or all their function from diseases such as stroke, injury, or aging. Much more research is needed to learn how to prevent such disabilities.

Last year the committee recommended an increased emphasis on training of scientists by the Institute. To meet continuing needs, it is important that the programs maintain a steady flow. This is particularly important since 3 to 5 years of highly specialized training and experience are required to prepare a physician-investigator or basic scientist to accept responsibility for independent research in the neurological and sensory areas. This continuing supply of well trained investigators is vital to the Nation's research efforts against stroke, epilepsy, parkinsonism, deafness, and many other disorders.

In conclusion, Mr. Chairman, the budget request of $103,485,000 is $219,500 more than the fiscal year 1969 estimated obligations. Within the budget, however, are requests for increases of $372,000 in research grants, and $587,500 in direct operations, offset by a decrease of $740,000 in the fellowship and training grant programs.

Special Reports

I shall be happy to answer any questions, and also I have special reports in the following areas: Parkinsonism, stroke, epilepsy, muscular dystrophy, multiple sclerosis, cerebral palsy, and hearing and speech disorders, if you would like these for your information.

Mr. Natcher. We will follow our usual practice and place these up-dated reports in the record.

(The reports follow:)

Special Report: Parkinson's Disease

THE PROBLEM

Parkinson's disease is one of the most crippling chronic disorders of the nervous system. It most frequently attacks people in their fifties and sixties, and is a matter of growing concern to the medical profession because it is thought to be increasing in prevalence along with the increase in the average life span. Epidemiological studies in New Zealand, Australia, England, Minnesota, and Sweden all indicate an overall prevalence rate of about one case per 1,000 population; however, estimates from United States voluntary agencies suggests a prevalence of one case per 200 population.

Symptoms

First described in 1817 by James Parkinson, a London physician, the disorder affects the brain centers involved in the control and regulation of movement. The intellect, however, is ordinarily unimpaired. Due to disordered control of movement, rigidity of the muscles develops with uncontrollable trembling of the extremities, stooped posture, lethargy, loss of facial expression, and difficulty in walking, talking, writing, or any action requiring a high degree of muscular coordination.

Although the symptoms are usually progressive, and in most cases gradually produce disability and often complete helplessness, there are stationary periods in some patients of 5, 10, or more years duration, during which there is little

or no visible progression of the symptoms. Parkinson's disease is rarely the primary cause of death, but it often weakens the victim so that he falls prey to other diseases.

Causes

The causes of Parkinson's disease are still unknown. Certain forms may result from a still undetected virus, and a few metallic poisons have been suspected. Recent work has shown that depletion of certain chemicals involved in nerve excitation accompanies parkinsonism, but how the depletion occurs is still not clearly understood.

While there is no cure for Parkinson's disease, drugs, surgery, and physical therapy offer three ways of alleviating the crippling symptoms. Drug therapy can reduce rigidity and tremor in many cases of parkinsonism. Intensive physical therapy can often bring patients from 50 percent of normal to 75 percent, under ideal conditions.

Surgery, although dramatic, and widely publicized, is of more limited use, because only 10 to 12 percent of all victims of parkinsonism are suitable subjects. Usually patients over 65 are not helped by surgery. The improvements, however, that are possible under any of the three forms of treatment, or combination, are substantial, and provide encouragement to many patients.

THE PROGRAM

The Institute's program in Parkinson's disease includes the grant support of many individual research projects in universities and other centers; projects centered around the surgical treatment of patients at the National Institutes of Health in Bethesda, Md.; the support of training in neurology, neropharmacology, neurosurgery, and the many other disciplines bearing on the problem; and efforts to coordinate more effectively all research being conducted through meetings, publications, and information services.

RESEARCH PROGRESS

Drug therapy

A major breakthrough in drug therapy for Parkinson's disease appears to have been confirmed this year by trials of the amino acid levodihydrophenylalanine (L-DOPA) in approximately 350 patients at Brookhaven National Laboratory, Columbia University, Cornell University Medical Center, and Northwestern University. Preliminary reports have indicated that up to 75 percent of the patients treated have benefited substantially, and efforts are in progress to speed analysis of the data produced, so that the compound can be manufactured in quantity and marketed for clinical use.

The work illustrates the importance of basic research combined with clinical observation, and flows directly from several converging lines of investigation at United States, Canadian, and European institutions. Studies at NIH in the late 1950's produced important new information on the role of a group of substances known as biogenic amines in the central nervous system, including the finding that the tranquilizing drug, reserpine, which produces symptoms similar to those of parkinsonism when given in heavy doses, also produces depletion of brain amines. Carrying the work farther, scientists at the University of Vienna reported in 1960 that they had found a marked depletion of the amine, dopamine, in the basal ganglia (an area normally richly supplied) of Parkinson patients at autopsy. This led to efforts to replace the substance, but it was found, largely through NIH-sponsored work, that it would not cross the blood-brain barrier—a protective biochemical mechanism separating the blood from the central nervous system. Then scientists in several countries found that L-DOPA, which is dopamine's metabolic precursor, or preceding link in a chain of brain cell metabolism, would cross the barrier. Early efforts with L-DOPA, administered intravenously and in small doses, showed favorable, but not remarkable or consistent effects. Then Dr. George Cotzias, and his associates at the Brookhaven National Laboratory succeeded in demonstrating the effectiveness of large oral doses of L-DOPA, and others, including Dr. Melvin Yahr at Columbia, Dr. Fletcher McDowell at Cornell, and Dr. Benjamin Boshes at Northwestern began achieving the same results, verifying the earlier findings.

Success with L-DOPA also illustrates the importance of communication in the medical sciences. The potential of the scientific groundwork which was reported in the medical literature by 1962 was not immediately recognized in the United States. A major stimulus to the recognition of the potential of L-DOPA was a large scientific conference on parkinsonism which took place in November 1965, at the Columbia University Parkinson Information and Research Center described below. Over 600 scientists from this country and abroad attended, and information obtained there helped stimulate American workers to begin experimental trials. The meeting was one of a series the center has sponsored with NINDS support.

Surgery

Surgery continues to be successful in a high percentage of carefully selected patients. Dr. J. M. Van Buren, an NINDS neurosurgeon, has reported that in a series of 200 selected patients undergoing thalamotomy at the National Institutes of Health, the failure rate was between 3 and 4 percent, and that although the bradykinesia (slowness of movement) is not helped by surgery, relief of tremor and rigidity has been highly successful. Research projects conducted in concert with parkinson surgery at NIH include microelectrode studies of responses of single nerve cells to stimuli; efforts to find out in what order various structures in the motor control system come into play, and studies of modifications in verbal behavior caused by depth electrode stimulation.

A similarly low failure rate was reported this year by Drs. Stanley Stellar and Irving Cooper of St. Barnabas Hospital in New York City. They have found that in a series of 2,868 consecutive cryothalamectomies for relief of tremor and rigidity in parkinsonism, the over all mortality was 1.5 percent and morbidity was 4.6 percent in the period up to 9 months following surgery. Arterial hypertension was one of the most important single factors related to increased risk advanced age was another, and it was also found that those having more than one freezing lesion at a given operation, and those undergoing second side surgery were exposed to increased danger.

INFORMATION CENTER

A major institute programing effort of the past few years has been the establishment and support of the Parkinson's Disease Information and Clinical Research Center at Columbia University in New York City. The information center, one part of the facility, is developing a comprehensive automated library service, including searching, evaluating, and computer storage and retrieval of the scientific literature on Parkinson's disease, and the publication of bibliographies, indexes, and critical reviews.

The clinical research center, the other portion of the facility, is conducting a comprehensive research program aimed at determining the cause, improving diagnostic techniques, and developing methods of treatment of Parkinson's disease and related movement disorders. The program closely integrates basic and clinical research, and serves as a training center for research workers. Reseach center scientists also serve the information center in an advisory and evaluative capacity.

Two of the primary tasks of the center as a whole have been to survey the entire field of medical research as it relates to Parkinson's disease, and to bring together scientists from the various pertinent basic and clinical disciplines so that a strong concentration of interest could be created. The center has produced two reviews based on its survey, and will continue this activity on a periodic basis.

OUTLOOK

The cause and cure of Parkinson's disease are still unknown. However, research on the bioamines offers exciting possibilities toward understanding the pathophysiology of the disease and revealing clues to its etiology. In the interim, new approaches are being developed to control its symptoms, and highly encouraging research is in progress in a number of medical centers. Gains made thus far, together with plans for the future, have justified an optimistic attitude among scientists, physicians, and others concerned that prevention and control can ultimately be attained.

Special Report: Stroke

THE PROBLEM

Strokes, known in the medical world as cerebrovascular accidents, continue to rank third among causes of death in the United States, exceeded only by heart disease and cancer. Each year about 400,000 people have strokes, and about 200,000 die. It is estimated that there are 2 million victims of stroke alive today, one-third of whom were wageearners before they were stricken. The economic cost of strokes has been estimated at more than $1 billion a year—$440 million for direct costs of medical care, and $700 million, or 179 million man-hours, in lost productivity. There are thus immense possible benefits to be achieved through research in this field—in both dollar and human terms.

Cerebrovascular disease may be a slow process, extending over many years. The basic causes are still poorly understood, but the acute stage of the disorder—the stroke—is usually preceded by one of three events: (1) thrombosis—the formation of a blood clot which remains at its point of formation in a blood vessel; (2) embolism—the sudden blocking of a blood vessel by a particle such as a blood clot, carried by the blood stream from a larger to a smaller vessel which it obstructs; or, (3) hemorrhage—the rupture of a blood vessel so that blood leaks into surrounding tissue.

All cells require oxygen, and most receive their supply entirely from the blood stream. The importance of an adequate blood supply to the brain is seen in the fact that although the brain comprises only 2 percent of the total body weight, it normally utilizes 20 percent of the total oxygen supply of the body. Brain tissue cannot store oxygen and is completely dependent from minute to minute on an adequate flow of blood. When brain tissue is deprived of oxygen for more than a few minutes, the cells die.

THE PROGRAM

The period from 1965 through 1968 has seen substantial growth in the institute's cerebrovascular research and training program. Since stroke is a problem of the blood vessels of the nervous system, the National Heart Institute also maintains a strong program in this area, supporting related research, and participating in program planning and management. This activity is accomplished by a joint subcommittee of the advisory councils of the two institutes.

Research Center

Eighteen cerebrovascular clinical research centers, located in major university medical complexes about the country, now make up the largest segment of the program. The centers vary considerably in their research emphasis: Several concentrate on single research approaches, as at John Hopkins University, where the epidemiological aspects of stroke are being studied—incidence and prevalence, methods for early detection of "high risk" segments of the population, familial aggregation of stroke, and similar questions. A center at Boston University devotes its efforts to research in aphasia—speech disorders following strokes. Here, anatomical studies of corticocortical connections in humans and animals, and studies of the neuropsychology and statistical properties of aphasic language are being carried out.

Some stroke research centers are broader in research focus, often working with several related approaches, such as the physical mechanics of cerebral blood flow, cerebral cellular metabolism, and efforts to control these factors with drugs, inhaled gases, and other means. All centers, except the two devoted to epidemiology, have interrelated clinical and basic research programs, and include accommodations for one to 30 research patients. Most of the centers also conduct training programs, and are staffed by 10 or more physicians and scientists from a wide variety of disciplines.

One center, headed by Dr. James L. O'Leary at Washington University in St. Louis, has just announced the establishment of an intensive care research unit especially equipped for special studies of acutely ill stroke patients. The unit is staffed around the clock, and monitoring equipment constantly records that patient's response to various forms of therapy. Coordinated with the unit are blood coagulations studies, efforts to find better indicators of "stroke proneness," and other investigations.

A very recent expansion of this program provides for grant support of research units for human studies on an outpatient basis. These units will greatly expand opportunities in epidemiology and other research areas where ambulatory patients can be studied.

Project grants

In addition to the broadly targeted work of the clinical research centers, about 50 research projects are being conducted with Institute support. These cover the entire spectrum from basic laboratory studies in such fields as neurophysiology and biochemistry to clinical investigations of drug effectiveness, the improvement of diagnostic devices and techniques, and development if improved surgical approaches.

Cooperative studies

Another approach to the problem of cerebrovascular disease is through cooperative studies. This technique is applicable to those problems where sufficient data can be collected and analyzed only through the combined efforts of a number of institutions. The Institute has been supporting a "Cooperative Study of Intracranial Aneurysms and Acute Subarachnoid Hemorrhage" among 24 university—based centers here and abroad. Personnel at a central registry at the University of Iowa have analyzed the accumulated data on over 6,000 cases, and have published a wealth of carefully derived information of value to physicians in deciding upon courses of treatment. As an example, a conclusion recently drawn from the study has been that surgery in the first 14 days after subarachnoid hemorrhage carries such an excessive risk, that its use need to be reserved for only very select cases. The first therapeutic task is to maintain the patient through his first two weeks without additional subarachnoid bleeding, and only then should surgery be considered.

Another cooperative study underway aims to provide better data on the effects of blood-pressure-lowering drugs on stroke. It is well known, for example, that the cerebral arteries make a protective adjustment to sustained high blood pressure. After this has happened, a sudden lowering of blood pressure by drugs, shock, or any other means, can produce a disastrous reduction in blood supply to the brain, usually because the vessels do not readjust fast enough. The study will provide information on how much blood pressure can be safely reduced in these patients, and how fast this can be done. Scientists will also learn more about the long-term effects on the brain of moderate high blood pressure, and the long-term effects of drug treatment.

The National Heart Institute is sponsoring a "Joint Study of Extracranial Arterial Occlusion." The purpose of this study is to improve the criteria for selecting patients for carotid (neck) artery surgery, and to enable surgeons to better predict in which types of patients they can expect success with the procedure. Twenty-seven invesigative teams are contributing to this study, and much valuable data are being produced.

Training

Since its establishment in 1951, the Institute has allocated about 25 percent of its budget to training support for teaching and research—well over 9,000 of today's physicians and research scientists have received training through this program—but it has only been within the past several years that it has been possible to begin training programs specifically on stroke. The Institute now has seven cerebrovascular training grants active at leading universities and hospitals, and these are supplemented by over 130 grants for training programs in neurology, neurosurgery, and all the other neurological disciplines involved in cerebrovascular disease research and medical care.

Direct support to individuals is also provided under cerebrovascular clinical traineeships. These are for practicing physicians seeking intensive study of the latest development in diagnosis and therapy.

A new program for clinical training of cerebrovascular nurse-specialists is planned. This program gives nurses who have the registered nurse degree 6 to 12 months of specialized "bedside" training in the field, and will give nurses holding the baccalaureate degree, specialized training necessary for developing improved methods of cerebrovascular care. Stipends for the trainees are to be paid by the Public Health Service's Division of Nursing, the training environment to be provided in the stroke clinical research centers described above.

Communication

The improvement of communication in the stroke field has been an urgent need. NINDS and NHI sponsor scientific conferences, both on specific aspects of the problem, such as aphasia, and rehabilitation, and on the whole field. The sixth in a series of biennial general conferences was held at Princeton, N.J., in 1968, and several smaller meetings, including a workshop for chiefs of the stroke centers, were held.

Communication projects include a quarterly Cerebrovascular Bibliography, a Cerebrovascular Survey Report reviewing the entire field, and a reprint service for physicians. Substantial assistance has been provided to the Division of Regional Medical Programs in preparation of guidelines for establishing cerebrovascular care facilities.

RESEARCH PROGRESS

Epidemiological studies of stroke are of utmost importance, because detailed and reliable knowledge of the distribution of the disease, correlated with genetic and environmental factors, diet, and other influences, can provide important clues to its causes, and possible means of prevention.

For example, accumulated data have suggested striking differences in the occurrence of death due to stroke in different parts of the United States. Incidence has appeared much higher than average in the southeastern part of the country, and lower in the Rocky Mountain area. However, scientists have not been certain of this; the statistical differences could have resulted from a number of unmeasured factors, such as reporting practices.

In late 1968, the difference was definitely verified. A nine-city epidemiological project headed by Dr. Abraham Lilienfeld of Johns Hopkins University and funded by NINDS showed a measurably higher rate among white males in the Deep South than in other parts of the country. The study involved the validation of death certificate information (a notoriously unreliable source) by hospital and home interviews, and will provide a firm basis for projects aimed at finding out why this group faces an increased risk.

Also of interest this year have been reports from a collaborative study being conducted by scientists at Kyushu University in Japan, and at the University of Minnesota. For years the Japanese have been reporting a higher incidence of brain hemorrhage in relation to infarction, or clotting, than seemed to be the case in the United States. The study has shown the reports to be incorrect—that the ratio in Japan is quite colse to that in the United States. It has also brought out an unexpected finding: That in Japan, cerebral infarctions occur more often because of obstruction in the smaller vessels of the brain; in the United States they occur more often in the middle-sized and larger vessels. The finding narrows the focus of research in this area, and may speed understanding of the mechanisms of cerebral thrombosis.

Cerebrovascular surgery is a field showing steady progress and constant refinement. NINDS grantees at the Medical College of Georgia have reported animal experiments in which they have joined small blood vessels with plastic adhesives. Although the technique is not yet ready for use in humans, the scientists have eliminated several types of plastic from consideration, and have found isobutyl cyanoacrylate to be the most promising of the materials tried.

Some scientists feel that an era of successful intracranial surgery is about to begin; yet the necessity for very rapid work, the inaccessible position of many of the brain's blood vessels, the friable vessel walls, and the problem of controlling bleeding all make suturing exceedingly difficult. One contribution toward a solution to this problem, reported by NINDS grantees, has been their development of clip grafts—teflon or dacron grafts attached to spring metal clips. The grafts were successful in 46 experimental animals, and in a limited number of patients. The investigators feel that they will come into wider use for human endarterectomies, embolectomies, aneurysms, and in the repair of major vessels injured in tumor surgery.

Stroke diagnosis is also a field exhibiting constant progress and refinement. Utilization of the familiar Doppler effect was reported on this year by Institute grantees, who have obtained profiles of the velocity of carotid artery blood flow in 30 patients. In the project, a sonic beam of 5 megacycles was directed transcutaneously along the carotid artery. The backscattered waves, being slightly more or less than 5 megacycles, depending upon the direction and velocity of the reflecting medium, in this case the red corpuscles, were picked up and converted

into an electrical signal on an oscilloscope. The researchers noted that arteriosclerotic disease at the carotid bifurcation causes easily recognizable changes in the velocity profile, and that the method may prove to be a useful adjunct to auscultation, angiography, thermography, and other methods of detecting lesions in this area.

A report from National Heart Institute grantees is of interest to stroke diagnosticians. Their project is a continuation of studies of the electrocardiogram in stroke patients. For several years it has been known that intracranial disease exhibits electrocardiographic changes consisting of dramatic giant T wave inversion; however, these investigators have observed less obvious and more subtle changes, consisting of prominent upright T waves frequently associated with prominent U waves, prolonged Q–T interval, and T–U fusion. Of 55 patients with electrocardiographic changes assumed to be related to intracranial lesions, 38 had the type with upright T waves.

There continue to be many needs in the field of cerebrovascular disease, many of which are still unmet. With increasing numbers of Americans moving into the age groups menaced by stroke, it becomes increasingly urgent that the Institute's research and training program continue to gain momentum. The Federal effort has already had a major impact on the field, and promises to more than repay its supporters in terms of better health.

Special Report: Epilepsy

THE PROBLEM

Epilepsy is a major health problem in the United States. It is generally estimated that there are at least one and a half to two million victims of epilepsy in this country. However, because of the social stigma and unfavorable economic and insurance position of sufferers from epilepsy, no reliable data are available about the true prevalence of this condition.

Epilepsy costs the Nation millions of dollars in patient care, research, and lost earning power. Overall, the economic burden in direct and indirect costs is probably well over one billion dollars a year. Unfortunately, much of this cost is unnecessary. Many, perhaps most, of the victims of epilepsy are intelligent, capable people with high potential earning power. Much greater efforts are needed in education and in placing victims of epilepsy in suitable employment.

Scientific opinion differs on the fundamental cause or causes of the disorder. Some believe that all forms of epilepsy arise from a single disease entity. Others feel that certain common mechanisms of neuronal discharge may occur in all cases, but that the specific etiologic, chemical, anatomical, or functional defect may vary widely. Epilepsy not infrequently results from injury or disease of the brain.

At the present time, physicians can control (but not cure) seizures in the majority of epilepsy patients by giving them anticonvulsant drugs. The recording of the electrical activity of the brain (electroencephalogram—EEG) is a widely used means for diagnosis and study of the disorder.

THE PROGRAM

The Institute's programs in epilepsy are attacking the problem through approaches designed to provide a better understanding of the basic chemical, structural, or functional mechanisms which are disturbed in the disorder; the factors that precipitate seizures; and the basis for effective treatment of epilepsy.

Five clinical epilepsy research centers are sponsored by the Institute. One is located at the University of Washington where studies of the fundamental mechanisms underlying epilepsy are being conducted by a multidisciplinary research team. Another center at the University of Wisconsin is conducting both clinical and basic research studies. A third center at the Brain Research Institute, University of California at Los Angeles, is concentrating on a study of the electrical process underlying the epileptic state in animals and in man. A fourth center at Yale University is conducting a program of research into mechanisms of epilepsy and of phenomena associated with seizure states. In addition, the Institute supports the Neuropharmacology Research Center of the University of Utah, which is primarily concerned with the mode of action of anticonvulsant drugs.

The Collaborative Study of Epilepsy, a large project supported by the Institute, concluded its pilot phase in December 1968. Four medical centers, Marquette University, the University of Virginia, Montreal Children's Hospital, and the New England Medical Center participated in this study. The immediate goal of this program was to establish a therapeutic baseline, or frame of reference, for seizure control. Information gathered in the pilot phase of this study is now under analysis and the results will be published. The methodology developed for data collection, storage, and retrieval will be employed in contracts solicited for the cinical investigation of anticonvulsant drugs.

The Institute has begun a program of encouragement and support for clinical trials of anticonvulsant drugs. A symposium, "Laboratory Evaluation of Antiepileptic Drugs," was held in Salt Lake City, Utah, May 1968. One anticonvulsant drug study began in 1968 at a state hospital. Additional new drug studies are anticipated so that pharmaceutical companies discovering promising agents may have an opportunity for an Institute-supported drug trial. The Institute plans to continue and expand these activities to provide opportunity for clinical evaluation of all promising new agents. This is to include the sponsorship of laboratory studies of promising anticonvulsant compounds.

In recent years, many basic research studies have contributed to the understanding of epileptiform seizure mechanisms in man. However, these studies have not been sufficiently applied to the specific problems of epilepsy. In a major effort to bridge this gap, the Institute and PHS Advisory Committee on the Epilepsies sponsored a symposium on Basic Mechanisms of the Epilepsies held November 18–21. At the meeting attended by some 400 scientists from 17 countries, basic researchers in such fields as neurophysiology, neurochemistry, biophysics, eletroencephalography, pharmacology, endocrinology, and genetics presented highlights of their own studies and their relationship to epilepsy. These papers will be published to provide reference guide to epilepsy researchers and to investigators in subspeciality areas whose work may be related to current investigations in the epilepsies.

This past year, the Institute sponsored a special medical exchange mission to the USSR. A group of six American medical scientists, designated as the delegation on Problems of Higher Nervous Activity, visited four major Russian medical research centers in May, 1968. Although the delegation was originally conceived as a mission to study epilepsy in the Soviet Union, Soviet neurologists urged that the delegation be broadened to include higher nervous functions. A report will be published on the mission at a later date.

An important part of any concerted attack on a disease is communication. It is essential that investigators be aware of what colleagues are doing, and what their results are; that practicing physicians are properly apprised of new possibilities in therapy; and that administrators have a firm basis for program planning. This past year considerable progress has been made in this direction. The Institute published a new monograph, "The Clinical Neurophysiology of Epilepsy: A Survey of Current Research," which surveys current electrophysiologic research in man which is pertinent to an understanding of the epilepsies. The monthly publication "Epilepsy Abstracts," first issued in November 1967, has been enthusiastically received by the scientific community. Some 2,250 scientists have subscribed to this Institute-sponsored publication.

RESEARCH PROGRESS

Despite a good deal of special attention to epilepsy research over the past several years, progress has not been rapid in the areas of drug therapy, surgical treatment, electroencephalography, or basic research. During the past 2 years, however, the Institute's epilepsy research program has been reorganized and new goals have been established. It is hoped that a greater emphasis on this serious problem will accelerate research progress. However, despite the relatively slow pace of ongoing research, several new advances have been reported this past year.

Drug therapy research

Important work is underway in the study of drug effects. In one study, for example, Dr. Henn Kutt of Cornell University, an NINDS grantee, describes two unusual responses which may occur from the usual treatment with diphenylhydantoin (Dilantin): a low tolerance to the drug and refractoriness to it. A

few patients have been found to have low tolerance to the drug that in normal doses causes a very high level of the drug in the patient's body. This is due to an inability to metabolize the drug and eliminate it from the body. Refractory patients include those who for various reasons do not respond to treatment with Dilantin and continue to have seizures. In some of these cases the drug was metabolized very rapidly and produced only quite low drug levels in the blood. Not only does this study provide guidance to the physician in the treatment of epileptic patients with the drug Dilantin, it may be a source of information toward developing new therapeutic agents.

In another important drug study, a gas-liquid chromatographic method for measurement of diphenylhydantoin in serum has been developed. Knowledge of the blood level of an anticonvulsant drug will make it possible for the physician to relate therapeutic effect and side effects to dose, and thus be able to manage his patient more effectively. Accurate data on drug blood levels will help to provide some needed information on the action of drugs in the body and how they are eliminated. Reliable methods for measuring amounts of a drug in the blood should also prove invaluable in research for new, improved anticonvulsants.

One drug has been found to have a special application in surgery. Dr. Mary A. B. Brazier of the Brain Research Institute of the University of California at Los Angeles reports that small doses of thiopental, a rapidly acting barbiturate commonly used to induce surgical anesthesia, can be used to pinpoint areas of diseased brain tissue responsible for epileptic seizures. Gradual administration of thiopental evokes specific brain wave patterns that can be used as markers. By exact localization of the diseased area, surgeons are able sometimes to remove it, relieving seizures.

Possible factors influencing epileptic seizures

In the past, there has been some evidence pointing to genetic factors causing or predisposing to generalized epilepsy. However, it has been assumed by some that heredity was not likely to be important in focal seizures. In a study of the families of 31 focal epilepsy patients, Dr. Eva D. Andermann, of McGill University, reported findings supporting the view of a genetic basis for temporal lobe epilepsy. Dr. Andermann found that incidence of abnormalities among families of epilepsy patients was significantly higher than in control subjects, with a predisposition to both generalized and focal epilepsy.

Another group of investigators studying central nervous system phenomena have found evidence that the excitatory level of the cortex and subcortical structures may be dependent upon release of specific amino acids. Liberation of these amino acids appears to be dependent upon activity of neurons in the nonspecific or midline thalamic nuclei and rostral midbrain regions. These data, considered preliminary by the investigators, may provide a better understanding of the mechanisms responsible for electrophysiologic alterations which accompany normal physiologic states as well as pathophysiologic phenomena characteristic of certain of the epilepsies.

Other research findings

One of the greatest needs of epilepsy investigators is a better animal model for research. A number of relatively good experimental animal models have been used over the years. The chief fault with these models has been that none were found in which epileptic seizures occur spontaneously; all seizures in these animals were induced mechanically. Scientists have discovered a baboon (Papio papio) in Senegal, Africa, that sustains an epileptic seizure in response to a flickering light stimulus. This animal model should provide the basis for research into the physiology of this pathological response to light as well as a model for testing drugs with a potential efficacy in this condition.

An Institute scientist has been able to pinpoint selective intellectual deficits in children with temporal lobe or centrencephalic epilepsy. Specific patterns of intellectual impairment were observed in children with unilateral temporal lobe or centrencephalic epilepsy. The left temporal patients showed learning and memory deficits on verbal tasks while their performance on nonverbal tasks was unaffected. The converse was true for children with right temporal involvement. In contrast to the two temporal groups, the centrencephalic patients were without significant memory defect; instead, they showed lower scores on a test of sustained attention. The results are similar to those obtained in studies of adults with comparable cerebral dysfunction. The findings suggest that cerebral differentiation of intellectual processes is established in childhood.

Four critical periods in the epileptic's life occur at ages 6, 14, 35 and 60, according to a neuro-physiologist at Northwestern University. Brain waves are most likely to show epileptic patterns during these years, possibly because they represent periods of major change in the lives of most people. At six, the child first enters school. At 14, he enters puberty and adolescence. Around 35, he experiences a peak in the struggle to succeed, often accompanied by soul-searching on his course in life. And at 60, he faces the prospect of retirement. The investigator has pinpointed these danger years by a study of the brain-wave patterns of 1,355 patients with epilepsy.

A search team under the direction of Dr. Maitland Baldwin at the Institute's Bethesda laboratories reports successful results in treating 15 children suffering from intractable and frequent epileptic attacks. An effective therapeutic regimen consisting of a combination of anticonvulsants, Valium, and corticosteroids on the one hand, or a high ketogenic diet on the other, produced complete control of attacks in these children who had been averaging between 10 and 100 seizures per day.

OUTLOOK

While many persons with epilepsy are able to live normal, productive lives, many still suffer from seizures that cannot be controlled. The Institute's epilepsy research programs have two aims: to develop effective treatment methods, and to understand the basic defect so that epilepsy can be "cured."

Great attention is now being focused on studies to develop and evaluate new anticonvulsant drugs that will be effective for those patients who are not helped by drugs currently available. Epidemiological studies are needed to supply more information on who develops the disorder before physicians can understand various aspects of epilepsy.

Special Report: Muscular Dystrophy and Other Neuromuscular Disorders

The neuromuscular diseases affect primarily America's greatest asset—her children and young adults. Estimates of the number of people affected by the disorders of muscle weakness, wasting, or paralysis range between 250,000 and 1 million. The two most prevalent neuromuscular ailments are muscular dystrophy (MD) and myasthenia gravis, the former affecting mostly children and the latter young adults.

Research on the neuromuscular diseases conducted and supported by the National Institute of Neurological Diseases and Stroke is concentrated in three main areas: genetic research, cell biology and chemistry, and drug treatment. Over $4 million has been spent this year on research conducted both in the Institute's Medical Neurology Branch and on over 100 research projects at medical institutions throughout the country. Voluntary organizations such as the Muscular Dystrophy Associations of America, the Myasthenia Gravis Foundation, Inc., and the National Foundation for Neuromuscular Diseases, Inc., maintain extremely active research programs as well as supporting patient care and rehabilitation facilities.

Many basic research studies are designed to elucidate the precise biochemical or metabolic defects causing each neuromuscular disorder. Other studies are concerned with the fundamental physiological and chemical characteristics of both normal and diseased muscle cells. As these studies provide us with greater knowledge of what is normal in muscle cells, we will be better able to understand, identify, and correct disease processes. Some therapeutic trials are being conducted.

MUSCULAR DISTROPHY (MD)

Several important research findings have been reported this year in the muscular distrophies. Investigators have been concerned with both genetic and cell abnormalities in this disorder, as well as with developing effective treatment for these diseases of progressive weakness and wasting of skeletal muscles.

Scientists in the Institute's Medical Neurology Branch have found that clincally normal carriers of Duchenne dystrophy, the most common type of MD, demonstrate atrophy and architectural derangement of scattered or slightly grouped muscle fibers. Histochemical techniques used in this study showed high RNA and oxidative enzyme stains for both types of muscle fibers and should per-

mit researchers to identify, through chemical testing and muscle biopsy, the women who carry the gene for this X-linked disorder.

In a separate study, another group of investigators have found that carriers of the gene for MD have increased amounts of the enzyme creatine phosphokinase (CPK) in their blood serum. Physicians can detect 75 percent of the carriers by measuring this enzyme. This is important for genetic counseling.

In other studies, Institute grantees at the University of Connecticut have made an observation which may represent a significant contribution toward understanding the progressive degeneration process in muscular dystrophy. In chickens with hereditary MD, the researchers have demonstrated that a decrease in the enzyme alkaline phosphatase in the capillaries and small arterioles precedes degeneration of muscle fibers. High oxygen therapy (70 percent oxygen) has been shown to retard progress of the steps in muslcle breakdown in the chickens.

Studies to establish a protocol for testing drugs which may be useful in treating muscular dystrophy are being conducted by two Institute-supported investigators. After several years of planning, the researchers—one at Case Western Reserve University and one at the University of Utah in Salt Lake City—are conducting a double-blind study.

One goal of research on muscular dystrophy is to find a biochemical defect for each form of the disease, so that physicians will be able to prescribe specific treatment for each form. Several forms of MD already have been found to be to be characterized by the absence of a specific enzyme. In some patients, the missing enzyme is phosphorylase, in others it is phosphohexosisomerase. Institute grantees at the College of Physicians and Surgeons, Columbia University, have recently found a third metabolic defect—an absence of phosphofructokinase.

MYASTHENIA GRAVIS (MG)

Myasthenia Gravis is a disorder characterized by widespread failure of impulse transmission at the nerve-muscle junction producing impairment of normal muscle function, fatigue, and eventually paralysis of the muscle of movement and respiration. The weakness may fluctuate from mild to severe and may affect different sets of muscles at different times.

In addition to research on the basic defect in this disorder, such as a study on the basic neurophysiology of myasthenia underway at the Johns Hopkins University, researchers are studying possible treatment methods. The value of thymectomy (removal of the thymus gland) has been studied for several years. Analysis of data on almost 300 thymectomies showed that this therapy is effective in young women who have had the disease for less than 5 years and who do not have a thymoma. Another form of therapy that has been used in myasthenia is ACTH.

In two studies at the Institute's Medical Neurology Branch, researchers found 1) that long-term ACTH gave marked therapeutic success in a case of atypical childhood myasthenia gravis and 2) that they could immunologically characterize and distinguish between antinuclear factor (an antibody seen in patients with systemic lupus erythematosus) and antimuscle factor in the serum of MG patients.

An Institute grantee at Harvard University has been studying the action of germine diacetate on skeletal muscle in a project to develop a new type of drug for treating MG with promising results in the first group of patients. A number of researchers are investigating the possibility that myasthenia gravis and other neuromuscular disorders may be auto-immune. One such research study, being conducted at Maimonides Medical Center in New York City, is concerned with antibodies or proteinaceous substances produced in patients with myasthenia gravis.

FINDINGS IN OTHER NEUROMUSCULAR DISEASES

Laboratory techniques such as histochemistry, biochemistry, immunology, autoradiography, electron microscopy, tissue culture and electromyography are also being applied to the study of neuromuscular disorders other than muscular dystrophy and myasthenia gravis. These include such categories as peripheral neuropathies, congential and other myopathies, and periodic paralysis. Central nervous system degenerations are also being studied. This year some research progress has been made in all of these areas.

Familial recurrent neuropathy (Tangier disease) in two sisters has been identified as being related to a specific biochemical abnormality. Physicians from this Institute cooperated with the National Heart Institute in studying the two patients who were found to have alpha-lipoprotein deficiency accompanied by low plasma cholesterol and neurological symptoms. This abnormality differs biochemically from similar syndromes that have been described previously and can be specifically diagnosed by careful study of plasma lipids and lipoproteins.

Two additional congenital myopathies have been identified and described by the Institute's Medical Neurology Branch. One disorder is characterized by segmental loss of cross-striations in the muscle fiber. In the second disorder, type I muscle fiber hypotrophy (selective atrophy of type I fiber) with central nuclei, an experimental model of the disorder was produced by neonatal sciatic denervation in rat gastrocnemius muscle. The researchers studying this experimental model believe it indicates that the disorder is not a myopathy but rather an alteration of the neural influence of the muscle fibers.

A functioning linkup outside the animal between nerve and muscle has been achieved by an Institute grantee at Albert Einstein College of Medicine. The characteristic transmission of signals across the neuromuscular junction develops after maturation in tissue culture. After growing pairs of isolated fetal rat cord and skeletal muscle fragments (0.5–1 millimeters part) in tissue culture, electrophysiological studies demonstrated that characteristic neuromuscular transmission was present at 1 to 2 months in vitro. Studies of the ultrastructural and bioelectric properties of these tissues during critical stages of maturation in culture may provide researchers with a useful model system for studying problems of development and regeneration.

While basic research studies continue to provide information about the basic defects producing neuromuscular disorders, investigators also are developing treatment methods to alleviate the effects of the disorders. In some instances, even though the basic defect still has not been elucidated, treatment methods have been developed which provide symptomatic relief. Studies at the NINDS Medical Neurology Branch have developed therapies for three such disorders this year.

A number of patients with poorly controlled attacks of hypokalemic periodic paralysis have responded to the drug acetazolamide (Diamox). Patients suffering from severe and frequent episodes of extreme weakness to the point of quadriplegia associated with low serum potassium were often able to lead normal lives while being treated with this drug. The actual mechanism of the drug's action in this disorder remains to be clarified.

In a second study, azathiaprine (Imuran) has brought about clinical and laboratory evidence of improvement in patients with dermatomyositis (polymyositis), a collagen-vascular disorder characterized by severe muscle weakness, erythematous skin lesions, elevated serum transaminases and inflammatory myopathy on muscle biopsy. A third study, in collaboration with investigators from the National Heart Institute, has shown a liquid formula diet low in phytol and phytanic acid to be effective in reversing the nerve abnormalities in Refsum's disease (hyperphytanicacidemia).

In the course of electromyographic studies which employ hypodermic needles and muscle biopsy studies, NINDS scientists have discovered that microscopic changes can be produced in the muscle by the hypodermic needle. They strongly suggest that muscle biopsies not be taken from a site that has been needled previously because the biopsy may show the needle-produced changes which cannot be distinguished from disease-produced pathology.

OTHER INBORN ERRORS OF METABOLISM

A specific diagnostic test has been developed for detecting patients with metachromatic leucodystrophy (MLD), a progressive degenerative neurological disease characterized by a defective enzyme. Researches in the NINDS Laboratory of Neurochemistry found that white blood cells from MLD patients show only 10 percent specific activity of arylsulfatase A compared with normal controls and patients with other neurological disorders. This new clinical technique is significantly more practical than the current screening method of urinalysis which is confused by several variables, or other earlier methods which depended upon brain or peripheral nerve biopsy.

The same laboratory two years ago developed tests to diagnose two other enzymatic disorders, Gaucher's disease and Niemann-Pick's disease. These re-

searchers now believe they are able to diagnose both disorders in utero through the techniques of amniocentesis and growing the withdrawn fetal cells in tissue culture. Laboratory tests have shown that activity of the enzymes involved in these disorders can be seen clearly in tissue cultures. In other tissue culture studies of Gaucher's and Niemann-Pick's disease the investigators have cultured small skin biopsies from patients and have been able to identify each disorder in culture. This same method may make it possible to identify heterozygous carriers of the disorders as well.

Tay-Sachs, another disorder but one which affects many more people, has until now resisted biochemical elucidation. However, Institute investigators have been successful in demonstrating for the first time the metabolism of the ganglioside which accumulates in the neurons of Tay-Sachs patients, which causes the symptoms of the disorder. They have synthesized this ganglioside and labelled it radioactively for use in experiments to study the specific abnormal enzymatic reactions producing the metabolic defect. It is only through successful studies of the basic nature of these diseases that rational therapeutic procedures can be devised. Furthermore, diagnosis of these inborn errors of metabolism during pregnancy and detection of the heterozygous carriers of these diseases now permit the important possibility of genetic counseling of families in which these diseases have appeared.

NINDS Research support for muscular dystrophy and other neuromuscular disorders

1966	$3,704,000
1967	3,931,000
1968	3,375,000
1969	3,494,000
1970	3,520,000

Special Report: Multiple Sclerosis

THE PROBLEM

An estimated 250,000 Americans are afflicted by multiple sclerosis (MS), and many more by related disorders. Although the disease was recognized more than 100 years ago, its cause is still unknown, and no effective treatment is available in spite of extensive research and many approaches to the problem. Its solution presents one of the most urgent problems of basic neurology.

MS exacts a very heavy annual toll of disability among men and women throughout the world, striking them mainly in their most productive early adult years. The estimated cost of patient care in the United Staes alone is more than $250 million each year. Additional millions are spent on research while the economic loss to the Nation is incalculable.

Multiple sclerosis is a disease of the central nervous system in which myelin, the fatty, protective tissue sheathing the nerve fibers, disappears in scattered patches. The disorder, which is progressive in most cases, proceeds in a series of unpredictable attacks. In earlier stages, attacks are often followed by periods of remission. With successive episodes, resulting lesions in the brain and spinal cord become more dense and destructive, causing more severe disability.

PROGRAM DEVELOPMENTS

The NINDS has developed a number of programs in the search for the etiology of multiple sclerosis. Especially significant are studies now being conducted on the epidemiology of multiple sclerosis, the implication of viruses in neurologic disease, and the biochemistry of the sclerosing and neuromuscular disorders.

Since multiple sclerosis is largely a disease of temperature climates, early studies were largely concentrated on the epidemiology of the disease. Epidemiology continues to be a major research path explored by Institute scientists in the search for answers to the riddle of multiple sclerosis. The fact that the incidence of multiple sclerosis is higher in colder climates is well established. Studies are underway in New York City investigating immigrants from Ireland and Italy and their first-generation descendants, to determine whether the propensity to develop multiple sclerosis in a common climate is altered by family background.

The Institute has continued to expand its program in "slow virus" research. Much of this research is conducted at a special virus laboratory established by the Institute at Patuxent, Md., in cooperation with the Fish and Wildlife Service, Department of Interior. Here, experimentally inoculated hosts are being held for a period of 5 to 10 years. In addition to multiple sclerosis, a number of other diseases are under study.

In another program, partly supported by the National Multiple Sclerosis Society, Institute scientists are using viral antigens to detect virus antibodies. They are using these antigens to search for such antibodies in patients with multiple sclerosis. Although several groups have reported higher measles antibody titers among patients with multiple sclerosis than matched controls, the role of viruses in the etiology of multiple sclerosis is still not established. Additional studies are now in progress in which a variety of antigens and sera from different groups of patients are being examined.

Another major research effort is being directed toward understanding the biochemistry of the disease. Scientists are seeking a possible biochemical defect as the cause of demyelination, a major characteristic of multiple sclerosis. The Institute has developed an important program on the biochemistry of myelin to investigate this possibility.

Institute scientists are investigating the possibility that multiple sclerosis is due to an autoimmune disease—a process wherein the body's antibodies are being directed against its own brain tissues. The Institute is supporting a number of studies to determine the nature of the chemical which initiates the autoimmune response, the body mechanisms involved, the evidence that such a process might be operative in patients with multiple sclerosis, and the means to prevent such destructive processes.

One of the most potentially valuable projects in multiple sclerosis research is a double-blind cooperative study to evaluate the use of adrenocorticotrophic hormone (ACTH) in acute exacerbations of this disease. Ten university treatment centers conducting this study recently issued a preliminary report. The investigators feel that they have attained the primary purpose of the study by determining a means by which a proposed agent can be tested. In their first report, the researchers presented evidence demonstrating that adequate randomization for all testable variables can be attained. A conclusive report on the benefits or lack of benefits of short-term use of adrenal steroids and ACTH will soon be issued by the 10 centers.

RESEARCH PROGRESS

Viruses

A number of events this past year add support to the belief that infective agents may contribute to multiple sclerosis (MS). The first strong evidence that viruses may be implicated in the etiology of certain neurological disorders, including multiple sclerosis, was gained about 3 years ago by the transmission of kuru to an animal host, the chimpanzee. Kuru, a degenerative neurological disease found only in a small population of New Guinea natives, resembles multiple sclerosis in some respects.

Further proof was gained this past year that kuru is of infectious origin when it was transmitted to the spider monkey in the special NINDS "slow virus" laboratory. Since the study of persistent and slow virus infections in the brain requires long-term observations of animals, the discovery of another laboratory animal susceptible to the disease is of great importance to researchers. Spider monkeys are less expensive and easier to obtain in large numbers than are chimpanzees. Use of this new experimental animal should help efforts to characterize the virus and to study the pathogenesis of the disease.

The disease which in America and elsewhere throughout the world bears the closest resemblance to kuru is Creutzfeldt-Jakob disease, also called spongiform encephalopathy of gray matter. It is a nervous system disease usually fatal within several months, which occurs sporadically throughout this country. At the special NINDS virus laboratory, brain biopsy from a case with the disease has been used for successful transmission of the same neurological disease to the chimpanzee after 13 months incubation. Both this disease and kuru bear striking resemblance to scrapie, a widespread fatal brain disease of sheep.

NINDS workers last year isolated a virus from lung and brain explants of sheep dying of Montana sheep disease, which is an enzootic disease of long standing in the United States. It has now been shown that this virus is similar to maedi and visna disease in Iceland. In the neurological form, visna, this slow virus infection causes widespread demyelination somewhat similar to that seen in multiple sclerosis. This finding among Montana sheep is of special interest because of work conducted for the past 12 years at the Institute for Experimental Pathology, University of Iceland, Reykjavik, Iceland. Scientists at the center in Iceland, supported in part by a grant from NINDS, injected brain material from different Multiple Sclerosis patients into Icelandic sheep. (These sheep have existed for a thousand years in ecologic isolation.) This resulted in a central nervous system disease in some of these sheep after an incubation period of more than 1 year.

Subacute sclerosing panencephalitis (SSPE), a fatal disease of children, has been shown to be caused by a measles virus persisting in the body for many years after acute measles infection. The Institute was among the first to accumulate evidence for the role of measles in this disease, and called a symposium on this important subject.

Work here at the Institute and elsewhere has since further incriminated measles as the cause of SSPE, which claims the lives of several hundred American children each year. Recently, experimental work at the Wistar Institute, supported by a grant from NINDS, has produced a similar disease in ferrets from brains of human cases of SSPE. The earliest sign of this disease was an electroencephalographic (EEG) abnormality in asymptomatic animals. As the disease progressed, other signs appeared and were associated with the development of distinct histologic lesions.

NINDS research support for multiple sclerosis

1966	$3,019,000
1967	3,301,000
1968	2,709,000
1969	2,795,000
1970	2,816,000

Special Report: Cerebral Palsy

THE PROBLEM

The term cerebral palsy refers to symptoms of nervous system damage to the brain's centers for muscle control. The disorder, which afflicts an estimated 600,000 Americans, is not a single disease, but a condition characterized by a multitude of causes and resultant degrees of impairment. The discovery of causes and prevention for cerebral palsy (CP) damage thus remains one of the most puzzling problems in medical research.

Such damage can be limited to motor difficulties affecting a few spastic fingers or can extend throughout the body. CP can be tragically obvious in the birth of a hemiplegic baby with spastic paralysis or strangely elusive, impairing development several years later. The condition is neither contagious nor progressive. The brain lesions which produce CP damage have been shown to be associated with physiological events surrounding pregnancy and birth, events which until recently were little understood.

Prognosis for treatment and recovery ranges from excellent to extremely poor. Braces to support weak muscles, exercise to stimulate development, special coaching for patients handicapped by complications like deafness, blindness, and speech disorders, have enabled some CP children to reach a level of functioning close to normal. Even those afflicted with almost total motor involvement and mental retardation have been helped to make some progress. Although research to improve rehabilitation methods can make many CP victims more productive, the hope for the future rests with scientists working to uncover, prevent, and remedy the complications which cause the crippling damage in the first place.

PROGRAM DEVELOPMENTS

From its inception in 1951, the National Institute of Neurological Diseases and Stroke has awarded CP research high priority as a major mission. The causes and complications of CP damage are being investigated through four major research avenues.

The collaborative perinatal research project

A major purpose of the project is to ascertain causes of cerebral palsy, mental retardation, congenital blindness and deafness, and other related deficits which rob children of their fullest developemnt.

This project, the first massive, longitudinal study of perinatal development ever attempted in American medicine, has been collecting data on 58,000 pregnant women and the development of their 55,000 offspring since 1959. The program was initiated to provide the detailed data which has been difficult or impossible to obtain in retrospective investigations of the causes and developmental course of neurological disorders. By selecting women as early in their pregnancies as possible and following them through delivery, and their offspring through age 7, the project has made possible a prospective study to identify neurological abnormalities and their relationship to events during pregnancy.

To provide an additional safeguard for scientists wishing to use project findings, a specially appointed committee under the chairmanship of Dr. Abraham M. Lilienfeld of the School of Hygiene and Public Health, The Johns Hopkins University, has reviewed the data collected by 14 outstanding medical institutions participating in the study. After evaluating the reliability and quality of the data, the committee concluded in a report published in December 1968 that "the data can be readily used for testing relationships between perinatal factors and various pregnancy outcome characteristics." The report also recommended that "increased use of the data for this purpose by investigators in other institutions and agencies should be stimulated."

Although the last study baby was born in September 1966, it will be 1974 before this child has completed the 7-year exam and the data can be completely analyzed. Already West Germany, impressed by the value of the United States effort, has established a similar prospective study using NINDS protocols in which 19 universities are participating to study babies beginning with the first trimester of pregnancy.

The institute intramural research program, surgical neurology branch

Scientists in this laboratory conduct intensive studies of the etiology, pathology, and prevention of cerebral injury and developmental disorders of the nervous system. Their approach extends from the examination and treatment of living patients to the study of disease processes in autopsy specimens, chromosome research, and research on the effects of radiation dosage on the human fetus.

The Laboratory of Perinatal Physiology, San Juan, P.R.

Directed by Dr. Ronald E. Myers, the Laboratory serves as a valuable counterpart to the Collabroative Project's human study. Using the rhesus monkey, whose gestational physiology closely resembles that of man. Laboratory scientists attempt to replicate the various kinds of nervous system damage in the monkey which human studies have suggested are responsible for neurological disorders in man. This experimental approach in helping doctors understand the cause and results of different types of human CP. There are now more than 1,000 rhesus monkeys in caged and free-ranging colonies in which pregnancy and infant development can be studied.

Extramural Grant Program

Through its awards of funds to support qualified scientists investigating causes of CP and related disorders in both humans and animals, the Institute is able to broaden its research into specific areas and to provide fundamental data which can benefit clinicians confronted with CP cases.

RESEARCH PROGRESS

Spastic Diplegia

Spastic diplegia is a type of CP in which both arms or both legs of the body have tense, stiff muscles. Collaborative project scientists reported earlier that

spastic diplegia appears to be almost invariably a disease of the small (under four and one-half pounds) and early-born (under 36 weeks) child and that such infants suffered a postnatal weight loss of more than 10 percent. New studies this past year suggest that the cause of this type of CP may be internal hemorrhage.

Normal infants usually lose 6 to 8 percent of their body weight after birth in the form of fluids, and the loss is associated with a rise in their red blood cell concentration. Spastic diplegic infants, however, show a lowering of red cell levels, which may be explained by internal hemorrhaging. Collaborative project scientists have recommended further studies of newborn weight loss, protein intake and change in red cell levels to test this theory.

Hemiplegia

New explanations for two types of hemiplegic CP, a condition which involves spastic paralysis on one side of the body, have been reported this year. Reviews of patients' records reveal that in spastic hemiplegia complicated by epilepsy there is an association beween the side on which the hemiplegia occurs and the position of the infant's head during birth. Epileptic hemiplegia sometimes appears as acquired infantile hemiplegia, a condition in which the spastic hemiplegia suddently appears during fever-producing illness. These findings suggest that epileptic hemiplegia results from bruises suffered by the brain during birth. Small lesions may form which become more extensive during infections and which then cause spastic hemiplegia.

Records for nonepileptic hemiplegics show that many of these patients experienced postnatal collapse (an episode of circulatory failure after birth). This type of spastic hemiplegia may thus be caused by blockage of the blood flow in the arteries which supply the brain. The episode of postnatal collapse may represent the moments when such blockage, possibly caused by clots in these arteries, occurred. These studies were directed by Dr. John A. Churchill at the Lafayette Clinic in Detroit, Mich.

In an effort to study further the relationship between head position at birth and the location of nervous system lesions, the Institute is working with scientists in Montevideo, Uruguay, where measurements of infant heartbeat, the brain's electrical pattern (electroencephalogram), and the intensity and frequency of contractions during delivery are being analyzed.

Laboratory of perinatal physiology: Experimental models of nervous system damage

Doctors have known for some time that one of the main causes of nervous system damage results during pregnancy from compression of the umbilical cord which supplies blood-carrying oxygen and nutrients from the mother to the fetus. Cord compression produces a condition called asphyxia, which means suffocation of the tissues. Studies in the rhesus monkey now show that the severity and type of damage caused by asphyxia depend upon when during gestation the injury occurs.

Thus the earlier in gestation asphyxia occurs, the less vulnerable the fetus and the longer the period of oxygen deprivation it can withstand. Fetuses at 3½ months (pregnancy in the rhesus lasts 6 months) can withstand oxygen deprivation twice as long as a full-term monkey infant. Moreover, the earlier in gestation the asphyxia is introduced, the less the overall damage to the brain and, particularly, the less the damage to the higher parts of the brain.

Another important finding is the discovery this past year that it is long-term, partial oxygen deprivation during gestation, rather than sudden, total deprivation, that produces the types of CP seen in humans. Experiments which induced acute, total asphyxia produced a pattern of neuropathology which bore little resemblance to the various well-recognized patterns seen in humans who are afflicted with CP or mental retardation on the basis of perinatal brain damage. Prolonged partial hypoxia, however, produced evidence of brain swelling associated with varying degrees of cortical necrosis. Under less severe insult, the damage appeared as two forms of pathology (ulegyria and status marmoratus of the basal ganglia) which represent the classically recognized and common patterns of change seen in the brains of humans damaged during gestation or at the time of birth.

Prolonged hypoxia is a naturally occurring condition for the fetus under a wide variety of circumstances consisting of depression of partial pressure of oxygen in the blood and mixed metabolic and respiratory acidosis. The scientists' ability

to replicate human types of brain damage through experimental procedures in the fetus means that for the first time researchers have a long-sought animal model to aid them in developing preventive measures and treatment for humans.

The barbiturate nembutal has been shown to have a strikingly protective effect against brain damage from asphyxia during delivery by Caesarian section in the monkey. Scientists believe that the barbiturate lowers the metabolism of the brain tissue, thus reducing its need for oxygen and making it less vulnerable to asphyxia.

Another series of experiments has revealed that if the blood supply to the brain is cut off early in gestation and remains cut off, the higher part of the brain may fail to develop at all, the space filling with fluid instead of tissue, which results in a condition closely resembling hydroanencephaly in the human. At intermediate stages of pregnancy, however, the damage is more likely to take the form of localized lesions in the higher parts of the brain. After blocking blood flow in the major arteries and the vein which serve the brain by tying them off in the neck of each fetus, the scientists found that 45 percent of the fetuses were aborted.

Such experiments also have produced a new explanation for one cause of severe mental retardation in humans. The brains of some animals surviving the vascular ligation procedure showing no signs of focal brain lesions, but did exhibit varying degrees of cerebral malformation. Researchers have found that the earlier in gestation the vascular ligation is introduced, the greater the probability of cerebral malformation unassociated with evidence of discrete anoxic lesions. The particular pattern of malformation is closely similar to the pattern of pathology frequently seen in severe retardees confined to mental hospitals. Because there was no evidence for focal lesions in the brains of these patients, there had been no suspicion that the damage was related to injury involving blood-oxygen deficiencies. The present study makes it appear almost certain that the brain alterations seen in such patients results from reduced blood flow to the brain early in gestation.

Hypoglycemia and CP

Severe and prolonged hypoglycemia in childhood (a condition of low blood sugar levels) has been further confirmed as a cause of CP and mental retardation. Scientists under Dr. Anatole Dekaban in the Institute's Surgical Neurology Branch have conducted examinations of living children and autopsy specimens in this research. Treatment methods, consisting of a special diet with feedings every 3 hours, have been worked out for exceptionally severe cases of hypoglycemia of unknown cause.

Studies of hypoglycemic children who are sensitive to the amino acid leucine, found in most proteins, have shown that this variety of the disease often clusters in families and that it often improves spontaneously after 3 to 6 years of age. This finding makes it possible for physicians to counsel families in which the disease tends to occur and demonstrates that if hypoglycemia can be controlled during infancy, permanent brain damage can be prevented in this not uncommon disease.

The surgical neurology branch is using a three-phase investigative approach to study the pathogenesis of cerebral birth injury. In the past neurologists have been limited by a poor conception of the causes and mechanisms behind such injuries. Under the present study, clinical findings in living patients are correlated with autopsy findings in cases of both acute and chronic lesions. This approach is providing an inventory of all types of lesions and is helping to clarify patterns of transition between acute and chronic lesions. Hopefully the effort will enable physicians to interpret the disease process in individual cases and will eventually make possible preventive measures and treatment for certain categories of CP patients.

Toxoplasmosis

Toxoplasmosis, a disease which can cause severe neurological damage to the developing fetus, has long been a puzzler to medical science because its mode of transmission remained a mystery. Collaborative perinatal project investigators have now detected a human-borne parasite whose presence is closely associated with evidence of exposure to the infection in Puerto Rican children. To clarify the nature of the association, doctors from the project's infectious disease laboratory will survey 200 children from each of the two Puerto Rican

villages this year, collecting and culturing parasites obtained from the children and from soil samples, and checking the children's blood for toxoplasmosis antibodies.

Although 30 percent of American women show evidence of exposure to the infection, the rate is twice as high for Negroes as for whites, and four times as high for Puerto Ricans, in whom 50 percent of children under 2 carry evidence of exposure, according to project data. The Puerto Rican rate is similar to that in Western Europe where poorly cooked meat has been demonstrated to be the source of infection. Estimates are that of the 88 percent of congenital toxoplasmosis cases which survive, 85 percent are mentally retarded and more than 60 percent are spastic. Once the disease carrier is pinned down, work can begin on development of preventive treatment.

In-utero test for one cause of CP

In 1968, scientists of the Division of Biologic Standards and the National Institute of Arthritis and Metabolic Diseases reported their discovery of a means of identifying the enzyme defect of Lesch-Nyhan syndrome in the developing fetus.

The disease, which causes a relatively uncommon type of CP characterized by spasticity, choreoathetosis, and psychomotor retardation, was shown earlier to be due to a defect in an enzyme of protein metabolism. The new test involves withdrawing a little of the amniotic fluid surrounding the fetus and culturing the cells. This procedure increases the possibility of satisfactory counseling of families in which this or other hereditary diseases have been detected.

Mental deficiencies and factors in pregnancy

Acetonuria: Mental retardation has been found to be three times as frequent in children of mothers who had acetonuria (an excess of acetone bodies in the urine) in the last third of their pregnancies in comparison with children of acetone-free pregnancies. This finding, the result of a collaborative perinatal project study by Drs. John A. Churchill, Heinz W. Berendes, and Lee Willerman, has expanded upon earlier project surveys which showed that diabetes accompanied by acetonuria during pregnancy is associated with evidence of subnormal intellectual and neurological function in children, while nonacetonuric diabetes during pregnancy is not. The new finding supports the theiry that acetonuria signifies episodes when the nutrient supply of a pregnant mother is insufficient for the fetus, since a fetus usually triples its weight in the last trimester of pregnancy and then is most in need of nutrients. Although only 1 percent of pregnant women are believed to have diabetes, three to 5 percent of pregnant women may have acetonuria alone, and project data shows that twice as many pregnant Negroes are acetonuric as whites.

To further test whether acetonuria can be interpreted by obstetricians as a sign of inadequate maternal nutrient supply, the project is sponsoring a study of pregnant Negro women in a Detroit clinic to check for acetonuria, assess dietary intake, and to develop simple biochemical measurements of dietary insufficiency. In the project's Bethesda, Md., laboratories pathologist Dr. Jack H. Carleton is examining brains of mice born of protein-deprived pregnancies for evidence of morphological abnormalities.

Maternal weight and prematurity

Studies by collaborative project scientists have raised questions about the advisability of a traditional American obstetric teaching: that weight gain during pregnancy should be restricted to a minimum. An investigation of factors associated with prematurity in newborns (defined as birthweight under 2500 grams) has demonstrated that both the mother's prepregnancy weight and her weight gain during pregnancy are positively associated with the birthweight of her baby. The research was based on a survey of project data on 15,000 full-term pregnancies, which included 8,295 white and 6,909 Negro mothers whose pregnancies were considered normal (uncomplicated by such factors as diabetes, toxemia, organic heart disease, and asthma).

The data also showed that regardless of prepregnancy weight, the incidence of low birthweight babies decreases for those mothers who gain heavily during pregnancy. Project scientists have designed additional studies to determine whether or not a true cause-and-effect relationship exists between weight gain and birthweight. Assuming it does, the data suggests that if women who gained 29 pounds or less had increased their average weight gain by 5 pounds, the rate

of premature white babies in the project could have been reduced by 20 percent and that of Negro babies by 17 percent. The association between weight gain and birthweight diminishes markedly as prepregnancy weight increases, however, according to analyses performed by Drs. Kenneth Niswander, Judith Singer, Milton Westphal, and by William Weiss.

A second study, based on separate data from Johns Hopkins Hospital on 6,675 white and 5,236 Negro mothers, and conducted by Nicholson J. Eastman of the Johns Hopkins Medical Institutions and Esther Jackson of the Office of Biometry, NINDS, has confirmed the collaborative project findings. This research is regarded as particularly important since prematurity (defined as low birthweight) is known to be associated with a high incidence of neurological damage and newborn mortality. Project studies have also shown that the higher the maternal weight gain, the higher the infant's birthweight and the better his growth and performance record during his first year of life. Should a definite casual relationship be proven between prepregnancy weight, maternal weight gain, and birthweight, the project findings may be especially applicable to the low-weight woman (whose prepregnancy weight is under 120 pounds). Such a patient may need expert help to maintain an average weight gain and to counteract the effect of low prepregnancy weight in causing the birth of a low-weight baby. For other women the objective in weight control during pregnancy would be to keep weight gain reasonably close to average.

An investigation of data on 7,000 mothers who had more than one pregnancy while enrolled in the collaborative project will be undertaken to examine the relationships between varying prepregnancy weights, weight gains and birthweight within the same woman. Variables such as toxemia, dystocia, abnormal lengths of gestation, and cigarette smoking during pregnancy and their association with birthweight will also be studied. Although independent research has shown that any apparent relationship between maternal height and birthweight is produced through the medium of prepregnancy weight, studies of mothers belonging to different height sub-groups will be conducted to determine the possible influence of genetic factors on birthweight. To define more clearly the mechanisms which determine birthweight, further research involving the manipulation of both quantity and nutritional quality of diet will be performed on pregnant rhesus monkeys.

Much of the Institute's cerebral palsy research is conducted within the collaborative perinatal research project, where a growing body of knowledge on perinatal events give medical scientists a better understanding of some of the many factors causing cerebral palsy. Other studies are being conducted to learn more about the factors which influence the development of the neurologically handicapped. When these factors are more fully understood, it will be much easier to develop better procedures for remediation.

NINDS Research Support for Cerebral Palsy and Related Neurological Disorders of Early Life

1966	$13,819,000
1967	9,973,000
1968	11,116,000
1969	11,216,000
1970	11,300,000

Special Report: Hearing, Speech, and Language

The Problem

A recent review and analysis of available data more than doubles previous estimates of the prevalence and cost of hearing, language, and speech disorders in the United States. As a part of its report on a two-year study of the field, the Subcommittee on Human Communications and Its Disorders, of the National Advisory Neurological Diseases and Stroke Council, states: "about 8,500,000 Americans have either bilateral or unilateral hearing impairments of handicapping magnitude; another 2 million have central communicative disorders; and 10 million have speech disorders. We probably should assume modest overlap in these totals, but we must still recognize that approximately 20 million persons in this country have communicative handicaps worthy of our concern. Moreover, at least a third (about 7 million) suffer either substantial or severe educational,

social, and economic disadvantage. Finally, approximately one-fifth of the grand total (about 4 million) consist of persons under 21 years of age."

Further on, the report adds: "The direct costs of coping with communicative disorders (special education, vocational rehabilitation, hearing aids, speech therapy, training of professional personnel, etc.) totals at least $400 million. The annual deficit in earning power among the communicatively impaired approximates $1,750 million. No price tag can be assigned to the personal tragedies and social misunderstandings which communicative disorders impose on their possessors."

THE PROGRAM

Since its establishment in 1950, the National Institute of Neurological Diseases and Stroke (formerly Blindness) has been deeply concerned with communicative disorders. This category comprises: deafness resulting from malformations or malfunctions of the ear, the auditory nerve, and sound-receiving centers of the brain; late speech acquisition or failure to talk; defects of articulation, including those caused by cleft palate, facial malformations, and other speech-affecting organic disorders; and inability to receive, interpret, retain, and express language, including aphasia and central disorders of perception.

Major emphasis continues on training of urgently needed personnel to conduct research in this field which has high priority in NINDS's overall effort. Currently, 389 postdoctoral students are studying with Institute support through 78 grants to institutions for advanced research training in otolaryngology, audiology, sensory physiology, and other related disciplines.

The Institute conducts the largest of all Federal programs of research into the mechanisms of human communications and the disorders which afflict them. Currently, NINDS supports:

174 separate research projects at 82 U.S. medical centers;

Five multidisciplinary clinical research centers—at Princeton, Central Institute for the Deaf in St. Louis, the University of Chicago, the Kresge Hearing Research Institute of Ann Arbor, Mich., and the University of Florida;

Three human communications out-patient clinics—at Stanford, the University of Pittsburgh, and Northwestern;

Four temporal bone banks for the long term study of structural and pathological changes relating to functional disorders of hearing—at the University of Chicago, Johns Hopkins, the San Francisco Medical Center of UCLA, and Baylor University in Houston;

An information center for hearing, speech, and disorders of human communications at Johns Hopkins to speed the interchange of scientific information between researchers; and

A long term collaborative study of some 50,000 children which includes evaluating their hearing and speech.

The Institute also publishes reviews and other documents of professional interest. Three monographs published this past year have made available to many physicians, educators, and therapsist new information relating to communicative disorders.

The Subcommittee on Human Communications and Its Disorders of the National Advisory Neurological Diseases and Stroke Council provides guidance to the Institute in its present programs and its planning for the future. This committee, organized in 1965 to review the state of research relating to problems of communicative disorders has completed its assignment and submitted an extensive report, which will be published in 1969.

RESEARCH PROGRESS

The Subcommittee on Human Communications and Its Disorders, after thorough review and analysis of current knowledge about hearing, language, and speech functions and dysfunctions, has identified gap areas and made specific recommendations for research concentration. Unquestionably, this impetus will speed the Institute's research program in preventing communicative handicaps and improving the lives of persons who are afflicted by them.

Ear transplants

Successful homograft transplants of complete middle ear structures were reported by several investigators. The transplants were made from cadavers to patients whose hearing had been destroyed by chronic otitis media. Transplants

of part of the middle ear had been made previously, but the recent work involves the complete middle ear which includes the eardrum and the three tiny middle-ear bones. Of 16 cases reported by Drs. Michael Glasscock, William F. House, and James L. Sheehy, of the Los Angeles Foundation of Otology, the hearing results were very good in three cases, improved in two cases, and six cases will require a second-stage procedure to obtain good results. Dr. Glasscock said, "There are many problems inherent in the use of this homograft technique which have not been solved, such as tissue preservation and prevention of adhesions in the middle ear. Dramatic results have been achieved in a few patients, and this has encouraged us to continue using this technique in selected cases."

Implanted tack relieves Meniere's symptoms automatically

Meniere's disease, resulting from increased pressure of fluid in the membranous labyrinth of the inner ear, is the most common of the inner-ear disorders and usually presents three symptoms at the same time—ringing in the ear, dizziness, and deafness on one side. While its cause is still unknown, various means have been developed to treat it, medically and surgically.

Among the new surgical techniques for managing the affliction is an operation under local anesthesia, in which a stainless steel tack is implanted through the footplate of the stapes—the tiny stirrup-shaped bone of the three middle-ear bones—in such a position that it will puncture a swelling membranous labyrinth before dizziness occurs. This procedure affords Meniere's disease patients, who otherwise would suffer frequent severe attacks of dizziness, an excellent chance of automatically controlling the symptoms with minimal morbidity and no serious complications.

In 57 cases the tack operation reduced dizziness in 95 percent of the patients, improved hearing by 20 decibels or more in 18 percent, reduced the sensation of ear fullness in 92 percent, and lessened ringing of the ears in 42 percent.

Antibiotic found destructive to hearing

Because of the increasing use of drugs by otologists in treating ear diseases, the Institute has emphasized studies of the relation of chemical agents to hearing disorders. An NINDS-supported study suggests that topical application of the broad-spectrum antibiotic chloramphenicol succinate may actually cause deafness. The drug has been used widely following surgery, and in cases of chronic refractory otitis media because of its effectiveness against infection. Topical application of the drug to the middle ears of a large number of guinea pigs showed significant damage to the hair and supporting cells in the organ of Corti, vital to hearing processes. The findings have alerted otologists to the possible danger of using chloramphenicol topically in the middle ears of human patients.

Electrodermal auditory technique used

Involuntary (electrodermal) audiometry was used by a NINDS grantee to help to resolve the controversial question about the site of the damage responsible for hearing impairment associated with Rh incompatibility. Results of a study using the technique strongly indicate that damage in Rh deafness is localized low in the central auditory nervous system (cochlear nuclei) or in the peripheral sensorineural mechanism (cochlea), not at high levels in the central auditory system.

This localization of damage is an important step in understanding the nature of the impairment and in facilitating more effective aid to afflicted individuals.

X-ray as a diagnostic tool

An advance in the diagnosis of inner-ear hearing loss was made this year through research conducted at a temporal bone laboratory. The bony changes which radiologists have observed and diagnosed as cochlear otosclerosis have now been confirmed histologically.

In the past, some persons with a severe hearing loss have been diagnosed, through use of X-ray, as having cochlear, or inner-ear otosclerosis. However, questions existed concerning the interpretation of the X-ray findings of inner-ear hearing loss. Some of these persons have willed their temporal bones to research and now, after death, the inner ears have been studied histologically and the X-ray diagnosis confirmed. This recent advance concerning inner-ear diagnosis gives further support to the value of temporal bone banks.

Temporal bone banks

Much of our knowledge of the causes of hearing loss has been gained through the study of middle- and inner-ear structures after death. There are now many temporal bone laboratories and four regional temporal bone banks. These are sponsored by the Deafness Research Foundation and the American Academy of Ophthalmology and Otolaryngology and supported by NINDS.

Surgery relieves one type of hearing loss

A surgical procedure has been developed this year to relieve the blocking of the eustachian tube which sometimes causes hearing loss. Air is necessary for effective hearing and the new procedure, conducted from above the tube, removes the block, provides air, and prevents the tube from filling with fluid.

Evoked response audiometry used in diagnosis

Early diagnosis of auditory nerve lesions, such as neuromas, is most important because they threaten life when ear tumors grow into brain tumors. Symptoms of such lesions are so similar to those of Meniere's disease (a nonfatal affliction characterized by fluid-accumulation swelling of the inner ear) that even the best audiometric tests so far devised cannot always positively distinguish which is which.

Evoked response audiometry, a valuable new research tool reported last year, which uses EEG (electroencephalograph) tracings to accurately evaluate hearing ability in patients too young, too retarded, or unwilling to cooperate, was applied experimentally this year by a Johns Hopkins University scientist to the problem of differentiating between VIII nerve lesions and Meniere's disease.

Results of the experiments on a limited number of patients suggest that evoked response techniques may prove valuable for diagnosis in this important area.

Unit simulates patient, speeds training

Bioengineering made a significant contribution to audiometry education. At the Johns Hopkins Medical Institutions, a physician and an electrical engineer teamed up to develop a valuable training tool called an audiometry training unit.

The machine simulates test procedures in air conduction, bone conduction, and speech audiometry to speed the training of audiologists, speech pathologists, audiometric technicians, and resident physicians. It consists of a conventional audiometer console linked to a preprogramed simulated test subject and can be set for an infinite variety of test patterns—simulated hearing loss cases. Additionally it replaces expensive audiometers and sound-treated rooms, takes only two persons to operate it, is reasonably mobile, and may be operated by battery.

Fiber-optics improves laryngoscopic techniques

NINDS grantees at the University of Tokyo devised a thin, flexible, fiber-optics cable which can be inserted through the nasal passage to provide clear observation of laryngeal conditions in the course of normal speech. Glottal conditions during articulations of consonants, not visible in ordinary laryngoscopic techniques, and during various other phonations, can now be observed and photographed. A significant recent accomplishment in speech research, this technique will hasten the acquisition of knowledge about the ways that our speech is produced in the different registers and the fundamental frequencies.

A better artificial larynx

In the area of artificial organ development, efforts continue to improve artificial larynxes. During 1968, Dr. Richard L. Goode, a Los Altos, Calif. surgeon, developed such a device to provide speech for those postlaryngectomy patients who fail to learn esophageal speech and cannot use a conventional artificial larynx. He reports that only minor surgery is required to place this inconspicuous artificial larynx. He also indicates that the unit remains in place for spontaneous speech, produces a loud intelligible voice, with minimal external sound radiation.

Preschool screening for rubella damage

Rubella (German measles), a mild disease of children and young adults has been a vicious destroyer and crippler of unborn babies when contracted by mothers in the first weeks of pregnancy. It is hoped that new vaccine will drastically reduce the prevalence of the disease in the future, but in 1964–65 one of the worst epidemics in our history affected almost 2 million persons and

damaged 20,000 to 40,000 babies before birth. At least half of those children have impaired hearing, the most common and persistent defect found in rubella babies.

In August 1967, in Montgomery County, Md., NINDS sponsored a 4-day preschool communications screening program which was conducted by the county health department and the Easter Seal Treatment Center. This program was one of the early efforts to find children having hearing, language, speech, and memory abnormalities and to determine, where possible, those who had been damaged by the rubella epidemic. In response to radio and newspaper advertising, 136 children between 6 months and 5 years of age whose parents or physicians suspected communications disorders, were brought in for examination.

Study results, completed in 1968, revealed that 79 children had definite abnormalities, and that seven were suspect. Of the overall total, 17 were found to have rubella antibodies. Additionally, of five children born shortly after the epidemic, four (three of them previously undetected) had congenital damage like that known to be caused by rubella. The report concluded that there probably are many more children in the county who have congenital rubella damage resulting from the epidemic which is as yet undetected but will be found later.

Since this typical program was conducted, many others have been held throughout the country. However, much more needs to be done to find all the rubella-affected children so that they may be helped early. Failure to do so may prevent the full development of their speech capabilities and mark them for life as handicapped.

NINDS research support for hearing, speech, and language

1966	$6,533,000
1967	7,929,000
1968	8,443,000
1969	9,000,000
1970	9,061,000

TRANSFER OF ACTIVITIES TO EYE INSTITUTE

Mr. NATCHER. Dr. MacNichol, what guidelines were used in determining what activities that were in your Institute stayed and what went to the new Eye Institute? What guidelines did you use?

Dr. MACNICHOL. Essentially, 20 percent of the total activities of the Institute could be clearly identified as eye-related research. Some of these things were quite obvious. For example, things that have to do with corneal and lens transparency, glaucoma, and other diseases of the eye itself obviously belong in the Eye Institute. In other areas the distinction is not as clear and will probably remain not very clear. It is something that will have to be worked out between the two Institutes. These areas are the central pathways serving vision and the use of other senses and the direct stimulation of the nervous system by devices designed to assist the blind. Here the two Institutes have overlapping responsibility, just as the Heart Institute and our Institute both have overlapping responsibility in the area of stroke, and Child Health and our Institute have overlapping responsibilities in the area of studies of the development of the nervous system.

Mr. NATCHER. Do you think the activities transferred to the Eye Institute will be more effectively carried out than they have been in the past, Doctor?

Dr. MACNICHOL. Personally I do not think it will make a great deal of difference. I think certainly they will get more emphasis. I frankly was one of those who did not feel that a separate Eye Institute was necessary, but since it has been created I want to do everything I can to launch it effectively.

Dr. MARSTON. Mr. Natcher, one specific area that we are working on is the strengthening of the intramural program. Even though we have serious personnel problems, this is one area in which we should expect to devote more resources within our intramural program. This is not an easy thing to accomplish, but we do plan to generate more activities in that area than we would have if we did not have an Eye Institute. Would you agree?

Dr. MACNICHOL. Yes, if there is space in the clinical center for it. The space is the thing that is restraining the intramural eye program at this time.

EVALUATION OF NEWLY DISCOVERED DRUGS FOR EPILEPSY

Mr. NATCHER. Last year in our report we urged that you initiate a broader program to evaluate newly discovered drugs for epilepsy. You have explained to us somewhat in detail concerning drug therapy for epilepsy. Is there anything you would like to add, Doctor?

Dr. MACNICHOL. We have one collaborative program going which is quite interesting and is coming along very well. This is a study of the type of epilepsy that occurs in children called petit mal absence where they just blank out for a short time. It is a relatively mild form of epilepsy, and it can be brought on by deep breathing. Thus an attack which is not harmful can be produced at will and an electroencephalogram clearly records changes which occur.

Mr. NATCHER. If a child 3 or 4 years of age is a victim of petit mal absence, can this condition be detected with the usual encephalogram?

Dr. MACNICHOL. An encephalogram can detect a malfunction at any age. Most of the children being studied are children of school age where this can be of some importance. Such things as lack of attention in school can be caused by this kind of attack. But the reason for using this kind of attack for studies is that it can be brought on readily and does not hurt the child the way a grand mal seizure would. These children can then be given the drugs, and we can see whether or not these attacks are eliminated or lessened by the drugs.

STROKES

Mr. NATCHER. We also expressed interest last year, Doctor, in the work that you are carrying on toward being better able to determine that a person is likely to have a stroke so they can be treated before it actually happens. Do you have any new developments you would like to explain to the committee other than the matters you pointed out in your statement, Doctor?

Dr. MACNICHOL. This is a very tough area. Getting at the circulation inside the skull without opening it up is not an easy problem. I wish I could tell you we are moving with some good programs in this area that are likely to give immediate results. I am afraid that I cannot. Of course, we do have the stroke centers. They are moving ahead and I think learning a lot of little things, but at present there is no major breakthrough in sight. I am trying to get together a workshop in collaboration with Dr. Cooper to find new methods for studying the cerebral circulation. The idea is to get the people who know the problems thoroughly together with a group of engineers and

applied physicists who are working on techniques in other areas that might be applied to this area, and see if they can come up with good ideas for studying cerebral circulation, particularly for finding rapid and relatively innocuous methods of discovering incipient strokes.

VIRUSES

Mr. NATCHER. And also in each of the last few years we have talked about the possibility that viruses may cause some of the neurological diseases. Have you any new findings to report, doctor?

Dr. MACNICHOL. Yes; there is quite a bit going on in this area. I did mention in my statement that subacute sclerosing panencephalitis has been show to be caused by a virus similar to measles. Further work has been done on this, and it has been found this agent is a modified form of measles virus. Tissue cultures of infected brain cells have been made to produce viruses that are indistinguishable from measles. So the agent seems to have been definitely identified.

BRAIN AND SPINAL CORD INJURY

Mr. NATCHER. There is increasing interest in improving the treatment of head and spinal injuries, as you well know. What are we doing and what should we be doing at this time?

Dr. MACNICHOL. In the case of head injuries we have a program, a so-called head model construction program, which is making a synthetic model to represent the head and brain and other structures which have as nearly as possible the same mechanical properties as the skull and brain tissues and the membranes of the brain. The idea is that this model can then be subjected to various kinds of accidental situations and stresses and strains in its various parts. It can then be measured to try to find out just what goes on in head injuries, and this information can be used in the development of safety devices.

There are other Institute studies which seem promising that have to do with the swelling of the brain after injury and drug therapy to reduce this swelling.

PUERTO RICAN FACILITIES

Mr. NATCHER. Can you briefly bring us up to date on your Puerto Rican facilities and activities?

Dr. MACNICHOL. We have the Laboratory for Perinatal Physiology there; and it uses, for experimental material, monkeys originally put on the island by a private group for research. They did not want them any more so we assumed responsibility for this facility, and the monkeys are being used primarily for studying birth-related defects. Experiments are conducted on the pregnant monkeys in a number of ways. For example, the blood vessels to the placenta can be partly closed off, and the effect of such action on the development of the fetus is studied. The mothers can be injected with various infectious agents and subjected to various situations at the time of birth. The newborn monkey is then studied to determine what effect that has on the central nervous system or the senses.

Also, because we have these free-ranging monkey colonies on the

four islands, behavioral studies are being made by visitors who come down and study the monkeys in what approaches a wild condition.

Dr. MARSTON. Mr. Natcher, could we go off the record a minute?

Mr. NATCHER. Yes.

(Discussion off the record.)

TRAINING PROGRAM

Mr. NATCHER. Doctor, I notice on page 202 that your small direct-training program has an estimated annual cost of $37,000 per trainee. Why is it so high, Doctor? Tell us something about the expenses that it covers and why it is this high amount.

Dr. MACNICHOL. I think Mr. Wipf knows more about that.

Mr. NATCHER. All right, Mr. Wipf.

Mr. WIPF. This is a program where staff members are given training outside the service from 1 to 3 years to better enable them to do particular jobs on their return. We have done this with several of our neurosurgeons and they have come back better equipped to do research. It is a separate activity in the budget. I think the Heart Institute has it too, and possibly Mental Health. Most of them do this type of training under their individual budgets.

The reason the cost seems quite high is that the quoted figure includes their total expense, salaries, and allowances, et cetera.

Mr. NATCHER. On page 202 of your justifications, other than salary, it runs $22,000 in other expenses per individual.

Mr. WIPF. We are training three doctors from PHS hospitals which are not part of NIH. The Service as a whole does this. They refer to the Institute individuals who are doing some research work and have a continued interest in it. We justify sending them away to school to finish their training, and they then go back in the Public Health Service's hospitals. There are two trainees from the Baltimore hospital and one from Seattle. They and their institutions make a commitment to us that after they get back to their institutions they will continue to spend part of their time on research. So we pay their salaries for their time away from duty; their positions however, are not charged to our appropriation.

Mr. NATCHER. Am I correct about the $22,000 each for expenses? That is right high, it is not?

Mr. WIPF. It is for salaries and expenses for these three people I am talking about; the average cost is thus about $14,000.

Mr. NATCHER. But you list it as "Other expenses." Does that include salaries?

Mr. WIPF. Yes.

Mr. NATCHER. Under your $30,000 item, just above it, you have personnel compensation and benefits. Isn't that where you have your salary figure?

Mr. WIPF. Those are for our Neurology Institute employees only. On the other expenses this includes three people who are from the hospitals' rolls which we support for training under an agreement under which we pay their salaries and expenses.

Mr. NATCHER. Insert at this point in the record, if you will, please, a concise statement on this.

Mr. WIPF. Yes, sir.

(The information follows:)

The NINDS, through its direct training activity, supports "outside the Service training" of selected staff, generally from 1 to 3 years. The purpose is generally to provide advanced clinical and research training for career staff.

During fiscal year 1969 and fiscal year 1970, NINDS supports two of its own employees in such training at an estimated cost of $30,000.

In addition, we are currently supporting, and will continue in fiscal year 1970, three doctors from the PHS hospitals of the Federal Health Programs Service, Health Services and Mental Health Administration, for advanced training in neurology and otolaryngology. They were selected on a basis of research competence and we arranged for their training in programs noted for the excellent research and clinical environment. On their return to their Institutions, they will spend a portion of their time in research. Budgetwise, we show their support under "Other expenses" ($44,000 in 1969 and $42,000 in 1970). We transfer the funds to the Federal Health Programs Service's reimburable account; they expend the money for the salaries and expenses of the three trainees involved. The average cost is thus about $14,000.

Mr. NATCHER. Mr. Michel.

SPINAL CORD INJURIES

Mr. MICHEL. Doctor, I was glad to see in the opening page of your statement that priority has also been given to immediate and effective treatment for the thousands afflicted each year with brain and spinal cord injury.

Are you acquainted, Doctor, with Dr. Paul Bucy?

Dr. MACNICHOL. I am, indeed. He is one of the Institute's strongest supporters.

Mr. MICHEL. We have had correspondence in the past and Dr. Bucy has made the point in his last communication that we ought to be moving ahead in the field of pilot centers, spinal injury centers. Looking at the long-range need it is probably impractical from the standpoint of the facilities we have immediately to do the job properly, but do you think the suggestion he has of starting out on one or two pilot projects is a valid suggestion?

Dr. MACNICHOL. I think it would be a very good idea. Also, the Social and Rehabilitation Service has considerable interest in this field and I think we should be able to get together with them and pool our resources.

Mr. MICHEL. I am glad to hear you say that because while we recognize there is a very great need, we also recognize that in rehabilitation they obviously have more than a passing interest in it, too. Working in concert one with the other we ought to be able to do something. There has been a lot of interest in this, particularly in Illinois, because of the discharge of a number of these spinal injury cases from the VA facilities in and around Chicago. I am not so sure that the general public is altogether aware of what is involved here except that when you see these unfortunate people so handicapped as they are getting short-shrift it creates a stir. While I know we are doing something in this area, I don't know if we are doing all we can. We have pressure put on us back home that with the amount of money we are spending we ought to make more progress.

Dr. MACNICHOL. With automobile accidents becoming more and more of a problem, the matter of spinal injuries is more serious. I am

no expert in this, but from what I am told, the sooner a spinal injury person gets treatment the sooner and more effective the rehabilitation will be.

Mr. MICHEL. And the shorter period of time he has to stay in the hospital, the more people we can take care of.

Dr. MACNICHOL. One of the things we are doing is our intramural program is research on such things as interruption of the spinal cord.

INCREASE IN AVERAGE EMPLOYMENT

Mr. MICHEL. On page 174 of the justifications I note there is an increase in the average number of employees of 53. That is a sizable increase, up from 660 to 713. Where are all these people going to be? Does that suggest you have some unfilled positions now?

Dr. MACNICHOL. I think Mr. Wipf had better answer that.

Mr. WIPF. These are largely man-year increases in permanent positions. It also includes intermittents, summer employees, and youth opportunity program employees.

(The following was subsequently submitted:)

The increase of 53 for average number of all employees represents the added man-years to be supported in 1970. This is the full-year support of positions that were on duty for less than a year during 1969.

The increase of $478,000 shown directly below for personnel compensation is directly related to the increase in man-years. Man-year increases always affect dollars and, therefore, are synonymous.

YOUTH OPPORTUNITY PROGRAM

Mr. MICHEL. What is this youth opportunity program?

Mr. WIPF. It is a total Government-wide program.

Dr. MARSTON. We participate in a Government-wide program which is primarily a summer program that brings in young people. It has two purposes. One is a broad recruitment purpose. These young people have an opportunity, at an early age, to see the various parts of government functioning and determine career choices. The actual increase of permanent positions in the Institute, I think, is five rather than the 53.

Dr. MACNICHOL. These represent a real need. One is in the epilepsy area, where the need is great.

DRUGS FOR TREATMENT OF EPILEPSY

Mr. MICHEL. I remember reading in your statement that there have been no new drugs in the last 8 or 9 years to cope with this problem of epilepsy.

Dr. MACNICHOL. No new drugs on the market, but there are promising new drugs that for some reason or other have not gotten off the shelf.

Mr. MICHEL. Why haven't they gotten off the shelf?

Dr. MACNICHOL. I think it is partly because the pharmaceutical manufacturers do not feel there is enough volume. It has taken initiative on our part to get them off the shelf into this testing program that we have initiated.

Mr. MICHEL. Are they approved?

Dr. MACNICHOL. Not yet. It takes, as you know, a good deal of testing and rather expensive testing to get a drug aproved.

Mr. MICHEL. Whose responsibility is that, yours or the Food and Drug Administration?

Dr. MACNICHOL. Unless we do something about it, it is the manufacturer's obligation. Unless they can see a volume large enough to make an expensive testing program worth while, they will not undertake it themselves.

YOUTH OPPORTUNITY PROGRAM

Mr. MICHEL. Getting back to the youth opportunity program, is that true for every Institute in NIH or just this one Institute?

Mr. WIPF. All Institutes.

Mr. CARDWELL. It is a Government-wide program. The Department hires several thousands of these people every summer. This will be the third summer this program has been in effect. The prospective employee has to meet a needs test. The test is a family of four with an income of not over $4800 a year. The employees are paid about $1.50 an hour—not regular civil service rates. While I would not want to characterize it as a quota system, every governmental department is persuaded to employ these people in meaningful work.

Mr. MICHEL. So this does not really have anything to do with research activities?

Mr. CARDWELL. To the contrary, they could be employed as animal caretakers in a research environment. They could do various kinds of house cleaning chores, run errands, do landscaping and maintenance of grounds and perform other nonskilled labor that is needed in a research environment.

Mr. MICHEL. Are we talking about make-work projects that have to be financed in a sensitive budget like NIH?

Mr. CARDWELL. It is a Government-wide program. We employed about 270 in NIH as a whole last summer.

Mr. MICHEL. Is that because NIH is adjacent to the District of Columbia?

Mr. CARDWELL. No; this program has been operating nationwide. One of the objectives was to get young people off the streets and keep them busy. The program is also a part of a joint Federal-industrial project to give young people meaningful work. I cannot say there has not been some make work, but the objective is to give them meaningful work that has been postponed for some reason or other.

Mr. MICHEL. How much would you say is in this budget to employ these people just in summer employment? Is it broken out in a block figure?

Mr. CARDWELL. If we could have the man-years we would make an estimate.

Mr. SITHENS. It is less than $800 a person; we had 110 summer employees, of which 24 were from the youth opportunity program. The actual payroll for the 24 people last summer amounted to $16,896.

Mr. MICHEL. But there is a need test?

Mr. CARDWELL. Yes, $4,800 a year. I think they are now paid $1.65 an hour. The first year they were paid $1.25 and the second year it went up to $1.50 and I think now it is $1.65.

Mr. MICHEL. But as far as you know the program of this Institute is no different from that of the other Institutes?

Mr. CARDWELL. No. This Institute hired a proportionate share of the NIH total—about 10 percent. Further, the NIH hired about 10 percent of some 3,000 employed by the Department last summer.

Mr. WIPF. We are using a fair number for coding statistical data in our perinatal project.

Mr. SHRIVER. Will the gentleman yield?

Mr. MICHEL. Yes.

Mr. SHRIVER. How long has this been going on?

Mr. CARDWELL. This will be the third summer.

Mr. SHRIVER. It was not as the result of any law being passed?

Mr. CARDWELL. No, sir.

Mr. SHRIVER. How was it instituted?

Mr. CARDWELL. The Civil Service Commission and the White House—Mr. Macy, of course, at that time was serving in the joint capacity of Chairman of the Civil Service Commission and Presidential adviser on personnel matters, and he and the Cabinet got together, with the participation of the Vice President, and they designed this program.

They also called in leaders of industry and attempted to persuade them to voluntarily participate in the program. It would seem it is now a permanent part of the personnel system. These employees are not hired on a competitive basis. There are still summer programs for young people under competition. For instance, college students might compete for available summer jobs, usually to relieve people on leave and that sort of thing. And there are a number of student programs in the sciences where the government attempts to persuade people who are studying science to come for the summer with the idea they might become permanent Federal employees when they get out of college. So there are traditional programs and this was superimposed on it.

Mr. SHRIVER. We had a summer program in offices of Members of Congress but part of the reason for discontinuing it was the financial problem we had. We no longer have that.

Mr. CARDWELL. It is possible—I don't know—that the new administration might not continue the program, but I have no way of knowing that.

Mr. MICHEL. What are the age limits, if any, on these new people who have been superimposed on the regular employment?

Mr. CARDWELL. It runs from ages 17 through 21.

Mr. MICHEL. But they can qualify at the age of 17?

Mr. CARDWELL. Yes.

Mr. MICHEL. But not below?

Mr. CARDWELL. No.

Mrs. REID. Will the gentleman yield?

Mr. MICHEL. Yes.

Mrs. REID. I think the difficulty with some of these programs is that young people are taken in and given jobs but then there is not enough work for them to do.

Mr. CARDWELL. I have observed that myself.

Mrs. REID. That was part of the difficulty with our summer intern program.

Mr. CARDWELL. I think it actually does more harm than good in that case.

Mr. MICHEL. Precisely. If we give our young people the idea they can twiddle their thumbs and have it made, it can do more harm than good. One should perform.

Well, Doctor, we are getting far afield, but it is amazing sometimes what we can get in the record from a line of questions such as this.

TRAVEL AND TRANSPORTATION

The amount requested for travel and transportation is the same as last year, $372,000. Give me an idea what all this traveling is for, Doctor. The reason I raise the question, we have one of our fellow committee members on the full committee, Mr. Jonas, of North Carolina, who has made a point that maybe there is $1 billion involved in travel when you consider all agencies of Government and all the moving about. And, of course, that $1 billion comes about by one item like this added to another.

Dr. MACNICHOL. I think the biggest part of our travel is in the supervision of research and training grants throughout the country. Many of these, and all the larger ones, require project site visits. At least one member of the Institute staff, plus at least three advisers from outside, are taken to the site. They confer with the person whose grant is under review and with his collaborators and administrative officials.

There is really a tremendous amount of travel from this source. The committees that come to advise us in Washington travel from all over the country.

Mr. MICHEL. I think we recognize the need for some of it. What we have to do is see that it is not abused. That would go for Members of Congress, too. Of course we seem to get more publicity when we take a trip, but I am amazed when I see what is being spent by agencies and departments.

OTHER SERVICES

What is this item of $14,519,000 for "Other services"?

Mr. WIPF. About $9 million is for research contracts and $5.2 million is for reimbursements.

Mr. MICHEL. That reimbursement item, with the total figure being practically the same as last year, seemingly has been a static figure.

Mr. WIPF. This figure is reached by prorating against the Institute's budget based on services that are provided, such as ground maintenance, clinical center operations, administrative and technical services, et cetera, under a fairly well established formulae.

REDUCTION IN FELLOWSHIP AWARDS

Mr. MICHEL. I see the fellowshp awards have declined or are expected to decline from 1969 by about 25, due to what?

Dr. MACNICHOL. Due to limits in the amount of money that is available.

Mr. MICHEL. Is that principally due to the Revenue and Expenditure Control Act?

Dr. MACNICHOL. No. This is our share of the cut in training funds and it is NIH policy across the board.

Dr. MARSTON. This is due to the makeup of the budget for 1970 and is not a reflection of the Expenditure Control Act. It is a simple reflection of the priorities we established within the constraints we had for the 1970 budget.

Mr. MICHEL. Yes, because once a contract is entered into, unless it was renegotiated, it obviously could not fall within the category of that limitation.

Dr. MARSTON. As to training grants and, to a lesser extent, the fellowships, the determination for the expenditure for the following year is actually made in the spring.

For instance, right now we are making decisions that will affect expenditures next year, so this reduction in the 1970 budget is not a reflection of the Expenditure Control Act but purely a function of the 1970 budget.

PHYSICIANS ENTERING NEUROSENSORY FIELD

Mr. MICHEL. Doctor, what percentage of our doctors coming out of medical school these days go into this neurological field?

Dr. MACNICHOL. I do not have that figure, sir. I can supply it.

(The information follows:)

Percentage of physicians graduating from medical schools who enter neurosensory medical fields

[From a survey of 64,509 students]

	Percent
Neurology	0.98
Neurological surgery	0.81
Ophthalmology	2.71
Otolaryngology	1.41

Mr. MICHEL. Would there be any marked change in recent years?

Dr. MACNICHOL. Yes, I believe there has been a considerable increase in the last 10 years.

Mr. MICHEL. To what would you attribute that?

Dr. MACNICHOL. I think the training programs of our Institute have had a great deal to do with it.

Mr. MICHEL. Would that be short-changing some other areas, do you know?

Dr. MACNICHOL. I could not answer that question.

Dr. MARSTON. I think it is fair to point out this has been a matter of concern over the years, particularly with the increase of trauma from accidents, to have enough neurologists in the field.

It has been of sufficient concern that study was conducted during the past 2 years to look seriously not only at what is happening in terms of people going into the field but what is in the pipeline—that is, what the possibilities and outlooks will be over the next few years.

We can give you a summary of a reasonably up to date analysis of the needs.

That study did raise concern about having sufficient people in neurology and in neurosurgery. These are the areas that have much of the responsibility for the treatment of victims of accidents, automobile accidents particularly.

Mr. NATCHER. Mr. Casey?

BRAIN AND SPINAL CORD INJURIES

Mr. CASEY. I am interested in your statement about the brain and spinal cord injuries and your observations. There is no question but that it really affects everyone when the head of the household has brain damage or damage to the spinal cord. There is little that can be done in this regard at the present time, is there, other than just care?

Dr. MACNICHOL. Care and a considerable amount of rehabilitation is possible. People learn to get around in wheelchairs.

Mr. CASEY. That is physical therapy?

Dr. MACNICHOL. Yes.

Mr. CASEY. I mean so far as——

Dr. MACNICHOL. As far as actually repairing the spinal cord damage there is nothing we can do.

Mr. CASEY. Tell me about these pilot programs and multidisciplinary centers. How long have they been in existence?

Dr. MACNICHOL. About 2 years. Essentially these have been undertaken only in the last 2 years and this has been largely a planning operation to get this kind of activity going.

Mr. CASEY. Are they concerned primarily with rehabilitation programs rather than seeking basic solutions?

Dr. MACNICHOL. Primarily with seeking better methods of treatment, understanding of the problems involved.

TRAINING OF AMBULANCE OPERATORS

Mr. CASEY. Has any thought been given as to methods for preventing some of this particularly spinal cord injury? Here come a couple ill trained ambulance operators and they throw him on to a stretcher and the moment they do, snap, and you have a problem. Is any thought being given to that in the way of a national program for better training?

Dr. MACNICHOL. That is a serious problem, sir. I believe this has been considered. The National Academy of Sciences—National Research Council had a meeting on this subject and I have read their report.

Mr. CASEY. Everybody knows exactly what we are talking about but what I want to know is whether there is effort on a national basis to try to get local authorities, who have control over who runs the ambulances and who staffs them, to get them to realize that this is where, I dare say, most of your trouble comes from in spinal cord injuries.

Dr. MACNICHOL. I am sorry, sir. I do not know the answer to this. Perhaps Dr. Marston can help you.

Dr. MARSTON. Mr. Casey, there is concern about this throughout the services, especially in regard to the effectiveness of evacuation in

Vietnam. There has been an effort to institute a trial system utilizing a training program to fix the responsibility and have the people trained to carry on that responsibility from the ambulance driver to the people in the hospital. Programs to look into this area of emergency treatment are supported by other parts of HEW.

Mr. CASEY. This is just an observation. I would think that at these centers that you have they could offer just a 1-day course. This would be better than nothing.

Give just a 1-day course to encourage municipalities and whoever has the responsibilities involved here to come in and learn how to handle injured people so as not to paralyze them for the rest of their lives.

There is so little known about it, in my opinion, and it is so important. A lot of this could be avoided. There is no question about it.

Dr. MACNICHOL. I certainly agree this should be done. I think that the most effective way to do it would be for all of those who are involved in this—ourselves, the Veterans' Administration, Social Rehabilitation Service—to pool our resources to do something of this sort.

Mr. CASEY. There is a new device for carrying injured. I did not see the demonstration and some of my constituents wanted me to see it. They started to call it a litter, but they have now changed that and call it a body splint. This has been developed by a doctor and a number of engineers. It seems to me that the initial care of the injured person is most important, especially when you have the possibility of a spinal cord injury. This can be prevented to some degree through good initial handling. This is something we should concentrate on, because after that injury has occurred you can do nothing for him other than to see if there is some way of rehabilitating him.

I would hope that you might suggest to these various pilot institutes that they should include in their efforts seminars once a year or every 6 months and invite industry as well as municipal employees.

The skill and training of ambulance drivers still leaves a lot to be desired. I know it used to be that the fellow who drove an ambulance was a young fellow who liked to tear through the streets with a siren. I know you and I would like to see an intern riding in every ambulance, but there just are not that many interns.

RESEARCH ACCOMPLISHMENTS

What should I say, Doctor, if on the floor they asked, "What do we get for all this money?"

What would be the best thing we can point out in the way of accomplishment? Someone may ask, "What did we get for this money last year?"

What can we point out as the best accomplishment over the last couple of years?

Dr. MACNICHOL. I think the transmission of Kuru is a major accomplishment, recognition that a number of very serious neurological

diseases may be of viral origin, and the indication, although it is a long way from being proved, that some of the other serious diseases may also have a viral origin.

I think that is a very important thing, Mr. Casey.

Mr. CASEY. Now that you have discovered that, you are working on attacking the virus through drugs or how?

Dr. MACNICHOL. At this point it has simply been a matter of finding out what caused the disease, learning about the disease. I think the therapy is yet to come.

Mr. CASEY. That is your next step?

Dr. MACNICHOL. Immunization, of course, is one of the things. Our Institute was involved in the identification of the damage that rubella did, for example, to unborn children. Some of the scientists at our Institute made a considerable contribution to rubella research and then other institutes have gone on to develop a successful prevention which is just now getting underway.

Dr. MARSTON. This is a good parallel. For many years people regarded the congenital defects in children as being an act of God and something you could do nothing about.

We have looked at many of these neurological diseases, particularly the progressive types. In some instances, it looks as though viruses are a cause, which raises the possibility that some of the techniques useful in dealing with viruses—such as immunization and other things that are primarily the responsibility of the Institute of Allergy and Infectious Diseases—are also applicable to these diseases.

A few years ago no one thought about using these things for this type of neurological disease. Now Dr. MacNichol's Institute is working closely with the people interested in infectious diseases. It has opened up a sort of new world.

That is a dramatic and important step. There had been little progress for at least 50 years—or even in the entire history of medicine—in this field. Progress has been made only in recent years.

L-DOPA

Dr. MACNICHOL. As far as treatment is concerned, I think that the use of L-Dopa for parkinsonism is the most promising. L-Dopa is not the final answer. But it will help a lot of people, I am sure. It has given us some ideas for other things to try along with it to improve its action, and indeed there may be something like L-Dopa which will be more effective in the long run.

The fact that it works to a large extent has opened up a lot of new ideas for exploration.

Mr. CASEY. Can we say on the floor that due to the work of this Institute that 75 percent of those suffering from Parkinson's disease now have an opportunity of getting some relief?

Dr. MACNICHOL. I would not give our Institute the whole credit for this by any means. One thing we did do some time ago was to set up a Parkinson's Information and Research Center at Columbia which had a great deal to do, I think, with identifying the research that

had been done all over the world in this area and bringing it to the attention of those physicians who started to use L-Dopa successfully.

Dr. MARSTON. There is a major problem, at present, in the supply of L-Dopa. It simply is not available.

Mr. CASEY. I know that. It is still being used in the form of medical testing.

Dr. MACNICHOL. Actually we are not even conducting the tests. The drug industry itself is doing that successfully. They hope to build up large supplies.

As Dr. Marston says, these production facilities do not exist at the present time, and until they do exist the million-plus patients in this country who have parkinsonism will not be able to get the drug.

NEED FOR EVIDENCE OF RESEARCH ACCOMPLISHMENTS

Mr. CASEY. I do not mean to be picking on your Institute. Last year when they had a motion to recommit, to cut off $20 million from the National Institutes of Health, you had fellows running around saying, "With all the money they have they can take this cut." They say, "I don't know as they accomplish all they could with this amount of money."

They can defend this position at home because they merely point out the large amount of money appropriated and ask, "Do you know of anything this Institute has done for you?" You have to sell them on the floor by what you give them for their money—and when I say "you" I do not mean you personally but the whole program.

Dr. MACNICHOL. I should mention another area of success. The biochemists, largely in the intramural program, have been studying diseases of the nervous system which are due to what are called inborn errors of metabolism. Certain biochemical deficiencies which are genetically controlled, produce serious brain diseases. Often there is a piling up of too much fatty material in the brain which cannot be disposed of because certain critical enzymes are lacking.

In a number of these diseases these enzymes have been identified and the genetics have been worked out. The next step, of course, is to find ways of getting around this metabolic block either by supplying something which takes the place of the enzymes or some other treatment.

Mr. CASEY. We have the hard job of being up there talking to our colleagues who do not have the opportunity to talk to you and have the confidence in you people that we do. It is something like the space program. They say that these experiments enable them to collect a lot of data. The fellows on the floor ask, "What do you do with data, eat it with a spoon?"

You are in very much a similar situation. We have 400-plus colleagues up there who do not understand all of this and we have to pass on to them what they are getting for their money.

If they can see one child you have helped they are bowled over and they are strong supporters. Usually they do not know how much of

your work went behind a child who has been helped. They see only as far as the local doctor.

In my hometown they brag about certain transplant experts. They do not realize that that man acquired some of that skill and knowledge through the work that went on in your institutes.

Thank you, Mr. Chairman.

REDUCTIONS IN FELLOWSHIPS AND TRAINING GRANTS

Mr. SHRIVER. You pointed out that the committee last year recommended increased emphasis on training of scientists in the Institute. What about the fellowship and training grant program in 1970? Will that be increased?

Dr. MACNICHOL. No; unfortunately it will not, sir, not with the present budget.

Mr. SHRIVER. Why was an exception not made with regard to reducing the fellowship and training grants since you pointed out that the committee last year urged increased emphasis on training?

Dr. MARSTON. This reflects the fact that we have a very tight budget. We tried to do several things in putting this budget together. First, not to take any action which would disrupt the basic support of research in the country so that if, as Mr. Natcher mentioned the other day, we want to build up the research attack on these diseases after Vietnam, we do not have to go all the way back to rebuilding the basic framework and the basic network for research.

The second thing we put a high priority on was that we did not disrupt the institutions at a time when they not only are expected to carry out research but also are expected to be the training area for additional manpower, across the board, and, at the same time, are expected to do the most complicated patient care.

It was in the context of these very tough decisions that the training program and fellowships, despite the very serious attention we gave to the instructions of this committee, gave way. It is not something we are happy about.

SUBCOMMITTEE ON HUMAN COMMUNICATIVE DISORDERS

Mr. SHRIVER. Would you summarize for us the major recommendations of the Subcommittee on Human Communicative Disorders and the present state of research on problems of communicative disorders?

Would you supply that for the record?

Dr. MACNICHOL. Yes; I can supply it for the record.

(Information requested follows:)

Recommendations of the NINDS Ad Hoc Subcommittee on Human Communication and Its Disorders were presented to the NANDS Council for consideration as follows:

A. *Recommendation 1.*—We recommend that a permanent Subcommittee on Human Communication and Its Disorders be retained as a permanent advisory body to the National Advisory Neurological Diseases and Stroke Council.

B. *Recommendation 2.*—The subcommittee recommends a substantial increase in the funds awarded for extramural research on human communication and its disorders. Annual increments of 20 percent (beyond the usual additions to

cover general rises in the cost of doing research) are proposed for the next 5 fiscal years. Proportionately greater funds should be awarded in gap areas and areas of limited research to the degree that adequate projects and programs become available in these areas. Moreover, special efforts should be made to encourage grant applications in these areas.

C. *Recommendation 3.*—The subcommittee recommends that priority be given to research proposals for initial research grants in communicative science submitted by postdoctoral trainees about to embark on careers as researchers or teacher-investigators (as well as to proposals that are submitted by other recently graduated and otherwise similarly qualified young scientists).

D. *Recommendation 4.*—The subcommittee recommends the establishment as rapidly as feasible of new Inpatient Research Centers, Outpatient Research Centers and Cooperative Studies focusing particularly on clinical management of communicative disorders.

E. *Recommendation 5.*—Our subcommittee recommends that attention be given to encouraging strong and diverse programs of research on human communication and its disorders in educational institutions where predoctoral and postdoctoral training is performed.

F. *Recommendation 6.*—The subcommittee recommends that the plan to establish a Human Communication Branch (previously identified as the Neuro-Otolaryngology Branch) within NINDB's intramural program be put into effect as rapidly as feasible.

G. *Recommendation 7.*—The subcommittee recommends that all senior staff positions in communicative science within NINDB's intramural research program be at as high a grade level as possible and that opportunities for administrative scientists in NINDB's extramural program be likewise enhanced maximally.

H. *Recommendation 8.*—The subcommittee recommends that the rate of growth of funds allocated for training grants, traineeships, fellowships and career support in communicative sciences be increased during the next 5 years at a rate of 20 percent per annum.

I. *Recommendation 9.*—The subcommittee recommends that every reasonable effort be made to assure dependable long-term funding to those training programs that have demonstrated their worth, since only thus can the strongest and most productive educational ventures be maintained.

J. *Recommendation 10.*—The subcommittee recommends that those training programs in communicative science and communicative disorders which are now being supported and which are clearly engaged in preparing full-time researchers and teacher-investigators be given strong support and be encouraged to reasonable expansion.

K. *Recommendation 11.*—The subcommittee recommends that the distribution of training funds be such that areas in the communicative sciences which have to date received limited support (gap areas) are given substantial allocations in the next few years.

L. *Recommendation 12.*—The subcommittee recommends the development of a number of training programs dedicated to the preparation of scientists in multidisciplinary areas germane to research on human communication and its disorders.

M. *Recommendation 13.*—The subcommittee recommends that a major fraction of funding for every training grant awarded by NINDB be reserved for stipends and for the ancillary costs (i.e., tuition where it is necessary) that go directly to the support of trainees, either predoctoral or postdoctoral. The subcommittee particularly advocates adherence to this policy in all new awards for training in the area of human communication and its disorders.

N. *Recommendation 14.*—The subcommittee recommends that all training stipends awarded by the Federal Government to persons preparing for professional careers as researchers, as teacher-investigators or in the service professions be made commensurate with the maturity levels and the work outputs required of the recipients.

O. *Recommendation 15.*—The subcommittee recommends that strong support be given to funding of summer institutes and short-term clerkships for the purpose of recruiting talented young people for research and teaching in the communicative sciences.

P. *Recommendation 16.*—The subcommittee recommends that strong support, in the form of stipends that are at least comparable to those available from other Federal agencies, be given to funding predoctoral traineeships designed to prepare full-time researchers and teacher-investigators in the basic aspects of human communication and its disorders.

Q. *Recommendation 17.*—The subcommittee recommends that special efforts be made to induce younger investigators to undertake 2 or 3 years of postdoctoral training. This effort will require active cooperation both from training institutions and from the organizations that employ young scientists.

R. *Recommendation 18.*—The subcommittee recommends that increased efforts also be made to induce intermediate echelon investigators in the communicative sciences to seek special postdoctoral fellowships at strategic points in their careers.

S. *Recommendation 19.*—The subcommittee recommends that research career development awards for work on human communication and its disorders be increased in total number and that awards be allocated so as to represent as wide a range of interests and subspecializations within the communicative sciences as feasible.

T. *Recommendation 20.*—The subcommittee recommends that the added costs which will be incurred by adopting its suggestions for increased magnitudes of training stipends, for summer institutes, for clerkships and for increased numbers of predoctoral traineeships, postdoctoral traineeships, special postdoctoral fellowships and research career development awards be covered via the 20 percent per annum increase in training funds proposed in recommendation 8.

U. *Recommendation 21.*—The subcommittee recommends not only that the existing information center for hearing, speech, and disorders of communication be given strong support but also that the entire process of information and data exchange in the communicative sciences be reviewed for the purpose of determining what other services along this line, if any, might also have sponsorship by NINDB and how these might best be organized.

V. *Recommendation 22.*—The subcommittee recommends that NINDB develop an on-going program for making authoritative translations of foreign publications dealing with research on human communication and its disorders avialable to American scientists.

W. *Recommendation 23.*—The subcommittee recommends that NINDB sponsor and/or support an ongoing series of symposia, workshops, and conferences covering diverse and timely phases of human communication and its disorders.

X. *Recommendation 24.*—The subcommittee recommends that a mechanism be established for supporting short-term study by senior investigators who need to acquire new skills and to have special training in emerging phases of investigative technology.

Y. *Recommendation 25.*—The subcommittee recommends that a new study section be established within the Division of Research Grants of NIH and that this study section be assigned the task of reviewing all applications for support of research on education or on socio-economic rehabilitation of afflicted persons that are submitted to NIH, including applications for such studies with the communicatively handicapped.

Z. *Recommendation 26.*—The subcommittee recommends that the NANDB Council continue an Ad Hoc Subcommittee for Rehabilitation and that this subcommittee concern itself with advising the Council on research needs involving rehabilitation of all neurological disabilities, including communicative disorders.

NOTE: After a lengthy debate the Council did not accept some of the recommendations and made important modifications in others.

SPINAL CORD INJURY

Mr. SHRIVER. How much of your 1970 budget will be allocated toward research on acute spinal cord injury? This was referred to a while ago.

Dr. MACNICHOL. For 1970, we estimate that $1,308,000 will be spent on accident and injury in research grants.

Mr. SHRIVER. How does that compare with this year?

Mr. WIPF. $10,000 more.

Mr. SHRIVER. Then you are not really moving ahead in this area very much for the coming year, are you?

Dr. MACNICHOL. We cannot increase it.

Mr. SHRIVER. The same reason?

Dr. MARSTON. Same reason, yes sir.

Mr. SHRIVER. On page 195 of the justifications you say that information from the head injury field survey of Korean war veterans will be available early this year. Have you seen that up to now?

Dr. MACNICHOL. All available information has now been obtained. The National Research Council is now analyzing the data, and will issue their report in the fall of 1969.

Mr. SHRIVER. I think that is all I have.

Mr. NATCHER. Mrs. Reid?

AVAILABILITY OF L-DOPA

Mrs. REID. Doctor, is L-DOPA expensive?

Dr. MACNICHOL. Right now it is very expensive. There is no reason it should be expensive. It is a relatively simple compound. It is just a question of getting large volume manufacture of the drug going.

Dr. BERLINER. It is not very expensive but it will be quite expensive for any patient to be maintained on L-DOPA indefinitely.

Mrs. REID. Can you give us estimates?

Dr. BERLINER. Several hundred dollars a year for L-DOPA per patient, anyway.

Mrs. REID. Several hundred dollars?

Dr. BERLINER. Yes, sir.

Mrs. REID. You say this is not now available to doctors?

Dr. MACNICHOL. It is available in only very limited supply.

Mrs. REID. I had a request from a doctor in my district who wanted this drug for a patient. This was several months ago when we first started reading about it. I looked into it and found out that at that time he could not obtain it.

Could he obtain it at this time?

Dr. MACNICHOL. He would have to get an investigative new drug permit (IND) from the Food and Drug Administration before he would be allowed to use it. If he could qualify for the IND and goes through the necessary procedures, he should be able to get it.

Mr. CARDWELL. To qualify, he has to use it as an investigational drug. He cannot just decide he wants to give it to a patient. He has to really be experimenting with the drug.

Dr. MARSTON. This field has been moving so fast it is important to assess it almost day by day.

Perhaps it would help for me either to spend a couple minutes here or to put a brief one-page summary to supplement Dr. MacNichol's statement in the record here.

There is a major problem of supply. There is a major problem in terms of large doses that are required. There is a major problem of side

effects. However, because of the severity of the disease people are anxious to take additional risks. There is even a growing possibility of a dangerous black market in this area.

We began, last fall, to look seriously at what we could do to increase the supply and to accelerate the accumulation of information. By December it was apparent that several hundred patients had been treated but that the information had not been pooled so that it could be looked at it in terms of effectiveness and what might be needed in terms of licensing it.

The drug companies, which had not seen this as a potential profit-maker because it is not patentable, have now expressed greater interest in it. Indeed, one has been able to develop a synthetic process which has changed the whole view of the supply. As recently as two or three months ago, we were much less optimistic about the possibility of getting adequate supplies than since this synthetic process has been available.

However, plants are still not underway. There is a tremendous flood of mail which comes to our office, and I am sure to you office, asking for help.

The fact is that for a while, despite very earnest attempts to get a sufficient supply of the drug, it will be in very short supply and patients will not be able to be treated immediately.

Mrs. REID. I think it is unfortunate when there is publicity about something of this kind and patients read this that they cannot get it. They read it and cannot understand why it is not available.

Dr. MARSTON. It was the same thing with penicillin and the same thing in the early days of cortisone. We will be talking about some others before these hearings are over.

Dr. ENDICOTT talked about a drug which is arousing some of the same type of concern. Whenever there is a substance which is two or three steps back in the research area it brings up the same problem.

It comes back to the problem Mr. Casey talked about a moment ago. It is not hard to dramatize advances in health care but every time one does this one has keep in mind the very great risk of arousing hope in sick people who do not understand that it may be 1 year, 5 years, 10 years off the distance.

Mrs. REID. You mentioned there are four centers where patients are being treated. Where are these centers?

Dr. MACNICHOL. There are a number of others but the four happen to be the ones that we have had closest contact with.

Brookhaven National Laboratory, which is operated by Associated Universities Inc., mainly with AEC funding——

Mrs. REID. Where is that?

Dr. MACNICHOL. At Upton, Long Island, N.Y.

The College of Physicians and Surgeons at Columbia University is another one. Also in New York is the Cornell Medical Center. The fourth is Northwestern University. There are a number of other investigators throughout the country who do have licenses to use the

drug experimentally; for example, at the National Parkinson Institute in Miami, they have about 150 patients.

MULTIPLE SCLEROSIS

Mrs. REID. We hear a great deal these days about multiple sclerosis which seems to be attacking more and more young adults. I had a sister-in-law who had multiple sclerosis and a good friend who has had this disease for 30 years or more.

You mentioned this just briefly in your statement, but what progress is being made in this program?

Dr. MACNICHOL. Essentially, we are trying to understand the underlying cause of multiple sclerosis, what causes the myelin coating of the nerves to degenerate.

There are a number of ideas and one of them is that this kind of disease may be an auto-immune response, a situation in which somehow the body directs its immune defenses against its own tissues.

The possibility is that viruses may have some part in triggering this immune response.

There is a good deal of work now being undertaken to find the cause of multiple sclerosis. Until we really find the cause, there seems to be little we can do about the treatment.

Mrs. REID. Not too encouraging.

Dr. MACNICHOL. I think some of the progress that is being made is very encouraging indeed.

RESEARCH CAREER DEVELOPMENT AWARDS

Mrs. REID. On page 188 of your justifications you mention the career development award program and indicate this year you plan to provide 168 awards to young scientists who have completed their formal research training and need to establish themselves as independent investigators. On what basis is this selection made? Is this competitive?

Dr. MACNICHOL. Yes; this is competitive.

The Training Grant Review Committees look over the applications from these people. They are people who are usually well known by their colleagues. Their departments recommend them and they are very carefully screened so that only the most promising applicants get these awards.

STROKE CLINICAL RESEARCH CENTERS

Mrs. REID. You said there are 19 stroke clinical research centers?

Dr. MACNICHOL. Yes; that is correct.

Mrs. REID. Would you provide for the record where these are located?

Dr. MACNICHOL. Yes; I would be glad to do that.

STROKE CLINIC RESEARCH CENTERS
[In thousands of dollars]

	Fiscal year 1969, amount	Fiscal year 1969, amount
Cornell University, New York, N.Y	192	202
University of Minnesota, Minneapolis, Minn	397	442
Wayne State University, Detroit, Mich	280	280
University of Miami, Miami, Fla	283	324
Boston University, Boston, Mass	202	251
Johns Hopkins, Baltimore, Md	298	250
Duke University, Durham, N.C	228	261
Philadelphia General Hospital, Philadelphia, Pa	230	235
Bowman-Gray School of Medicine, Winston-Salem, N.C	119	119
Mayo Foundation, Rochester, Minn	194	203
University of Maryland, Baltimore, Md	120	138
Indiana University, Bloomington, Ind	186	125
University of California at Berkeley, Calif	96	305
University of Tennessee. Memphis, Tenn	179	237
Washington University, St. Louis, Mo	388	445
University of Kansas, Kansas C'ty, Kans	173	125
Presbyterian-St. Luke's Hospital, Chicago, Ill	98	80
University of California, San Francisco, Calif	115	140
University of Texas SW, Dallas Tex	182	157

Mrs. REID. Thank you very much.

MARKETING OF NEW DRUGS

Mr. CARDWELL. In the chain of questioning on the availability of L–DOPA, I think there is an interesting feature about how new drugs come on the market which might be helpful to you.

Following the thalidomide instances of the early 1960's there was a very severe tightening of the use of "experimental drugs." L–DOPA is still in the class of an experimental drug.

Now an experimental drug must be operated under protocol and very strict scientific observation and control.

The next step then would be for a drug manufacturer to propose to the Government a so-called new drug application, an application to bring the drug on to the open market for use by the medical profession. Until that happens, until these above-mentioned stages are followed, the drug really could not become available to the general public.

As Dr. Marston points out, the manufacturers have been slow to come forward with a new drug proposal because even if they had the approved application they would not have the supply.

Dr. MARSTON. We are following this very closely with the drug companies and we are concerned that it cannot move faster than it is moving.

Mr. SHRIVER. Where do these names come from? Where do you get L–DOPA?

Dr. MACNICHOL. That is an abbreviation. DOPA is Dihydroxyphenylalanine. L–DOPA means that the molecule is bent in a left-handed direction. There are two kinds. One is put together so that it is bent in a right-handed direction and the other is in a left-handed direction. Of the naturally occurring amino acids only the left-handed ones are generally found.

Mrs. REID. That is an unfortunate name. People think of it as dope. I should think you could find a better name.

Dr. MACNICHOL. It is an old compound and nobody ever thought when this acronym was given to it that it would be useful in treating disease.

Mr. NATCHER. Thank you for your testimony, Doctor.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

Amounts Available for Obligation

	1969	1970
Appropriation	128,934,500	103,485,000
Transferred to "Operating Expenses, Public Building Service, General Services Administration"	3,000	
Comparative transfers to "National Eye Institute"	-22,303,000	
"Salaries and Expenses, Office of the Director"	-615,000	
Cutback required by PL-90-364	-2,748,000	
Total obligations	103,265,500	103,485,000
Disposition of Cutback:		
To be returned to the Treasury	2,748,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
183	Research		$ 59,134,000		$ 59,506,000		+$372,000
	General research support grants		(5,818,000)		(5,818,000)		---
	Scientific evaluation and planning		(130,000)		(130,000)		---
	Categorical clinical research centers		(2,416,000)		(2,416,000)		---
	Specialized research centers		(850,000)		(850,000)		---
188	Fellowships		3,213,000		3,085,000		-128,000
190	Training		15,659,000		15,047,000		-612,000
	Direct Operations:						
191	Laboratory and clinical research	290	9,879,000	293	10,100,000	+3	+221,000
195	Collaborative research and development	199	9,742,500	201	10,092,000	+2	+349,500
198	Biometry, epidemiology and field studies	80	3,016,000	80	3,028,000	---	+12,000
202	Training activities	2	74,000	2	72,000	---	-2,000
203	Review and approval of grants	85	2,058,000	85	2,114,000	---	+56,000
204	Program direction	29	490,000	29	441,000	---	-49,000
	Total obligations	685	103,265,500	690	103,485,000	+5	+219,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	685	690	+5
Full-time equivalent of all other positions	55	45	-10
Average number of all employees	660	713	+53
Personnel compensation:			
Permanent positions	$ 6,837,000	$ 7,315,000	+$478,000
Positions other than permanent	331,000	343,000	+12,000
Other personnel compensation	113,000	120,000	+7,000
Total personnel compensation	7,281,000	7,778,000	+497,000
Personnel benefits	713,000	753,000	+40,000
Travel and transportation of persons	372,000	372,000	---
Transportation of things	83,000	83,000	---
Rent, communications, and utilities	222,000	225,000	+3,000
Printing and reproduction	119,000	139,000	+20,000
Other services	14,491,500	14,519,000	27,500
Supplies and materials	1,270,000	1,270,000	---
Equipment	710,000	710,000	---
Grants, subsidies, and contributions	78,006,000	77,638,000	-368,000
Subtotal	103,267,500	103,487,000	+219,500
Deduct quarters and subsistence charges	2,000	2,000	
Total obligations by object	103,265,500	103,485,000	+219,500

Summary of Changes

1969 estimated obligations	$ 103,265,500
1970 estimated obligations	103,485,000
Net change	+219,500

	1969 Base Pos.	1969 Base Amount	1970 Estimate Pos.	1970 Estimate Amount
Increases:				
A. Built-in:				
1. Annualization of the 1969 pay raise (in 1970)		---		$ 15,000
Subtotal, built-in increases		---		15,000
B. Program				
1. Research grants	---	59,134,000	---	372,000
2. Laboratory and clinical research	290	5,727,000	3	185,000
3. Collaborative research and development	199	9,531,000	2	397,000
4. Review and approval of grants		1,269,000	---	14,000
Subtotal, program increases	---	---	5	968,000
Decreases:				
A. Program				
1. Fellowships	---	3,213,000	---	-$128,000
2. Training grants	---	15,659,000	---	-612,000
B. Centrally furnished services from the National Institute of Health Management Fund:	---	5,265,000		-23,500
Total decreases		---		-763,500
Total net change requested		---	+5	+ 219,500

Explanation of Changes

Research grants--The increase of $372,000 will provide for approximately 7 additional ongoing or non-competing projects that were originated in 1969.

Laboratory and clinical research--The program increase of $185,000 will support three new positions and logistical needs for initial expansion in the new research facility at Bethesda, made available in October 1968 (40,000 net sq. ft.); a new program in neurotology, a major gap in the current intramural program, can now be initiated. The new experimental compound facility in Puerto

Explanation of Changes (con't)

Rico will be completed in March, 1969. In addition, the Laboratory of Neural Control will be expanded.

Collaborative research and development--An increase of $397,000 will finance 2 new positions and research support for Neurology's epilepsy and head injury programs. The epilepsy collaborative effort is concerned with the development and testing of improved anticonvulsant drugs. Research associated with head injury will be concerned with two major programs, the forces of injury and incidence and prevalence.

Review and approval of grants--An increase of $14,000 for program increases is requested to support additional administrative needs of the extramural and program analysis staffs.

Fellowships--The decrease of $128,000 will provide for 168 awards, a reduction of 25 from 1969.

Training grants--In 1970 the decrease of $612,000 will provide for 17 fewer awards than 1969.

Significant Items in House and Senate Appropriations

Committee Reports

ITEMS	
1969 House Report	
(1) The Committee urged the Institute to initiate a broader program to evaluate newly discovered drugs for epilepsy. (Page 23 of the House Report)	(1) One Institute-sponsored drug evaluation program has begun.
(2) The Committee expressed an interest in developing programs concerned with the development of new techniques for detecting strokes in the incipient stages. (Page 23 of the House Report)	(2) The Institute is initiating a study of new methods for detecting incipient stroke.
(3) Despite budget restrictions, the Committee expects the Institute to give considerable emphasis to its training programs. (Page 23 of the House Report)	(3) While there is a reduction both in numbers of grants and trainees, the importance of this program is fully understood and every effort is being made to maintain its quality.
1969 Senate Report	
(1) The Committee expressed active concern with the problem of Parkinsonism, and appealed for broader clinical trials to test the efficacy of L'Dopa. (Page 46 of the Senate Report)	(1) The evaluation of the effects of the drug is underway.
(2) The Committee also encouraged the Institute to expand its activities on brain and spinal cord injuries. (Page 47 of the Senate Report)	(2) Head injury studies have been expanded through centers, intramural research, and head model construction activities. Planning for increased studies in spinal cord injuries is underway.
(3) The Committee also directed the Institute to establish special isolated laboratories to study the possible effect of viruses in causes of degenerative neurological disorders. (Page 47 of the Senate Report)	(3) A Program of Requirements for a facility have been written, and actual design should begin during F.Y. 1969.

Legislation	1970 Authorization
Public Health Service Act Section 301--Research and Investigations in general.....	Indefinite
Title IV, Part D--National Institute of Neurological Diseases and Blindness.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Authorizing Legislation

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in section 301 of the Public Health Service Act.

Title IV, National Research Institutes, Part D, National Institute on Arthritis, Rheumatism, and Metabolic Diseases, National Institute on Neurological Diseases and Blindness, and other Institutes.

"Sec. 431 (a) The Surgeon General shall establish in the Public Health Service....an institute for research on neurological diseases (including epilepsy, cerebral palsy, and multiple sclerosis) and blindness...."

"Sec. 433 (a) Where an institute has been established under this part, the Surgeon General shall carry out the purposes of Section 301 with respect to the conduct and support of research relating to the disease or diseases to which the activities of the institute are directed, through such institute and in co-operation with the national advisory council established or expanded by reason of the establishment of such institute. In addition, the Surgeon General is authorized to provide training and instruction in such institute and elsewhere, in matters relating to the diagnosis, prevention, and treatment of such disease or diseases with such stipends and allowances (including travel and subsistence expenses) for trainees and fellows as he may deem necessary and, in addition, provide for such training, instruction, and traineeships and for such fellowships through grants to public and other nonprofit institutions."

Public Law 90-489
90th Congress, H.R. 12843
August 16, 1968

"Sec. 453. The name of the institute for neurological diseases and blindness is hereby changed to the "Institute for Neurological Diseases."

Public Law 90-639
90th Congress, H.R. 14096
October 4, 1968

"Sec. 7. The name of the National Institute of Neurological Diseases and Blindness is hereby changed to the National Institute of Neurological Diseases and Stroke."

Explanation of Transfers

Transfer to:	1969 Estimate	1970 Estimate	Purpose
"Operating Expenses, Public Building Service, General Services Administration"....	$ 3,000	---	To provide for rental cost.
Comparative transfers to:			
"Salaries and expenses, Office of Director".....	615,000	---	To provide funds covering expenses for the Office of Director, NIH, which were previously funded through the NIH Management Fund.
"National Eye Institute"....	22,303,000	---	To provide funds for the new institute established by PL 90-489.

National Institute of Neurological Diseases and Stroke

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$ 29,403,000	$ 33,613,000	$ 48,966,000	$ 41,487,000
1961	39,662,000	44,362,000	61,550,000	56,600,000
1962	54,100,000	57,624,000	80,000,000	70,812,000
1963	71,206,000	77,506,000	86,506,000	83,506,000
1964	88,407,000	87,675,000	88,407,000	87,675,000
1965	88,608,000	87,889,000	88,089,000	88,089,000
1966	96,403,000	96,403,000	102,153,000	101,153,000
1967	106,418,000	111,296,000	116,296,000	116,296,000
1968	128,633,000	128,633,000	135,633,000	128,633,000
1969	131,195,000	126,674,000	132,674,000	128,934,500
1970	103,485,000			

Justification

National Institute of Neurological Diseases and Stroke

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	685	7,994,000	690	8,531,000	+5	+537,000
Other expenses.....	---	95,271,500	---	94,954,000		-317,500
Total.....	685	103,265,500	690	103,485,000	+5	+219,500

General Statement

This Institute is concerned with a variety of diseases which afflict the brain and sense organs. Disorders such as cerebral palsy, epilepsy, multiple sclerosis, muscular dystrophy, parkinsonism, and deafness result in long-term disability while cerebrovascular disease (stroke) is the third largest cause of death in this country as well as invaliding many others. Progress against these inadequately understood diseases would relieve mankind of some of its heaviest disease burdens.

These neurological and sensory disorders fall into 13 major program areas, each subject of a specifically focused research effort. The research effort in these areas is carried out through extramural project research grants, center or program project research grants, intramural research projects, collaborative and field research projects and contract research projects.

(During 1968 and 1969, research and training activities relating to vision disorders have been financed from the "NINDB" appropriation. In 1969, this total authorization for NINDS and NEI is $103,265,000 and $22,240,000 respectively.)

The program areas and the distribution of the research effort for each NINDS category in 1968 was as follows:

The neurological disorders of early life include all those diseases of the nervous system which occur in early life whether they are acute or chronic. This is being pursued through some 293 projects, 99 of which are research grants, 49 are intramural projects, 113 are collaborative and field projects, and 32 are contracts.

The neurological disorders of adult life are those diseases of the nervous system which manifest themselves late in life, but are chronic and debilitating. In this area we have 63 projects, 47 of which are extramural grants, 2 centers, 3 intramural projects, 6 collaborative and field projects, and 5 contracts.

The cerebrovascular disorders include all those disorders of the central nervous system related to blood circulation including stroke. Here, there are 99 projects, 63 in grants, 17 in centers, 13 intramural, 4 collaborative and field, and 2 contracts.

Epilepsy and convulsive disorders are those conditions in which recurrent seizures require constant medication or treatment. There are 78 projects in this area, 55 of which are grants, 13 intramural, 3 collaborative and field projects, 3 centers, and 4 contracts.

Degenerative disorders of the nervous system include such diseases as multiple sclerosis, amyotrophic lateral sclerosis, and others which are chronic and incapacitating but for which there is no certain cause or treatment. There are 84 projects of which 76 are grants, 2 intramural, 3 collaborative and field, and 3 contracts.

Neuromuscular and muscular disorders of the nervous system are those diseases which involve both nerves and muscles in their interactions. These may occur at different periods of life, but are chronic and, again, incapacitating. There are some 126 projects here, 109 as research grants, 3 centers, and 14 intramural projects.

Inflammatory disorders of the nervous system are all those diseases caused by known infectious agents whether bacterial, virus, rickettsial, fungus, or other. There are some 23 projects in this area, 12 extramural grants, 1 intramural project, and 4 collaborative and field projects, and 6 contracts.

Accident and injury of the nervous system includes all those physical agents which can accidentally cause injury to the nervous system. In this area there are 55 projects of which 36 are extramural grants, 3 centers, 5 intramural, 2 collaborative and field, and 9 contract projects.

Tumors of the nervous system include all the neoplastic growths which occur within the confines of the nervous system and include the metastatic tumors of the nervous system which originate elsewhere in the body. There are 43 projects, 32 grants, 9 intramural projects and 2 collaborative and field projects.

Other neurological disorders (anatomical, chemical, and physiological base for neurological and behavioral functions) include all kinds of research which may relate to several of these disease categories or all of them. This is basic research on the nervous system which has wide application in many problems. There are 475 projects, 421 of which are extramural grants, 7 are centers, 25 are intramural projects, 4 collaborative and field, and there are 18 contract projects.

Hearing, equilibrium, and problems of the ear are being investigated in 170 projects, as 157 grants, 10 centers, 1 intramural project, 1 collaborative and field project, and 1 contract.

Speech, learning, language and memory disorders include 37 research projects, of which 30 are grants, 6 intramural, and 1 collaborative and field project.

Other sensory disorders (taste, smell, touch, etc.) encompass 79 research projects, 75 of which are grants, and 4 intramural projects.

The Institute maintains an overview of each of these areas through special task forces, Advisory Council Subcommittees, and its scientific information network now centered in four of the Nation's strongest university libraries and research laboratories. These facilities have been developed to advise the Institute staff of research needs and current progress.

From the outset, the use of focused and directed research efforts has been a major part of the Institute's program. For example, the cooperative study of retrolental fibroplasia, completed in 1955 at a cost of approximately $50,000, saved the country over $100 million for each year that this discovery was advanced by the study. The longest Institute study of this type is the Collaborative Perinatal Project, which is now in its ninth year. Other cooperative and collaborative studies are now in progress, and a major segment of direct research is devoted to the direction and coordination of these investigations, frequently using the contract mechanism.

Faced from the outset with a critical shortage of highly specialized scientists required for neurologican and sensory research, the Institute has devoted approximately 20 percent of its grant funds to the training of personnel. Former trainees form an important segment of developing programs, such as the newly established stroke centers. The expanding number and size of medical schools and specialty training programs are increasing the manpower demands from our training programs. These must grow to meet these needs.

The research supported by the Institute in these major program areas is discussed further within the following budget activities.

Research Grants

	1969 Estimates	1970 Estimate	Increase or Decrease
Research Projects.....	$ 49,920,000	$ 50,292,000	+$ 372,000
Special Programs.....	9,214,000	9,214,000	---
Total Research Grants.	59,134,000	59,506,000	+ 372,000

Introduction

The research grant programs of the National Institute of Neurological Diseases and Stroke include research projects, research program projects, outpatient clinical research projects, clinical research centers, and specialized research center grants in the cerebrovascular and head injury areas. The primary objectives of these grant programs are the identification, stimulation, and support of essential research on problems related to the diagnosis, treatment, and prevention of diseases of the nervous system, the neuromuscular apparatus, the ear, and human communication. Some of these diseases are among the major causes of death in the United States (stroke, head injury, and spinal cord trauma) and of permanent disability (paralysis, epilepsy, deafness, loss of speech). They include diseases of the young (cerebral palsy, epilepsy, aphasia) and of the aged (stroke, brain tumor, Parkinsonism, otosclerosis).

Program Plans for 1969 and 1970

In 1969, approximately 1,290 regular research projects totalling about $49,920,000 will be awarded by the Institute. It should be emphasized, however, that it was possible to maintain support for these projects only because the amount originally approved for each grant was individually negotiated downward an average of 10% to 15%. Therefore, by continuing the appreciable curtailment of activity on all projects, it will be possible to continue many of the ongoing projects at a minimal operating level and to initiate at pilot levels a limited number of new projects of special quality and importance. With the funds available for 1970, a similar compromise of progress will be required. This situation is aggravated by the increasing costs of doing research and increases resulting from policy changes in recent years pertaining to indirect costs and cost-sharing. The program will continue emphasis in the fields of stroke, parkinsonism, epilepsy, brain injury, brain tumors, deafness, and loss of speech. New programs at pilot levels will be directed towards special efforts in the neurological and sensory disorders as outlined below.

Research Project Grants

The importance to the mission of NINDS of some 1,300 regular research projects cannot be overemphasized since they constitute the major part of the extramural research program. They represent the ideas and approaches of the individual, independent scientists in laboratories and clinics throughout the nation. Some studies are largely clinical; others are effective and essential combinations of clinical and basic research. Many are fundamental studies on the important basic mechanisms by which cells, genes, protein molecules, and other fundamental biological entities reproduce and function in the nervous system. This information is vital to finding new approaches to the cause, treatment and prevention of diseases of the nervous system and human communication. Building upon this broad base of independent research, the Institute is establishing special projects and programs directed toward specific categorical objectives. In this way the most effective attack on each of the Institute's

disease problems is being developed and maintained.

Disorders of Human Communication (Hearing, Language and Speech)

The NANDS council's ad hoc Subcommittee on Human Communication and Its Disorders which was organized to review the present state of research on, and the problems of, communicative disorders, has completed an extensive report including twenty-six recommendations. These recommendations are under review by the Institute.

Other than prevention, the prime public health need with respect to communicative disorders is their early identification and management. Such disorders are frequently considered to be correctable solely by medical remedial measures followed by proper training and education. Therefore, it is especially important that they be diagnosed as early as possible before they become so firmly established that corrective measures will have limited effectiveness.

Clinical research centers and outpatient clinical research programs have been established to provide for comprehensive research programs on diagnosis and treatment of these communicative disorders. The centers are multidisciplinary and include experts in many aspects of human communication. Major developments in the detection, diagnosis, therapy, and natural history of communicative disorders are being perfected in them.

The development of improved instrumentation and sensory aids will be encouraged. In no other area is the participation of the engineer and the physicist more important for the design of mechanical and electronic aids. Every effort will be made in FY 1970 to at least maintain the present level of research in these crucial areas.

Epilepsy

Epilepsy is recognized as a major national health problem. It is generally estimated that there are at least one and a half to two million epileptics in the United States. However, because of the social stigma and unfavored economic and insurance position of epileptics, no reliable data are available about the true prevalence of this disorder. The economic burden in direct and indirect costs is probably well over one billion dollars a year. Despite a good deal of special attention over the past several years, progress has not been rapid in the areas of drug therapy, surgical treatment, electroencephalography, or basic research. This is true even though reasonably good experimental animal models are now available for laboratory studies.

Epilepsy has many manifestations and expert opinion differs on its cause or causes. Some believe that all forms of epilepsy arise from a single disease entity. Others feel that certain common mechanisms of neuronal discharge may occur in all cases, but that the specific etiologic chemical, anatomical, or functional defect may vary widely. At the present time seizures can be controlled, but not cured.

The Institute's program is built on a broad base of individual research project grants to scientists representing many disciplines in many laboratories. Studies on the structure, chemistry, and function of the normal brain are also essential to provide the firm base on which the abnormal brain can be examined. From basic studies on normal and epileptic brain tissue, significant advances are expected in such areas as microanatomy, neuropharmacology, neurochemistry, neurophysiology, and central nervous system circuitry that may underlie the basic mechanisms of the epileptic discharge. This requires sophisticated electronic and microchemical instrumentation. Such investigations will lead to the development of more effective anti-convulsant compounds and a better understanding of

the disease process.

Parkinsonism

The Institute is engaged in a broad attack on Parkinsonism, one of the chronic, disabling disorders of aging. In addition to the support of basic studies through research project grants, there are now two active clinical research centers for Parkinsonism and allied disorders. These disorders are important aspects of the national health problems since it is estimated that between one and one and a half million persons are afflicted with this disorder for which there was no effective form of therapy until now.

It was pointed out last year that the emphasis on new drug development would soon require the availability of extensive clinical facilities for testing and evaluation. This has now occurred in the development of the highly promising drug, L-Dopa (levodihydroxyphenylalanine), which may be a therapeutic breakthrough for the treatment of Parkinsonism. Preliminary trials of this amino acid have in many cases shown considerable relief of disabling symptoms, including rigidity, akinesia, and tremor. L-Dopa is still in the investigational phase and its use is still limited to clinical or basic research.

The Institute is considering arrangements for a carefully controlled clinical study of this compound. Because of the complex nature of the clinical manifestations of Parkinsonism, any therapeutic trial must include a very careful evaluation of the many factors involved. The short range effects of L-Dopa therapy may be apparent this year, but information about its long term usefulness and toxicity will require additonal time.

Because of this breakthrough, exciting new avenues of research have now become available, somewhat comparable to the stimulus that the discovery of penicillin had to the development of the wide spectrum of antibiotics now available.

Acute Spinal Cord Injury

The incidence of spinal cord injury as a result of both civilian and military injuries is increasing. These injuries, often resulting in paraplegia, have very serious consequences for the victim, his family, and the community. Although on-going, but financially limited research programs are already in existence, an intensified national effort is essential.

More information is necessary especially concerning what immediate damage actually consists of in the injured spinal cord. Preliminary data suggest that if the acute injury is properly treated, permanent damage may be prevented. The development of methods of treatment of the acute injury is of great importance since these provide the only hope for prevention of permanent damage, greater efforts are needed to develop instrumentation to utilize still viable muscles even though long tracts of the spinal cord have been damaged. Again, this is an area where the multidisciplinary approach of neurological scientists, biophysicists, and engineers is essential.

Head Injury

As a result of modern machines of peace and war, both the frequency and severity of head injuries are increasing. The Institute continues to intensify its attack on the medical aspects of this problem through the establishment of clinical research centers in order to provide a firm base for the important combination of clinical material, laboratory facilities, and experienced researchers. Much fundamental research is underway on the basic mechanisms of reaction to head injury. These studies increase the importance of providing clinical research centers to relate the findings in the laboratory to the problems of the patient.

Presently supported groups continue to direct their efforts to such problems as brain swelling after injury, the physiological and metabolic consequences of head injury, the physical forces involved in brain damage secondary to trauma, the structure and function of the blood-brain barrier, and the evaluation of new diagnostic and therapeutic procedures in the management of head injury.

Despite the great need, however, this research area has not moved ahead rapidly. Institutions with superb clinical material may not have the other requisites for a clinical research center. Consequently, seven specialized research center grants have been awarded to develop head injury clinical research centers. Additional institutions must be supported in their plans to develop centers and it is assumed that a number of the groups presently under development will show sufficient progress in the near future to warrant support as a full scale head injury clinical research center.

Stroke

Stroke continues to be one of the leading causes of death and disability, frequently occurring during the victims' most productive years. Survivors often suffer life long physical disability and/or mental incapacity.

Studies are desperately needed to insure more effective treatment of stroke by devising means to anticipate and prevent complete obstruction of cerebral vessels, and to supplement or replace vessels diseased beyond repair. Fundamental research on the cerebral blood vessels of laboratory animals and on regional and cerebral blood flow continue to provide the information which is essential prior to undertaking similar studies in man.

The main thrust of the Institute's attack on the stroke problem continues to be through the stroke clinical research center program, nineteen of which are presently supported. It is anticipated that several additional stroke research centers will be approved, but will have to await funding at some future date. Several of the present centers were first supported through a developmental phase in as much as some institutions did not have all of the essential resources required to justify a full scale center, but did have the potential for such development if given assistance.

Continued support of basic laboratory research also is essential to complement the clinical research center program as it provides the laboratory experimental base from which techniques applicable for human research are developed.

Support must be continued for the carefully designed national cooperative studies of the surgical and medical treatment of aneurysms and of the efficacy of drugs for the prevention of stroke due to hypertension. These are long term studies initiated several years ago and must be continued over the period of the research design.

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Chronic Neurological Disorders of Childhood	$ 3,295,000	$ 3,319,000	+$ 24,000
Chronic Neurological Disorders of Aging	2,297,000	2,312,000	+ 15,000
Cerebrovascular Disorders	4,843,000	4,876,000	+ 33,000
Epilepsy and Related Paroxysmal Disorders	2,646,000	2,665,000	+ 19,000
Sclerosing Disorders	2,895,000	2,916,000	+ 21,000
Muscular & Neuromuscular Disorders	3,694,000	3,720,000	+ 26,000
Infectious Diseases	449,000	453,000	+ 4,000
Accident and Injury	1,298,000	1,308,000	+ 10,000
Tumors of Nervous System	849,000	855,000	+ 6,000
General	14,726,000	14,836,000	+ 110,000
Disorders of Hearing and Equilibrium	6,940,000	6,987,000	+ 47,000
Disorders of Speech & Other Higher DNS Functions	1,547,000	1,561,000	+ 14,000
Disorders of Other Senses	2,296,000	2,314,000	+ 18,000
Multi-Categorical	2,145,000	2,170,000	+ 25,000
Total Regular Research Grants	49,920,000	50,292,000	+ 372,000

Distribution of Research Grants

	1969 No.	1969 Estimate Amount	1970 No.	1970 Estimate Amount	Increase or Decrease No.	Increase or Decrease Amount
1. Non-competing	889	$34,898,000	896	$35,270,000	+7	+$372,000
2. Competing	401	13,847,000	399	13,847,000	-2	-----
3. Supplementals	(110)	1,175,000	(110)	1,175,000	--	-----
4. Subtotal Regular Program	1,290	49,920,000	1,295	50,292,000	+5	+ 372,000
5. General Research Support Grants		5,818,000		5,818,000		-----
6. Scientific Evaluation		130,000		130,000		-----
7. Categorical Clinical Research Centers		2,416,000		2,416,000		-----
8. Specialized Research Centers		850,000		850,000		-----
9. Total Research Grants	1,290	59,134,000	1,295	59,506,000	+5	+ 372,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total fellowships...	3,213,000	3,085,000	- 128,000

Introduction

The research fellowship programs of the NINDS are designed to encourage clinicians and laboratory scientists to acquire the specialized advance research training and experience essential to prepare them for careers focused on investigation problems of the diseases and disorders of the nervous system, including stroke, and of hearing, speech, and human communication.

The program provides the indispensable financial support enabling scientists to become highly qualified in a diversity of essential skills such as neuroanatomy, neurophysiology, neuropathology, neurochemistry, neuropharmacology, audiology, otolaryngology, speech pathology, neuro-otology, biophysics, all of which are critical to the advances in solving the neurological and communicative problems. These scientists must become skilled in the use of the most up-to-date techniques and instrumentation as they apply to medical research. They must continue to up-date their skills as knowledge in their own and related areas advances. More than a decade of experience indicates that the fellowship programs have proven effective in meeting these objectives. A significant proportion of the research scientists whose projects are now supported by NIH research grants received support in the past under the fellowship programs.

Program Plans for 1970

Postdoctoral Fellowships

Postdoctoral fellowships provide financial support for scientists who have just completed doctoral training and are continuing advanced research training in highly specialized fields.

During 1970, emphasis will continue to be given to training in scientific fields relevant to laboratory and clinical research on problems of cerebrovascular disease, epilepsy, parkinsonism, speech disorders, deafness and vestibular disease.

Career Development Awards Program

Career Development Awards ensure salary support during a 5-8 year period for selected young scientists who have completed all or nearly all of their formal research training and who require additional research experience prior to assuming positions of scientific leadership. These awards provide them with an opportunity to become established as independent investigators in a chosen area of research. The awards are especially important for the clinician researcher, who is able for the first time during his training to devote himself completely to developing the experience essential to an academic and research career for which he has had a long prior period of clinical and research preparation. Many more individuals of this type are needed who can combine extensive knowledge in one or more of the basic sciences and firsthand experience with neurological or communicative diseases.

Funds requested for 1970 will provide for 168 awards, compared to 193 in 1969, a decrease of 25. This decrease reflects the priorities of the 1970 President's Budget which gives emphasis to the development of health services personnel.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	84	$2,061,000	81	$2,096,000	-3	$+35,000
b. Competing.....	52	615,000	55	662,000	+3	+47,000
2. Supplementals.....	(60)	53,000	(52)	49,000	-(8)	-4,000
3. New Grants.....	57	484,000	32	278,000	-25	-206,000
4. Total fellowships...	193	3,213,000	168	3,085,000	-25	-128,000

Fellowships (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral.....	77	$ 639,000	61	$ 518,000	-16	$-121,000
2. Research Career:						
a. Career.....	13	371,000	13	376,000	0	+ 5,000
b. Development...	85	2,053,000	83	2,104,000	-2	+ 51,000
3. Foreign.....	18	150,000	11	87,000	-7	- 63,000
4. Total fellowships	193	3,213,000	168	3,085,000	-25	-128,000

Training Grants

	1969 Estimate Amount	1970 Estimate Amount	Increase or Decrease Amount
Total training grants....	$15,659,000	$15,047,000	-$612,000

Introduction

The Training Grants program of the National Institute of Neurological Diseases and Stroke provides support to institutions for establishing, improving, or expanding training programs designed to prepare clinical and laboratory scientists for research and academic careers, and for careers in organized community service and public health in the disciplines relevant to diseases and disorders of the nervous system, the cerebrovascular area, the neuromuscular system, hearing, speech, and human communications.

The responsibility for future advances in understanding, preventing, and successfully treating neurological and communicative disorders rests essentially on this group of highly trained clinical and laboratory scientists from whose ranks emerge the leaders in teaching and research.

An Institute sponsored survey suggested that we would not be able to keep pace with the growing need for highly trained clinicians, teachers, and researchers in the areas of the neurological disorders, hearing, speech and human communication. The needs stem from the opening of new medical schools and increasing demands for highly skilled personnel in community and regional medical programs.

Funds requested for 1970 will provide for 405 awards, compared to 422 in 1969, a decrease of 17. This decrease reflects the priorities of the 1970 President's Budget which gives emphasis to the development of health services personnel.

National Institute of Neurological Diseases and Stroke
Distribution of Training Grants

	1969 Estimate No.	1969 Estimate Amount	1970 Estimate No.	1970 Estimate Amount	Increase or Decrease No.	Increase or Decrease Amount
1. Continuations:						
a. Noncompeting...	187	$9,450,000	187	$9,450,000	---	---
b. Competing.....	131	4,473,000	131	4,169,000	---	-$304,000
2. Supplementals.....	(40)	310,000	(40)	310,000	---	---
3. New Grants.....	104	1,291,000	87	983,000	-17	- 308,000
4. Scientific evaluation and planning	(4)	135,000	(4)	135,000	---	---
5. Total training grants.....	422	15,659,000	405	15,047,000	-17	- 612,000

Training Grants (by type of program)

	1969 Estimate No.	1969 Estimate Amount	1970 Estimate No.	1970 Estimate Amount	Increase or Decrease No.	Increase or Decrease Amount
1. Graduate.....	243	$13,500,000	234	$12,975,000	-9	-$525,000
2. Traineeships.....	179	2,024,000	171	1,937,000	-8	- 87,000
3. Scientific evaluation and planning	(4)	135,000	(4)	135,000	---	---
4. Total training grants.....	422	15,659,000	405	15,047,000	-17	- 612,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	290	3,880,000	293	4,113,000	+3	+ 233,000
Other expenses		5,999,000		5,987,000		-12,000
Total	290	9,879,000	293	10,100,000	+3	+ 221,000

CLINICAL RESEARCH

Medical Neurology

Clinical investigations of this Branch are concentrated principally on neuromuscular diseases and degenerative diseases of the nervous system. They involve application directly to the patient of the newest aspects of basic research techniques in histochemistry, biochemistry, immunology, electron microscopy, tissue culture, autoradiography and electro-myography. This systematic approach has been particularly successful in identifying new diseases and in developing new therapeutic procedures. It will be continued.

Neuroradiologic studies will be directed towards producing new and improved techniques in angiography of the brain and spinal cord. The use of radioisotopes by injection intravenously or intrathecally will be continued to follow the movement of the spinal fluid.

Neuropharmacologic studies will be continued to clarify the chemistry of relaxation and contraction of striated muscle. Other studies will be made on the effects of snake venoms on the blood brain barrier and neuromuscular junction.

Surgical Neurology

The surgical neurology program is concerned with the use of selected patients coupled to basic laboratory inquiry applied to the problem of head injury, epilepsy, cerebral palsy and mental retardation. Surgical techniques are being developed and refined.

Mental retardation is being studied by clinical, laboratory, chromosomal, and biochemical techniques in an effort to discover the nature and cause of these defects.

By means of high-speed photography, x-ray and various physiological recording devices, the immediate effects of brain injury are being identified. In addition, histochemical and electronmicroscopy studies of the injured brain are being made. A system of classifying and coding patients with head injury has been developed and is being used, while a few highly selected patients with severe injury to the brain stem are being studied directly.

Cerebral edema is an important complication of head injury and brain disease. The occurrence of brain swelling within the closed cerebral cavity greatly aggravates the results of injury. Investigations of the disturbed permeability of the blood brain barrier through the use of radioactive tracers and other specialized techniques are directed toward determining a method to modify this reaction.

The effect of cold and drugs on epilepsy and drugs on brain tumors are being studied. Using a new technique, the brain is cooled while anti-convulsant drugs are given by vein. Similarly, for the treatment of brain tumor, anti-cancer drugs are instilled directly into the brain cavities of the afflicted patient.

Children with inborn and acquired brain lesions as well as those suffering from mental retardation are being studied by clinical, laboratory, chromosomal, and biochemical techniques in an attempt to ascertain the nature and cause of these defects and afford better management and prevention.

Electroencephalography

The investigations of this Branch are directed toward an understanding of the essential brain mechanisms underlying epilepsy and related brain abnormalities in both human and experimental situations. The electrical activity of the brain cells is being recorded under normal and abnormal conditions. Such knowledge is basic to an understanding of the deviations of electrical activity underlying the epileptic seizure.

Other studies are concerned with the mechanisms of abnormal movements such as those occurring in Parkinson's disease and related disorders.

This Branch also maintains a diagnostic service in electroencephalography widely called upon by the entire Clinical Center.

Neuro-otology

With adequate funding and increased positions, this Laboratory will take steps to establish and expand a program of research into communicative disorders.

Human communication is a multifaceted product of complex neurological processes. Consequently, the scientific evaluation of both normal and abnormal communicative processes required a multidisciplinary approach to research. A Neuro-Otology Branch will have two missions: (1) to conduct long-range research on the normal processes of the sensory, central, and efferent mechanisms which are used for human communication, and (2) to study the identification, and amelioration of aberrations in these mechanisms.

LABORATORY RESEARCH

Neuropathology and Neuroanatomical Sciences

The program of this Laboratory is directed toward development of precise knowledge of the normal nervous system on the fine ultrastructural level, as well as a proper interpretation of basic abnormal (pathological) changes and mechamisms underlying neurological disorder.

With magnifications available up to 200,000 times, investigation of intimate details of the normal individual cells and studies of the organizational patterns of these neural elements are undertaken as well as the elucidation of this nature and function in the overall complex organization of the brain.

The basic abnormal mechanisms studies are those operative in brain edema, oxygen deprivation of the brain, hypertension, and the reaction of the nervous tissue of radiation.

Biophysics

This Laboratory is studying the basic mechanisms of activities in nerve and other excitable tissues. The principal objective is to determine the physical and chemical processes which underlie the ability of the nerve axon to transmit

an information-carrying impulse. The approach combines laboratory investigations on single axons, artificial membranes, and membrane models using mathematical analysis with the aid of computers.

Neurochemistry

The program of the Laboratory of Neurochemistry involves more than a dozen major projects concerned with the chemical organization of brain and nerve, the biochemical bases for nerve activity and excitability, the function of nerve cell membranes in transport processes, and the abnormalities of protein, lipid, amino acid and ionic components in various neurological diseases. These basic investigations are aimed at understanding such neurological disorders as epilepsy, concussion, stroke, cerebral edema, multiple sclerosis, lipidoses, viral encephalitides, amyotrophic lateral sclerosis, muscle diseases and genetically-determined neurological conditions. Representative recent work elucidates micromolecular organization of nerve membranes related to lipid and to ionic transport, the probable nature of the biochemical defect in Tay-Sachs disease, important diagnostic and genetic counselling procedures for various lipidoses, and new approaches to regulation of brain fluid and ion distribution in cerebral edema and stroke.

Neurophysiology

The purpose of this Laboratory is to study the fundamental functions of the nervous system. Investigations include studies of the cellular properties responsible for the orderly development of the nervous system; studies of the of the responses of sense endings; studies of the transmission of messages from cell to cell (synaptic mechanisms) and studies of the basic properties of single neural elements (cells). Many studies involve the less complicated neural structures of lower forms of life within which fundamental processes are more clearly elucidated.

Molecular Biology

The objectives of this Laboratory are to determine the mechanisms through which genetic material may be damaged and the processes whereby modifications of this material lead to developmental alterations of the body. Molecular biology is concerned with explaining these basic biological questions in molecular terms.

The mutagenic and chromosomal breaking alterations of DNA produced by various chemical and physical agents are studied by working primarily with bacteria and with isolated DNA. The mutant organisms are then examined for their alterations in protein synthesis and function and the resultant developmental malformations are analyzed. These studies are essential to the basic understanding of the mechanisms of the inborn errors of metabolism and to genetically determined disorders.

Neural Control

The objectives of this Laboratory program are to study the mechanisms through which the nervous system can be made to respond to external stimuli and to study how the nervous system controls voluntary and/or involuntary movement. In addition, studies will be made of ways in which the effectiveness of the normal or damaged control mechanisms can be increased by supplementing with or supplanting by artificial elements. There will be three facets to this program: research leading to development of direct neural control of external devices, i.e., outward information transfer; two, the development of direct control of the vervous system by external devices, i.e., inward information transfer; and three, to study central information-processing mechanisms and its representation through equivalent neural models.

Perinatal Physiology

The research program of this Laboratory is concerned with the perinatal period of life and its relationship to certain kinds of neurological disorders such as cerebral palsy and mental retardation. In humans, these conditions are believed to result from the presence of certain noxious influences during critical periods of early development. The reproductive processes of rhesus monkeys are similar to those of man and afford a convenient and significant approach to understanding the pathophysiology of these conditions. This Laboratory has developed extensive rhesus primate holding and breeding facilities which are necessary to provide the appropriate resources to this problem. The present studies focus on systematic and detailed study of the pathophysiological, biochemical and behavioral changes produced by events such as anoxia, asphyxia, placental abruption and hypoglycemia.

The requested increase of $221,000 for this activity includes $185,000 for program increases to support three new positions and the full year ulitization of permanent positions authorized in 1969. It will also support new programs in neurotology and logistical needs for the new research building. Also included in the total is $8,000 for annualization of the 1969 pay raise and an increase of $28,000 for centrally furnished services of the "National Institutes of Health Management Fund."

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	191	$1,891,000	201	$2,181,000	+2	+$290,000
Other expenses		7,851,500		7,911,000		+59,500
Total	199	9,742,500	201	10,092,000	+2	+349,500

HEAD INJURY

The head model construction program, started in 1967, has made considerable progress. The goal of this program is the development of accurate physical and mathematical models of the head which can be used for intensive studies of the characteristics and effects upon the head of various forces of injury. Three institutions, under NINDS research contracts, will continue during the forthcoming year to test the material properties of the human and animal head and will begin the design of a simple mechanical model. An excellent panel of expert consultants from the disciplines of neurology and neurosurgery, biophysics, and mechanical engineering is assisting the Institute in the direction of this program.

A field survey of some 850 head-injured veterans of the Korean Campaign and 200 non-injured controls is nearing completion. Interviews of the veterans and their relatives and employers have been carried out by the American National Red Cross Service to Military Families, and the interview schedules are being edited by the staff of the Head Injury Section. Information is being obtained on employment patterns over the past 15 years, the occurrence of post traumatic symptoms, and the incidence of epilepsy in the veterans and their immediate families. The National Research Council Follow-Up Agency is coding and storing the edited information along with data already obtained on the original injury and follow-up clinical studies. All available information will have been obtained by early 1969, at which time the National Research Council will begin analysis of the data.

An in-depth evaluation of research in the field of head injury throughout the country is currently underway. Educational institutions, industrial organizations, and government agencies concerned with basic mechanisms, treatment, and prevention of head injuries will be surveyed. Current and planned programs in this area will be reported to interested researchers, thus encouraging information exchange and hopefully reducing duplication of effort.

Under consideration for F.Y. 1970 are an incidence and prevalence survey to determine the role of head injury in the total picture of accidental injuries, and the development of field activities related to the physiologic problems of head injury.

The Institute continues to rely upon the advice and support of an ad hoc Subcommittee of the National Advisory Neurological Diseases and Stroke Council in the development and evaluation of its research programs in head injury.

EPILEPSY

Information gathered in the pilot phase of the NINDS-sponsored Collaborative Study of Epilepsy (concluded in December, 1968) is now under analysis and the results will be published. The methodology developed for data collection, storage, and retrieval will be employed in contracts solicited for the clinical investiga-

tion of an anticonvulsant drug.

Anticonvulsant drugs presently available are effective in controlling only about 60 percent of epileptic patients. Thus, there is an urgent need for new anticonvulsants for uncontrolled and poorly controlled patients; also of concern is the development of drugs having fewer, less severe side effects. A modest anticonvulsant drug program was begun in 1967 and continued in 1968 and 1969. Liaison with the pharmaceutical industry was established. One Institute-sponsored drug evaluation program was begun in 1968. Two symposia were held: "Laboratory Evaluation of Anti-epileptic Drugs," May 1968, at Salt Lake City, and "Basic Mechanisms of the Epilepsies," November 1968, at Colorado Springs. The Institute plans to continue and expand these activities to provide opportunity for clinical evaluation of all promising new agents. Institutionalized patients and outpatients will be employed. Sponsorship of laboratory studies of promising anticonvulsant compounds is also contemplated.

The monthly publication "Epilepsy Abstracts," first issued in November 1967, has been enthusiastically received by the scientific community. There are 2250 scientists who have subscribed to this Institute-sponsored publication. The magnetic computer tapes resulting from the production of the abstracts will be converted to a standard library format and made available to appropriate biomedical information centers. A retrieval system will also be developed and made available.

The Public Health Service Advisory Committee on the Epilepsies continues to provide excellent advice in establishing program priorities and assessing the value of these activities.

COLLABORATIVE PERINATAL PROJECT

The Collaborative Perinatal Project of the NINDS, which was initiated in 1959 in collaboration with 14 hospitals and university medical schools, is a comprehensive investigation of medical and obstetrical complications of pregnancy and of genetic and other factors operating in pregnant women. These factors are suspected of contributing to neurological and mental deficits and congenital defects in the offspring. Institutions participating are: Johns Hopkins Hospital; Boston Lying-In Hospital; Children's Medical Center, Boston; University of Buffalo; University of Tennessee; University of Minnesota; Charity Hospital, New Orleans; Babies Hospital, New York City; New York Medical College; Pennsylvania Hospital; Children's Hospital of Philadelphia; University of Oregon Medical School; Brown University; and Medical College of Virginia.

Data have been collected on 60,000 pregnancies and the children from these pregnancies are followed until eight years of age. It is expected that this follow-up will be completed by 1974.

Complete data are now available on all pregnancies under investigation, and the observations of children through the first year of life. Several thousand children have completed the examination schedule at age eight. However, the majority of children are still too young to have received this examination.

The analysis of data in a preliminary manner has been underway for sometime and has resulted in the identification of important obstetrical factors which appear to contribute to the neurological and mental deficits in the offspring. During the last year significant relationships to mental deficits in four-year old children have been shown for such complications like diabetes. Further evidence has accumulated on the correlation between the head position of the child at birth and the location of neurological lesions. Preliminary analysis also suggests that hypertensive disease with proteinuria appears to contribute to mental retardation as identified in four-year old children.

Additional evidence has come forth suggesting a mechanism for the occurrence

of a specific type of cerebral palsy in premature children. Promising leads also have come from the investigation of viruses and other infectious agents as contributors to neurological and mental aberrations in the young child. It has been known that German measles produce profound fetal effects when it occurs in the first trimester of pregnancy. The observation of adverse fetal effects when rubella occurs later in pregnancy has added considerably to the understanding of the nature of the German measles infection and the effects which it produces in the fetus.

With the completion of the data file of the obstetrical information and the information on children through the first year of life, and completion of the basic evaluation of the data collected by this program, the program has now outlined a basic plan for data analysis. This will permit the comprehensive analysis of the relevant information collected by this program in the pursuit of the basic objectives of this study, namely, the identification of factors of pregnancy and its complications which contribute to neurological, mental and other birth deficits of children.

Of the total $349,500 increase requested for Collaborative Research and Development, $396,500 is for program increases, $4,000 for annualization of the 1969 pay raise and offsetting decreases of $51,000 for centrally furnished services of the "National Institutes of Health Management Fund."

The program increases will be utilized for two new positions and the full year utilization of positions authorized in 1969, in support of the Institute's epilepsy and head injury programs. The epilepsy collaborative effort is concerned with the development and testing of improved anticonvulsant drugs. Research associated with head injury will be concerned with two major programs, the forces of injury and incidence and prevalence.

Biometry, Epidemiology and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	80	$ 901,000	80	$ 901,000	--	$ --
Other expenses.....	--	2,115,000	--	2,127,000	--	+12,000
Total.....	80	3,016,000	80	3,028,000	--	+12,000

BIOMETRY

The Office of Biometry provides consultation and assistance to the Institute's staff on mathematical and statistical matters, data processing and computer technology, and the formulation of programs in which biometry is important.

Continuing programs of the Office of Biometry include the development of mathematical and statistical methodology applicable to the field of neurology, i.e., investigation of a mathematical model for transmitting chemical substances from nerve endings to muscle fibers is an example of this basic research; the statistical design and analysis of clinical trials assessing new drugs for possible use in the treatment of neurological disorders; the design and analysis of animal, chemical and physiological experiments to provide insight into neurological mechanisms; the statistical design, analysis and interpretation of perinatal studies of the etiology of fetal mortality, mental retardation and other neurological deficits in children; and the development of new computer systems and applications to support mathematical and statistical activities of the Institute.

The increasing need for computer and biometrical formulas and concepts in the Institute's extramural, collaborative and clinical programs designed to find cures for neurological diseases and disorders places added emphasis and importance upon the work of the Office of Biometry.

EPIDEMIOLOGY

Studies of the incidence and prevalence of a wide range of neurological disorders are underway and will be continued. Diseases or disorders under investigation include multiple sclerosis, amyotrophic lateral sclerosis, cerebrovascular disease (stroke), epilepsy, peripheral nerve diseases, motion disorders, acoustic neuroma, dystonia musculorum deformans, and headache.

Studies of patients dying of amyotrophic lateral sclerosis on the island of Guam have revealed an uncommon pathology. Collaborative pathological studies on patients who have contracted ALS after living on Guam will be pursued to determine whether these changes are common in all ALS victims who have lived on this Pacific island. These studies will further illuminate the factors which contribute to an abnormally high incidence of ALS on Guam.

A nationwide cerebrovascular disease mortality study has been completed which verifies marked regional variations in the occurrence of strokes in the U.S. As an outcome, major studies have been developed, and are being supported by the Institute's Extramural Program. In addition, prospective epidemiologic studies are planned to develop sound information on possible precipatating factors which may relate to regional variations in climate, medical care, socio-economic status, diet, etc.

The fact that the incidence of multiple sclerosis is high in colder climates is well established. Studies are underway in New York City investigating

immigrants from Ireland and Italy and their first-generation descendants, to determine whether the propensity to develop MS in a common climate is altered by family background. In addition to these field studies in multiple sclerosis, studies on the immune reactions of peripheral lymphocyte cells promise to provide information on the role of auto-immunity in the etiology of multiple sclerosis, or in the susceptibility of individuals to the disease.

The true incidence and prevalence of epilepsy is extremely difficult to document due to a variety of causes, including social stigmata, and varying criteria of diagnosis. A study is underway in one community to test various methods, other than complete medical examinations, to ascertain the true incidence of convulsive disorders. These methods can then be applied by other investigators to communities across the nation.

Field studies have confirmed a genetic role in the etiology of dystonia musculorum defornams, a rare neuromuscular disease. Field studies of acoustic neuroma, a tumor affecting the function of the inner ear, are underway and will be expanded to evaluate methods of prevention and treatment in genetically susceptible groups.

Short term studies of other neurological disorders will be carried out using epidemiologic techniques developed during the past several years.

SLOW AND LATENT VIRUSES IN NEUROLOGICAL AND SENSORY DISEASES

For the past decade, the Institute has been pursuing a program to search for viruses as a cause of such chronic neurological diseases as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Parkinsonism and the subacute and chronic encephalitides of childhood. As part of this program, a strange subacute neurological disease, kuru, which had reached epidemic proportions in an isolated population, was selected for concentrated study because of its high and restricted incidence suggested the possibility of a focus on an infectious agent.

Kuru has many of the features of chronic neurological diseases seen throughout the world, which have been classified as degenerative diseases of the nervous system. It also had a familial pattern of occurrence with suggested genetic determination, at least hereditary predisposition. Its epidemic proportion, however, made it essential to consider infectious causes when toxic and deficiency possibilities had been ruled out. In the further study of this exotic disease, successful transmission with long incubation periods varying from one and a half to over three years to chimpanzees has been achieved by the inoculation of brain and other tissue from kuru victims. The stimulation that this success has given to investigation in the field of idiopathic neurological diseases has been far-reaching. Spurred by the successful elucidation of kuru, NINDS has launched into studies of other chronic central nervous system diseases. Subacute sclerosing panencephalitis, a fatal disease of children, has been shown to be caused by a measles virus residing in the body for many years after acute measles infection. The Institute was among the first to accumulate evidence for the role of measles in this disease, and called a symposium on this acutely important subject in September 1967. Workers from several nations who were contributing to this discovery were assembled to discuss the state of knowledge. Subsequent work here and elsewhere has further incriminated measles as the cause of this disease, which claims several hundred American children each year.

The disease which in America and elsewhere throughout the world bears the closest resemblance to kuru is Creutzfeldt-Jakob disease, also called spongiform encephalopathy of gray matter. It is a nervous system disease, usually fatal within several months, which occurs sporadically throughout this country. Brain biopsy from a case with the disease has been used for successful transmission of the same neurological disease to the chimpanzee after 13 month's incubation. Both this disease and kuru bear striking resemblance to scrapie, a widespread fatal brain disease of sheep.

Kuru and scrapie have thus become the experimental models for the study of persistent and slow virus infections in the brain. The work requires long-term observation of animals, particularly primates in the case of kuru, since other animals are not susceptible. Recently, NINDS workers have succeeded in transmitting kuru to the spider monkey, as well as to the chimpanzee. This is a great advance, since it now permits experimental work to be done on a laboratory animal much more readily available and easier to house. These slow virus infections, in which successful transmission has already been achieved, have indicated that for both the further study of the pathogenesis of these diseases and for the investigation of other more prevalent neurological diseases of still unknown etiology, long-term holding of experimental animals, including primates, will continue to be a necessary feature of the investigations. A series of animal infections of the nervous system, which have been proven to be caused by slow viruses, are also being used as experimental models. These include scrapie, mink encephalopathy, visna, maedi, Aleutian mink disease, and canine distemper.

NINDS workers successfully isolated, last year, a virus from lung and brain explants of sheep dying of Montana sheep disease, which is an endemic disease of long-standing in the United States. It has now been shown that this virus is similar to maedi and visna disease in Iceland. In the neurological form of this sheep infection (i.e. visna), this slow virus infection causes widespread demyelination, somewhat similar to that seen in multiple sclerosis and amyotrophic lateral sclerosis. There is no suggestion that the visna virus causes any of these human diseases, but the phenomenon of the slow virus infection producing essentially the same large areas of demyelination as seen in the human demyelinating diseases provides a compelling experimental model for numerous investigations. It is of interest that our endemic sheep disease in Montana has been shown to be related, or identical with, the maedi-visna complex of Iceland.

Because of the occurrence of diseases of these types in wildlife, as well as in farm animals, a collaborative program was established with the Bureau of Sport Fisheries and Wildlife, U.S. Department of Interior. Facilities at the Patuxent Research Center, Laurel, Maryland, were provided and augmented by the Institute's construction of a temporary primate holding facility. The scope of the program initiated in 1962 included inoculation of several species of apes and smaller primates, and small experimental animals, such as mice, guinea pigs, hamsters, rabbits and birds. The program also included studies using tissue culture cell lines in an attempt to grow the viruses in these. Such experimentally inoculated hosts are being held for a period of five to ten years. The diseases under study are multiple sclerosis, amyotrophic lateral sclerosis, the amyotrophic lateral sclerosis-Parkinsonism dementia syndrome observed in Guamanians, encephalitis, hemorrhagic leucoencephalopathy, Schilder's disease, progressive multifocal leocoencephalopathy, epilepsy partialis continue, subacute sclerosing panencephalitis, Boeck's sarcoid, lupus erythematosus, and Burkitt's lymphoma, as well as kuru, scrapie, visna, Montana sheep disease, mink encephalopathy and many others.

Kuru and Creutzfeldt-Jakob disease are to date the only chronic neurological diseases of man which have been transmitted successfully to the animal host. Subacute sclerosing panencephalitis, caused by the measles virus, progressive multifocal leucoencephalopathy caused by a polyoma-like virus, a subacute encephalopathy caused by herpes simplex virus, and persistent congenital brain infections with rubella virus and cytomegalo virus, are the other chronic infections which have been recently demonstrated to have a virus etiology. A further disease causing progressive epilepsy and dementia, called epilepsy partialis continua, is rather certainly of similar etiology, but the virus is yet unidentified. In none of these diseases, however, do we yet have an animal model which permits study of the disease under experimental conditions, with an aim toward treatment, cure and prevention.

The recent progress in identifying the causative virus for a large group of chronic degenerative diseases of the nervous system now necessitates large animal holding facilities for long-term maintenance of experimental animals, including

apes and monkeys, in conditions of isolation and good health. The success thus far now makes it urgent that in vitro studies in tissue cultures, using immunological, electron microscopic and pathological methods be expanded, in order to establish the factors responsible for the long-term persistence of viruses in the human subject and this activation.

The NINDS study has been a focal point of nation-wide and world-wide interest in slow, latent and persistent virus infections, and the investigational methods that are being developed are being applied not only to neurological diseases, but to the whole matter of rheumatic diseases (arthritis and collagen diseases), to human cancer virus research, as well as to the major neurological problems of multiple sclerosis, amyotrophic lateral sclerosis, Parkinsonism, etc.

NEUROLOGICAL INFORMATION NETWORK

The Institute has developed a National Neurological Information Network to facilitate the prompt exchange of information within the medical and scientific community through the establishment of information centers in four universities having outstanding library facilities: Columbia University — Parkinsonism and Related Neurological Diseases; The Johns Hopkins University — Hearing, Speech and Disorders of Human Communication; University of California at Los Angeles — Basic Neuroscience; and Harvard University — Vision and Diseases of the Eye. (This latter center will be financed in 1970 from NEI funds).

The Network is coordinated by the Office of Program Analysis, NINDS, and operates in close collaboration with the National Library of Medicine. It is engaged in a review of scientific reports, indexing for the MEDLARS system, publication of bibliographies, special reviews, symposia, and a review of articles on topics of special interest.

This Network has now developed to the point where there is a steady output of special relating service bulletins in a variety of areas such as Parkinson's disease, sleep physiology, electroencephalographic literature, enzyme chemistry of the brain, and communications disorders. Some of the special reviews which have been produced are now the standard words on the subject. The Vision Information Data Bank is conputerized and will serve anyone who wants to rent a terminal and pay the line costs to search it. Indexing in the area of neurological diseases and in visual sciences is being done for the Index Medicus of the MEDLARS system of the National Library of Medicine. These special indexing thesauri are being examined and incorporated into the new augmented indexing system for the second generation MEDLARS. Major symposia have been held on various subjects, results of which have generated major research programs.

Training Activities

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	2	30,000	2	30,000	--	----
Other expenses.....		44,000		42,000		-2,000
Total.....	2	74,000	2	72,000	--	-2,000

TRAINING

This activity supports the training programs for professional, technical, administrative, and clerical personnel, including job-related training at both government and non-goverment facitilies.

The primary objective of the program is to train scientists in particular skills which are needed to carry on various Institute research projects. Long term training is provided by the establishment of agreements and contracts with appropriate schools or institutions.

Program plans provide for training in otolaryngology, neurology, and epidemiology.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	85	$ 950,000	85	$ 964,000	--	+$14,000
Other expenses.....	--	1,108,000	--	1,150,000	--	+ 42,000
Total.....	85	2,058,000	85	2,114,000	--	+ 56,000

EXTRAMURAL PROGRAMS

Within the extramural program office of this activity, all grants and awards, such as research grants, program project grants, training grants and fellowship awards are programmed, examined, processed and continually followed by the professional, administrative, and clerical staff. Formal reviews are performed by several organized and ad hoc bodies of non-governmental authorities in the health and science fields, including the National Advisory Council of Neurological Diseases and Stroke, training review committees and study sections of this Institute and Division of Research Grants, National Institutes of Health.

The magnitude of the managerial and review processes in terms of number of grants, dollar volume, and programming complexities are imposing greater demands in terms of data for and advice on programming. Two mechanisms are being resorted to more frequently: Advisory groups or task forces expert in critical fields and gradual introduction of greater sophistication and capabilities in the retrieval and analysis of data regarding grants and programming. Both these types of activities are funded out of the Review and Approval activity, and the latter is directly coordinated and interdigitated with activities of the program analysis function in the Office of the Director, NINDS. During 1969, steps are being taken to concentrate the major institute facilities for information and data storage and retrieval, and to design the facility so that it can be tied into central NIH computing activities for analytical studies in the future.

The total increase of $56,000 includes $14,000 for additional administrative needs of the extramural staff, $3,000 for annualization of the 1969 pay increase, and $39,000 for centrally furnished services of the "National Institutes of Health Management Fund."

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	29	$342,000	29	$342,000	--	$--
Other expenses	--	148,000	--	99,000	--	-49,000
Total	29	490,000	29	441,000	--	-49,000

This activity supports professional and administrative direction of the Institute's activities. The Office of the Director provides for the centralized supervision, coordination and review of these programs, as well as for the direction of the administrative functions of finance, personnel, supply, travel, space utilization and management analysis. The decrease of $49,000 is associated with the National Institutes of Health Management Fund.

New Positions Requested
Fiscal Year 1970

	Grade	No.	Annual Salary
Laboratory and Clinical Research			
Medical Officer	GS-14		$21,406
Secretary	GS-5		5,732
Clerk-Typist	GS-4		5,145
		(3)	32,283
Collaborative Research and Development			
Medical Officer	GS-15		23,734
Medical Officer	GS-13		19,206
		(2)	42,940
Total new positions, all activities		(5)	75,223

National Eye Institute

WITNESSES

DR. EDWARD F. MacNICHOL, JR., ACTING DIRECTOR, NATIONAL EYE INSTITUTE
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ELDON L. EAGLES, ASSISTANT DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ECKART WIPF, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
ROBERT L. SITHENS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	410	587	777
Other personnel compensation	20	21	28
Total personnel compensation	430	608	805
Personnel benefits: Civilian employees	30	35	58
Travel and transportation of persons	58	51	51
Transportation of things	14	12	12
Rent, communication, and utilities	39	34	34
Printing and reproduction	19	16	16
Other services	798	928	942
Supplies and materials	35	30	47
Equipment	47	41	41
Grants, subsidies, and contributions	19,696	20,485	23,772
Total obligations	21,166	22,240	25,778

PERSONNEL SUMMARY

Total number of permanent positions	61	63	78
Full-time equivalent of other positions	5	5	6
Average number of all employees	60	60	76
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	14,086	16,206	19,660
(b) Fellowships	354	676	650
(c) Training	2,703	3,603	3,462
Total, grants	17,143	20,485	23,772
2. Direct operations:			
(a) Laboratory and clinical research	610	737	754
(b) Collaborative research and development	168	349	349
(c) Biometry, epidemiology, and field studies	267	303	317
(d) Review and approval of grants	366	366	466
(e) Program direction			120
Total, direct operations	1,411	1,755	2,006
Total program costs, funded [1]	18,554	22,240	25,778
Change in selected resources [2]	2,612		
Total obligations	21,166	22,240	25,778
Financing:			
Comparative transfer from other accounts	−21,166	−22,240	
Budget authority (appropriation)			25,778
Relation of obligations to outlays:			
Obligations incurred, net			25,778
Obligated balance, end of year			−13,613
Outlays			12,165

[1] Includes capital outlay as follows: 1968, $77,000; 1969, $41,000; 1970, $41,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $591,000; 1968, $3,203,000; 1969 $3,203,000; 1970, $3,203,000.

Mr. NATCHER. Dr. MacNichol, if you will change hats you can keep your seat and take up with us the request for the National Eye Institute.

Dr. MACNICHOL. I have an opening statement, sir.

Mr. NATCHER. We will be glad to hear from you.

GENERAL STATEMENT

Dr. MACNICHOL. Mr. Chairman and members of the committee, it is my privilege to appear before you in behalf of the National Eye Institute which Congress authorized the Secretary of Health, Education, and Welfare to create last August.

ESTABLISHING A NEW INSTITUTE

The administration of a separate institute for eye research of course requires both additional funds and additional personnel beyond those required for eye research as it has been conducted as part of the National Institute of Neurological Diseases and Blindness. Since these were not available during the fiscal year 1969, Secretary Cohen decided that eye research activities should continue to be carried forward as part of the Neurology Institute until sufficient additional funds and personnel were authorized.

The President's budget for 1970 requests the necessary additional resources to make a separate Eye Institute a reality. As Director of the National Institute of Neurological Diseases and Stroke, and Acting

Director of the National Eye Institute, I have therefore continued to administer eye research under NINDS while making plans for launching the new Institute as soon as the necessary resources are made available.

A National Advisory Council has been selected, invitations have been issued, and all have been accepted. An orientation and planning session has been scheduled during the first week of April; and the first official meeting to review applications will be held in June.

Much time has been spent in an effort to find a Director for the Eye Institute. The various ophthalmology groups who were in the forefront urging a separate Institute have been asked to help in this recruitment. We expect that a Director will soon be found and that the new Institute will be ready to operate by July 1.

As soon as funds are available for the administrative operation of the Eye Institute, the extramural vision research and training programs will be transferred from NINDS. Various intramural and collaborative programs will remain with NINDS for some time and then be transferred gradually or operated jointly, depending upon the needs of each specific program.

THE CHALLENGE OF EYE RESEARCH

I know of no greater challenge than the research relating to the eye. So much is still unknown about its normal functioning and many of the disease processes affecting it are still surrounded in mystery. Much new knowledge is needed concerning the normal structure and function of the eye as well as the disease processes affecting it before the prevention and treatment of eye disease can be significantly advanced.

If a serious eye disorder suddenly robs a person of his vision, long periods of rehabilitation are necessary before some semblance of normal life is again possible. Even then a blind person, deprived of his most important sense, cannot drive a car, or easily perform such simple activities of daily life as finding his way alone in a building or street, pursue his former occupation except under very unusual circumstances, or participate in most kinds of recreation. The development of devices and techniques to allow the visually handicapped to live more normal and independent lives is a matter of the utmost importance.

RESEARCH POTENTIALS

Of particular interest to this committee, I am sure, is the present status of these programs and their research potential. One area which is certain to receive early consideration is diabetic retinopathy. In patients who have had diabetes for 15 years, approximately 70 percent show aneurysms in the capillaries supplying blood to the retina. Comparatively little is known of the disease process of diabetic retinopathy which causes damage and often blindness. Various types of present therapy slow down the progress of the damage but the results are most discouraging. Therefore, special efforts are being made to stimulate research and to search for new approaches to the problem.

Another area deserving much more attention relates to retrolental fibroplasia—RLF—a disorder which develops in some newborn premature infants who must be given oxygen to overcome respiratory

distress. An excess of oxygen results in this serious eye disorder causing blindness.

In the early fifties, RLF was a leading cause of blindness in the United States. Through a collaborative study supported by NINDS, it was discovered that the disorder was caused by an excess of oxygen. Hospitals throughout the Nation were notified and in a very short time the disease almost disappeared. Recently, oxygen therapy has emerged as an effective treatment for premature newborns suffering from the respiratory distress problem called hyaline membrane disease. In such cases the physician now faces the difficult task of preventing the infant from suffocating and at the same time preventing RLF and blindness.

An Institute grantee has found that frequent sampling of arterial blood oxygen can provide a means of avoiding the dangerous oxygen levels. However, the precise arterial oxygen levels that cause retinal damage are not known; and few hospitals are equipped with either the instruments or the trained personnel to monitor the oxygen levels. New tools must be developed which will aid the physician in maintaining the delicate balance between enough oxygen to preserve life and too much oxygen which will cause blindness.

A major cause of blindness in the United States is glaucoma. It is estimated that 2 percent of the population over 40 years of age have the disease and many do not know it, since the disease is usually symptomless in the early stages. Much progress has been made in identifying and treating the disease. One of the encouraging new avenues of attack has been opened by recent studies of the change in intraocular pressure that occurs when compounds related to cortisone are applied to the eye. By this method, it may be possible to identify the persons who have a genetic predisposition to the disease many years before the disease develops. The Institute is presently engaged in a directed research project using this approach in which the responses of identical twins are compared.

Research has greatly improved surgical treatment for retinal detachments but it is still not possible to repair many of the larger ones. One of the most promising innovations of the past year was the use by grantees of injected air inflatable balloons, and other devices in freeing adhesions and treating these more extensive detachments.

One of the causes of uveitis, which has been particularly resistant to therapy, is toxoplasmosis. Institute grantees were successful last year in using lasers to create scar tissue around the site of the infection and thus to seal it off. Recurrences of the disease were much fewer than with the best previous available treatments.

Among the new diagnostic techniques under study, one which appears to hold great promise is ultrasound. It has been found useful in locating tumors, retinal detachments, and foreign bodies in the eye when cataracts and corneal scars prevent accurate examination of the eye by ordinary means. It carries no radiation hazard, and can be used repeatedly without harm or discomfort to the patient.

In no other area are artificial aids more greatly needed than for the blind. Recent research has provided data regarding the way information is transmitted from the retina to the brain. This research indicates that it may be possible to construct an apparatus that will provide for long-continued direct contact between an array of external light-

sensitive devices and the nervous system; thus bypassing the eye and feeding a crude sort of visual information directly to the brain. Recent reports have shown that such direct stimulation of the brain is possible; but much remains to be done before any practical application can evolve. The difficulties are great, but the importance of the successful development of such devices is obvious.

RESOURCES FOR RESEARCH

As the new Institute develops its program, it will be building on the many resources developed by NINDS over the years. These will include an outstanding intramural research branch in ophthalmology, nine clinical research centers for blindness and eye disorders, 14 outpatient clinical research units, a model reporting area for blindness in which 16 States are participating, a well developed ophthalmological epidemiology program, and a Vision Information Center. Results of a survey of disorders of vision conducted during the past 2 years by a subcommittee of the NINDS Council are now available. Some 250 of the Nation's leading scientists have cooperated in this report of research potentials, gap areas, and special needs.

The new Institute will also be relying on a pool of highly qualified teachers and investigators trained under NINDS supported programs. Some 4,000 persons trained in investigative ophthalmology and the related visual sciences from 1953 to 1968 are making a tremendous contribution, but many more are needed. This past year over 300 advanced students benefited from the various vision training programs supported by the Institute. A continuation of this support is necessary in order to continue to meet the demand for clinical and laboratory scientists prepared to be investigators and teachers in the visual sciences.

The budget request of $25,778,000 is $3,538,000 more than the fiscal year 1969 estimated obligations; $3,454,000 of the increase is for research grants and $251,000 is for direct operations. The fellowship and training grant programs are $167,000 less than the 1969 estimate.

I shall be happy to answer any questions.

Mr. NATCHER. Thank you, Doctor.

SPECIAL REPORT ON BLINDNESS

Dr. MACNICHOL. I also have a special report on vision and its disorders if you would like a copy for your information or for the record.

Mr. NATCHER. We will place that in the record.

(The statement follows:)

INTRODUCTION

Visual impairment and blindness constitute major health, educational, and economic problems. The Department of Health, Education, and Welfare has instituted a broad range of programs to cope with the many types of problems presented. These include programs of education, vocational rehabilitation, and income maintenance which directly assist the visually afflicted; programs to train the health professions and associated personnel who must provide required care; programs to improve the quality and delivery of eye care service; and the long-term programs of medical research and the training of research scientists.

Among all of these departmental efforts, the ones that have probed most deeply into the fundamental questions of cause and cure and which provide hope of ultimate prevention and control are the research and training programs which have been conducted under the National Institute of Neurological Diseases and Blindness, and hereafter will be conducted largely under the National Eye Institute, authorized by Congress in August of this past year.

Visual disability and blindness already can be reduced significantly by early detection and treatment. However, fundamental knowledge is still lacking in the understanding of causes and mechanisms of many blinding diseases. Therefore, the Institute supports a broad basic research program together with clinical research. Since not only the eye but the nerve pathways and the brain are necessary for vision, basic neurological research is involved. Also considered must be the systemtic disorders that may involve the eye, such as diabetes, disorders of the blood vessels, and various diseases of the brain and central nervous system.

The Institute's program includes research at its laboratories and the Clinical Center at Bethesda, Md., a collaborative and field research program; research grants, fellowships, and traineeships to individual scientists in academic institutions throughout the country; and training grants to aid universities and other centers in educating more ophthalmologists and research scientists.

In addition to individual research projects, the Institute supported 9 multidisciplinary research centers in vision and 14 outpatient research centers; a model reporting project in blindness in 16 States; and various collaborative and field projects relating to vision. These vision programs are currently operating at a level of $21 million.

Many of the Institute's vision programs relate to the major causes of blindness: cataract, glaucoma, retinal disorders, disorders of the optic nerve, vascular disorders, uveitis, infections, myopia, retrolental fibroplasia, neoplasms, and accidents, injuries, and poisonings.

PROGRAM DEVELOPMENTS

A permanent Subcommittee on Vision and Its Disorders, appointed by the National Advisory Neurological Diseases and Blindness Council, has assisted the Institute in reviewing and planning vision research and training. It has conducted a continuing assessment of the status of knowledge in eye research and training, and in the identification of problem areas and special needs. A report of this subcommittee, including recommendations, developed over a 2-year period with the help of 250 of the Nation's leading scientists was published shortly before the beginning of the year. It has served as an important guideline for research efforts, particularly focusing attention on areas requiring special and immediate investigation.

Task forces, such as the ones on refractive anomalies and ocular pharmacology, served to review current research, supervise programs for the dissemination of scientific information, and organize programs of directed research and development. An ad hoc committee on visual rehabilitation made a number of recommendations including the establishment of a new review committee for rehabilitation of the blind. Plans were made also for the establishment of a diabetic retinopathy planning committee.

Information network

A Vision Information Center (VIC), established in 1966 under a contract with Harvard University served as the focal point for the collection, storage, retrieval, and dissemination of information relating to vision, eye diseases, and blindness. The center is located in the Francis A. Countway Library of Medicine at the Harvard Medical School.

The VIC is part of the national information network of specialized centers for neurological information. Its scope embraces those areas of vision and diseases of the eye which are the province of this Institute. These include: (1) All clinical aspects of ophthalmology and optometry, including eye manifestations of systemic diseases, and (2) physiological, biological, biochemical and biophysical research related to the eye and vision. The VIC scans the literature in its field for depth indexing and entry into a computer-assisted retrieval system. This Center offers literature searches on eye diseases and vision, a listing of periodical publications, or abstracting of newly-published journal articles, and computer-assisted instructional services.

Vision research centers

In addition to the program of regular research projects, support is being provided for nine clinical research centers for blindness and eye disorders, each concentrating on special clinical problems such as glaucoma, cataract, retinal disorders, corneal disease, infections of the eye, and disturbances of eye movements. Even though highly specialized, each centr maintains a broad approach to the overall problem of blindness. For example, as a basis for approaching the problem of the sensory and perceptual disorders, several centers are developing needed information about fundamental mechanisms by which light impulses are converted to nervous energy and transmitted to the brain for interpretation.

Outpatient clinical research centers

The program of eye outpatient clinical research grants, initiated on a pilot basis in 1967 and 1968, has been successful and currently includes support for 14 units. These programs have made available outpatient populations with eye disorders for research study. They provide the environment to carry out clinical and epidemiological studies, drug evaluations, developmental studies, long-term followup, and other investigations of ocular disorders which affect only humans and cannot be duplicated in animals. They offer an opportunity for continuing research which has reached its limits in the laboratory or in animal trials.

Model reporting area

Through its biometric branch, the Institute maintains a model reporting area for blindness statistics (MRA). Its purpose is to make available better blindness statistics and to stimulate blindness research. Ultimately the goal is a national reporting system for all States which will standardize pertinent information on severe visual impairment cases.

MRA provides uniform data by State on each blind person's visual acuity, and the blinding condition and its cause. A program of evaluation has been undertaken to assist in the future direction of this program. Almost one-third of the U.S. population is now covered. Currently, member agencies represent the following 16 States: Connecticut, Georgia, Kansas, Louisiana, Massachusetts, New Hampshire, New York, North Carolina, New Mexico, Oregon, Rhode Island, South Dakota, Utah, Vermont, Virginia, and New Jersey.

The training program

The training grants program of the Institute provides support to institutions for establishing, improving, or expanding training programs to prepare clinical and laboratory scientists for careers in research and academic medicine in the biomedical and medical disciplines relating to research on the eye. The scientists trained under these programs can be expected to assume the responsibility for future advances in knowledge leading to the prevention and successful treatment of eye disorders and for training of the next generations of eye scientists. These programs have been growing steadily in number and quality, thus beginning to increase the pool of well-trained scientists available to fill the many vacant positions of leadership as researchers and teachers.

Research fellowship programs are encouraging advanced, specialized research training by providing the financial support necessary for clinical and laboratory scientists to become qualified for research on problems relating to diseases of the eye. The fellowship programs are a most effective means of providing this training and of encouraging individuals to enter research careers. Postdoctoral fellowships provide financial support during the 3 years of research training immediately following the doctoral degree. Career development awards assure support over 5- to 8-year periods for selected scientists who have completed formal research training, and are by this means provided with an opportunity to become established as independent investigators in a chosen line of research.

This year, a contract was entered into with the University of Minnesota for a manpower study in the visual sciences.

NINDB is supporting a training program at the University of Puerto Rico School of Medicine. This is the Western Hemisphere's first intensive course in the basic sciences for young Latin American doctors in the field of ophthalmology. The program is being conducted in cooperation with Columbia University, New York.

Development and use of the cryoprobe for surgery has advanced far in the past year. This has facilitated the extraction of lenses in cataract surgery as

well as the production of pigment in retinal detachment work. New instruments are aiding in cryo (cold) extraction, making the surgical procedure easier.

Glaucoma

Glaucoma, which causes a great deal of avoidable blindness, results from lack of control of fluid pressure within the globe of the eye. A major emphasis of Institute glaucoma research has been toward a better understanding of the processes for maintaining proper pressure within the eye, including the early use of medications that save vision by correcting pressure. Therefore, Institute researchers have studied the effects of many drugs on eye pressure and have developed diagnostic tests of intraocular pressure abnormalities.

Epidemiologists are defining the characteristics of individuals for whom special vigilance is required because they are especially prone to develop glaucoma. Efforts have been made to improve techniques for detection and testing which are highly consistent and accurate. Advances have been made in understanding the basic dynamics of introaocular pressure, in applicable diagnostic techniques, in pressure variations and aqueous humor drainage and formation, and in understanding the activity in those parts of the brain believed to serve a pressure-regulating function.

This year, the genetic determination of ocular pressure, aqueous outflow, and open-angle glaucoma by multifactorial inheritance has been substantiated through various studies. When investigators cannulated (inserted a tube within) the optic nerve to measure the tissue pressure and to determine its relationship to intraocular pressure, they found optic nerve pressure to be directly affected by cerebral spinal fluid (CSF) pressure. (Tissue pressure in the anterior segment of the optic nerve posterior to lamina cribosa was found, however, to be independent of acute changes in intraocular pressure). The investigators demonstrated that elevated intraocular pressure compromises the small vessel structure of the distal optic nerve segment and hypothesize that this accounts for the glaucomatous disk changes in man. Extensive clinical testing and elevation of drugs in relation to glaucoma were made at several medical schools in the expectation that they might help in treating glaucoma or might yield information fundamental to understanding glaucoma. Drugs currently being used in this treatment were tested for their safety. A valuable contribution was made this report year in the systemic studies of the pressure in the episcleral vein with the aid of a newly designed instrument, a modified force displacement transducer with a lucite cone applantation tip.

Analysis of tonometry data, with and without drugs and before and after drugs, were made, and relationships between aqueous inflow, intraocular pressure, and venous blood pressure in the eye were interpreted. Design and analysis of a study of correlations between eye pressure differences (differences between blood pressure and intraocular pressure) and aqueous inflow took place. Findings made through three separate communitywide surveys suggested the need for further investigation of tonometric screening for glaucoma. Other findings suggested that the time of measurement can influence comparability of tonometry data collected for epidemiological investigation.

Corneal disorders

Corneal scarring, caused by injury and infection, is responsible for about 10 percent of the blindness in this country. Research has led to effective treatment for one common infection, herpes simplex, before scarring occurs. Other investigators have improved methods of freezing and dehydrating corneas for transplant when this is necessary to restore vision. Institute studies have concentrated particularly on effective drugs which can be used to fight inflammation without harmful side effects; microsurgery; better understanding of mechanisms of graft rejection; improving techniques for tissue transplants; use of synthetic substances which may be used to restore sight to persons blinded by severe cases of clouded or damaged corneas. New approaches to the broader study of antiviral drugs have been made. Increased understanding of the mechanisms by which antiviral drugs accomplish their task may lead to much improved treatment of systemic virus diseases as well as eye disorders.

New knowledge gained through a recent animal study of the tensile strength of corneal wounds should aid in the management of corneal wounds by both drugs and surgery. The study provided a theoretical basis for the clinical use of flaps (tissue grafts) in corneal ulcers, with frequent beneficial results in restoration of found healing. Scientists have demonstrated that it is possible to remove

the epithelium and replace it with a membrane of plastic material having a smooth optical surface. Thus a contact lens may be bonded directly to a damaged cornea. The final evolution of favorable results necessitates long-term observation.

Reasons for graft failures were explored in a series of studies and new recommendations offered. The effectiveness of systemic steroid therapy in suppressing rejection of corneal grafts during the period of drug administration was successfully demonstrated. Prolonged followup after termination of drug therapy indicated that systemic corticosteroids are capable of inducing a state of tolerance or "graft adaptation" in a high percentage of recipients. Use was made in successful experiments of an artificial endothelium made of silicone rubber to be used in corneal grafts. Drs. David Paton and Miguel Martinez, Wilmer Institute, Johns Hopkins University and Hospital, has undertaken a project designed to develop improved surgical and eye bank techniques. Doctors are studying what they call "prefabricated corneal grafts"—grafts which are precut, presutured, and preserved until used in the operating room, and "composite grafts" made up of corneal tissue with a synthetic membrane bonded to the posterior surface. Such procedures, still in early stages of development, may be expected to help in solving the problem of too few donor graft materials for transplantation.

Uveitis

Uveitis is an inflammation of the iris, ciliary body and choroid in which the cause is often unknown. Institute scientists were among the first to recognize the parasitic infection, toxoplasmosis, as a major cause. This year's research has revealed that the use of antimetabolites, such as methotrexate and cytoxan, may be beneficial in the management of some types of uveitis even after steroid treatment has become ineffective. The beneficial value of these immunosuppressive drugs in the treatment of one form of uveitis—sympathetic ophthalmia—was found due more to its anti-inflammatory properties than to the immunosuppressive action. A final evaluation of the usefulness of these properties particularly, in combination with steroids, must be postponed until the results of prolonged therapy with these drugs become available.

Recurrence of toxoplasmosis, which accounts for 30 to 50 percent of all posterior uveitis, was beneficially treated with employment of laser energy to create scar tissue around the lesions of the retina surrounding the initial focus of infection.

Tumors

Collection of data for study of malignant tumors of the eye among residents of the United States has been completed. These data, based on the review of death certificates, provide the first description of mortality in the United States due to specific ocular tumors. These data will be analyzed and reported in the near future.

Far more sophisticated methods of diagnosis and detection of malignant tumors of the eye are urgently needed. Research has concentrated on a search for the origin of eye tumors and early clinical detection of malignant tumors. NINDB research has revealed some promising new methods, using fluorescence angiography and radioactive tracers. These new techniques appear to hold promise. Successful malignant transformation of ocular tissue with oncogenic DNA viruses in vitro was accomplished for the first time in a joint effort with investigators from the National Cancer Institute. Ultrasonography of the orbit has been used successfully to locate intraorbital tumors and Institute grantees have found the method easy to perform and useful in the routine investigation of unilateral exophthalmos.

Cryosurgery was used successfully by Dr. Harvey Lincoff to destroy tumors growing on the inner surface of the eye. Treatment of malignant melanoma—generally regarded as radiation resistant—with a combination of cobalt 60 and freezing, is being tried. The combined technique may be of value in managing a number of malignant intraocular tumors formerly treatable only by removing the eye.

Retinitis pigmentosa

Electrophysiological and psychophysical examination of patients with various forms of retinal degeneration were conducted on the offspring of families afflicted by retinitis pigmentosa before the characteristic features of the disease had developed.With the Ganzfeld technique and balanced light stimulation, deficits of the rod and cone components in the electroretinogram could be differentiated and correlated with different genetic types of the disease entity. Family studies were conducted in patients with dominant retinitis pigmentosa, sex-linked retini-

tis pigmentosa, a recessive cone-rod degeneration, dominant retinitis pigmentosa with incomplete penetrance and dominant cone degeneration. The combination of the tests contributed to the understanding of underlying defects in retinal degenerations. Genetic studies of early or atypical cases of retinitis pigmentosa furthered the clarification of various types and allowed a limited prognostic evaluation.

Twin registry for eye examinations

Eye examinations, perinatal medical histories, zygosity determinations, and various anthropometric measurements were completed on over 450 pairs of twins. These studies of identical and nonidentical twins will provide important information regarding the role of inheritance in glaucoma, myopia, and other eye disorders.

Oculo-motor problems

Electromyography (EMG) is amplifying our understanding of the oculomotor involvement in brainstem lesions. Findings support the theory that inhibitory and excitatory influences on the oculo-motor nuclei may travel along different pathways. Before electromyography, descriptions of oculo-motor involvement in the brainstem lesions were confined to clinical observations of eye movements.

Scientific data on how the eye focuses, provided through the ultrasonographic technique, have modified a century-old theory by demonstrating that it is not the lens alone, as had previously been supposed, but also the globe that changes shape as the eye shifts focus. Through ultrasonography, it may now be possible, in a matter of minutes, to determine the degree of myopia in a child.

Myopia

Advances have been made in ability to correct errors of refraction, such as myopia. Broadly based epidemiological and genetic studies are under way to assist in solving the problems of refractive anomalies. Theories have been confirmed that myopia, an inherited condition, may be influenced by environmental factors.

Color vision

Just as our understanding of psychophysical phenomena in the visual process has come from a knowledge of electrical events and their relationship in different areas in the visual system, so may it be stated for studies of the visual pigments. The nature of the pigments, their change during various conditions, and their relationship to other known properties of the eye all contribute to a basic understanding of the psychophysics of vision. The use of various disciplines within the province of ophthalmology is especially marked in this area.

Visual physiology

Scientists have evidence that the ability to see things in three dimensions exists because objects at different distances from the eye excite different neurons in the brain.

Animal trials are now in progress that will soon be given large-scale human testing. Some scientists now believe that hyaluronic acid, a giant molecule common to many tissues of the body, may hold the key to such eye diseases as retinal detachment, vitreous opacities, and hemorrhages, and to such joint problems as rheumatoid arthritis and osteoarthrosis.

Examination of the physiological responses of the visual system to light has been one of the major interests of physiologists in the past year. The complex responses and interactions of various areas of the visual system is far from being resolved, but an understanding of these complexities is being achieved. Nowhere is this more apparent than in studies of the receptive fields of the retina and higher pathways.

A new method of extracting rhodopsin from the retina was discovered. This may well prove to be a major assist to workers on the chemistry of visual processes.

Drugs

Medrysone, a new synthetic corticosteroid, was shown to be an effective anti-inflammatory agent for the eyes when tested through comparative studies. Useful in the treatment of certain forms of conjunctivitis, it exhibited no propensity to raise the intraocular pressure even in patients known to respond to other steroids with pressure rise, or in patients with glaucoma. Prolonged treatment with Medrysone kept symptoms under control and produced no outward side effects.

Herpes simplex

The rate of recurrence of herpes simplex keratitis in man is 25 percent within 2 years. Patients with more than one attack have a 43 percent chance of having additional episodes within 2 years. Chronic infection of the conjunctiva and lacrimal gland with herpes simplex virus is now believed to be a probable source of virus for recurrent corneal infection. It was an Institute grantee who just a few years ago discovered the first effective treatment for the herpes virus—IDU—and later extended his work to testing other improved drugs for the same purpose. This year, evidence that interferon stimulation can cure an acute viral eye infection in rabbits (NIAID project) has strengthened the hope that interferon inducers may also be useful in treating viral infections in man.

Trachoma

Research on an eye ailment transmitted venereally may cause a reevaluation of mass treatment of trachoma, which is a leading cause of blindness in underdeveloped countries. The presence of the agent of the disease-inclusion conjunctivitis has been confirmed in both the eyes of the children and genital tracts of the mothers. Local treatment with antibiotics can suppress but not eradicate or prevent recurrence, but oral treatment with sulfa drugs usually eliminates both symptoms and the disease agent. Since the causative agent is similar to and perhaps identical with that causing trachoma, investigators believe that trachoma, too, may require treatment with systemic or chemotherapeutic agents rather than the topical drugs now employed.

Fluorescein angiography

Technical refinements have been accomplished in methods of fluorescein angiography. Its use is becoming increasingly widespread in the investigation of both clinical and research problems. Improvements permit not only wider application of the method but also more detailed morphological and hemodynamic (blood flow) studies, and greater accuracy in interpretation of results.

Retrolental fibroplasia

At one time retrolental fibroplasia (RLF) was the leading cause of blindness in the United States. Then it was discovered through a study supported by NINDB that the disorder was due to exposing premature infants to oxygen in excess of the usual atmospheric conditions. With this knowledge, the incidence of RLF was dramatically reduced until it was nearly an unknown disease in the United States. Recently, however, a new problem has arisen leading to a resurgence because of the treatment of the respiratory distress syndrome which may cause the newborn to suffocate. The usual treatment for this syndrome is an increase in the incubator oxygen concentration. Thus the physician faces the difficult task of preventing the infant from suffocating and at the same time preventing RLF and blindness.

Dr. Arnall Patz, Wilmer Institute, Johns Hopkins University and Hospital, reported that frequent sampling of arterial blood-oxygen could provide a means of avoiding potentially retinotoxic oxygen levels. Two serious difficulties, the investigator pointed out, are (1) the fact that the precise arterial oxygen levels that cause retinal damage are not known, and (2) few hospitals are equipped to monitor arterial oxygen tensions, for this requires expensive instrumentation and the services of highly skilled pediatricians and specially trained technicians. A standard must be established which will provide sufficient oxygen for metabolism but yet not stimulate retinal vessel proliferation. New tools must be developed which will aid the physician in maintaining this delicate standard in the premature. The approaches to this highly important problem are under evaluation and support is being planned for a series of workshops and for in-depth studies of the problem, then for development and evaluation of the required clinical tools.

Meanwhile, the oxygen treatment appears necessary until relief of the life-destroying respiratory distress syndrome becomes more adequately documented.

Effect of light on the retina

A series of electron microscopic studies of rat retinas has served to establish the pathogenetic mechanisms whereby exposure to very bright light (750 foot-candles) damages the retina. Scientists have found that the rods and cones have regenerative capability if not too extensively damaged by continuous exposure to light. This regeneration capability is a major step forward in retinal pathophysiology.

Retinal degeneration

Macular degeneration may result from hereditary disturbances, trauma acquired lesions, lesions secondary to other retinal abnormalities, or senile changes. Treatment is most successful in the acquired secondary type of macular lesions. New study techniques developed at several university hospitals disclose that some of these lesions are due to breaks or leaks in Bruch's membrane. Some of these may be sealed by using a photocoagulator or laser beam. New laboratory clues suggest that a person with a problem of hereditary macular degeneration should avoid prolonged exposure to bright light.

Retinal detachment

Retinal detachment, a cause of blindness, is a separation of the retina from the underlying structure. Extensive studies relating to the cause as well as improved methods of treatment are underway. A successful innovation of the past year in retinal surgery was the use of inflatable balloons, air, and other products in vitreous surgery. These were used in an attempt to free adhesions so that the vitreous and the retina may be restored to their usual positions. Liquid silicone sometimes has been used successfully in rare cases where the retina has become "glued" in the detached position.

Diabetic retinopathy

Diabetic retinopathy is a degenerative disorder of the retina which occurs as a complication of diabetes. The incidence of retinopathy in diabetic patients increased from less than 1 percent in 1930 to over 18 percent today. This increase occurred as insulin and other modern medication has lengthened the life for the diabetic patient. Vascular complications of the disease develop over a period of time and as a result are more common in the older patient.

Institute-supported research is evaluating present treatment and attempting to discover the mechanism of the disorder. Investigators have found a specific and highly significant loss of pericytes in diabetes, regardless of age. Loss of these intramural cells is associated with an increase in ghost cells, shunt vessels, and the number of microaneurisms (ballooning of small blood vessels). A simple, semiquantitative method of measuring tear glucose which provides the practicing physician with a new, easy, practical, and readily available procedure for screening patients for diabetes, and a rapid, indirect measurement of excess of sugar in the blood, was developed. The effectiveness of currently available treatment, notably photocoagulation, was probed in a series of studies which examined the long-term visual programs for this condition and analyzed the most often used forms of therapy.

A symposium of diabetic retinopathy was held in October at which a number of the controversial views on treatment were discussed, particularly hypophysectomy as opposed to coagulation. It was agreed that rigid controls on procedures should be established. A future conference has been planned to delve deeper into these problems.

Laser beam

A study of the possible injury to the eye resulting from scleral transmission of laser light was concluded with the evaluation of the extent and type of lesions produced in animal eyes.

Ultrasonography

Although ultrasonic energy has been used for diagnosis for only a few years, it has already proved its worth. It is an aid to diagnosing eye disorders that cannot be examined with ordinary instruments. It carries no radiation hazard, and can be used repeatedly without harm or discomfort to the patient. During the past year, experimental work has been performed in the field of ultrasonography related to breaking the lens material so that it can be successfully aspirated. The technique appears to hold promise but also some risks. So far the principle application of ultrasound has been for diagnosis. It is useful in locating tumors, retinal detachments, and foreign bodies in the eye, when cataracts and corneal scars prevent accurate examination of the eyes by ordinary means. Distance within the eye can be measured electronically to within 0.05 mm. of tissue thickness.

Optic nerve and visual pathway

New methods of measuring activity of the visual centers of the brain by means of electroencephalography are yielding valuable data concerning the human visual process. Both the electrically evoked response (EER) and visually

evoked response (VER) have proved useful in studying the eye. When two methods of electrical stimulation of the retina were compared, investigators found that small stimuli moving across the visual fields are more efficient in producing VER responses to light.

Microelectrode recorded data from the visual cortex of animals has indicated that diffuse light stimulation of the retina is less efficient than target movement across the retinal fields. In normal vision, even if objects seen are perfectly still, the eye itself moves by a series of quick flicks and drifts. Dr. Christopher Evans of Middlesex, England, uses stabilized images on the retina to study what happens to the afterimage. More has been learned about the rules of the fragmentation process which occurs when pattern perception breaks down.

Model of the eye

The development of a more accurate mathematical model of the eye, using high speed computation, opens the door to a better understanding of its optical performance. This has a great potential for the improvement not only of diagnostic and therapeutic instruments but also of optical aids to the visually handicapped.

Mechanical aids to the blind

In no other area are mechanical aids more greatly needed nor are the long-range possibilities more promising than for the blind. Recent fundamental research has provided extensive data regarding the nature of the coded signals whereby information is transmitted from the retina to the brain. Implanted electrodes have been used extensively in animals and man. A crucial need, however, is for a precisely located array of inert stimulating devices which will provide for long-continued direct contact between an external light-sensitive device and the nervous system. To greatly oversimplify, a blind person might wear or carry a miniature television camera which would transmit impulses to the brain which will be translated into vision. The first attempts, of course, will be crude. However, even the detection of rather large differences between light and darkness would be a great improvement over total blindness.

Feeding electronic information directly into the brain or optic nerve at the present time offers some serious problems. These might be temporarily circumvented by using the chest, the abdomen, or the inside of the arm as the sensory receptor. That is, a blind person might learn to use a small device with many tiny "fingers" on or near the skin so the "fingers" could be actuated by a light sensitive device. The patient could learn to interpret the pressure patterns in terms of the objects before him. The ultimate answer, of course, is the direct input of signals into the optic nerve.

The importance of the successful development of such devices is obvious. The difficulties are unusually great but some initial progress is being made though accomplishment is far off.

Television ophthalmoscopy

Observations of the visible blood vessels and other structures in the fundus of the eye have a great value in studies of cerebral arteriosclerosis and degenerative disorders of the optic nerve and the retina. For such studies to be meaningful, precise methods of evaluating and measuring these vessels must be developed. The use of television scanning devices and advanced television technology presents a promising avenue of research and development. In collaboration with the National Center for Health Services Research and Development of the Health Services and Mental Health Administration, a workable television ophthalmoscope and techniques for its employment are being developed. A contract is now in effect to undertake an analysis of the relative merits and projects costs of specific applications of television ophthalmoscopy.

Ophthalmic survey of two defined groups in the South Pacific isles

Institute surveys of two defined groups in the South Pacific isles provided insight into the ocular status of people unexposed to Western civilization. Marked differences were found in the prevalence of disorders common to our society. Such conditions as hypertension and diabetes mellitus were virtually nonexistent. Even in the older subjects, there was little retinal vascular disease, no elevated determinations of intraocular tension, and almost no significant refractive error. In particular, no myopia was found, which raises the question regarding what portion of this type of refractive error might be due to environmental causes.

SUMMARY

As can be seen from this brief review of recent activities, the causes of blindness are many and research in vision and its disorders involves lengthy, complex study. Achievements take time, but there are many hopeful elements, and a number of great strides in research have been made within the past few years. Most encouraging is the ever-increasing interest of the public in improvement in research training, betterment of facilities for research, an increase in well trained investigators to develop the field, and the mounting number of research projects which bring the probability of good sight for all closer to reality.

NINDS research support for blindness

1966	$12,454,000
1967	15,808,000
1968	21,166,000
1969	22,240,000
1970	25,778,000

INCREASE FOR EYE INSTITUTE COMPARED WITH OTHER INSTITUTES

Mr. NATCHER. Doctor, the only very significant change in the budget for 1970, compared with the level of funding for these activities in 1969, is an increase of $3,454,000 for research grants. This is an increase of over 20 percent, considerably more than any other institute.

Dr. MacNichol, perhaps I had better direct this question to Dr. Marston. I assume this decision was his responsibility more than yours.

Dr. Marston, why was this Institute favored over the others to this extent?

Dr. MARSTON. Mr. Natcher, this is a very important question. As you know, the National Institutes of Health did not recommend the establishment of an eye institute, particularly during a time of fiscal constraints and constraints on personnel.

However, we feel very strongly that now that we have an Eye Institute we should have the resources that make it possible to establish a very excellent Eye Institute, and in order to do this, one is going to have to put in additional resources. For this reason we do have in the 1970 budget, as our recommendation, an increase in the dollars for research. Without this I think we would have great difficulty in recruiting the type of staff that is necessary to launch the Institute in the form Congress expected.

CREATION OF NEW INSTITUTES

Mr. NATCHER. You said a few days ago when you appeared before us that there was considerable opposition within the executive branch to more institutes and you, personally, were opposed.

Dr. MARSTON. Yes, sir.

Mr. NATCHER. Dr. Marston, if new institutes are to be favored to the extent of the increase I just referred to, it seems to me that this would encourage the proponents of more institutes to redouble their efforts. Am I right or wrong?

Dr. MARSTON. I think you are absolutely right, Mr. Natcher. It is clear that in our minds the priority goes to the point that if you are going to have an institute that you put in the resources to make it the type of institute that one needs. My staff and I have taken the position that we will work very hard to make this a very good Institute despite the fact that the better the Institute is the more it proves

that we were wrong, I guess, in our recommendation that it should not be established in the first place.

I think it is more important on this to maintain the quality of the Institute and the nature of the Institute than it is to get off into these other areas of what the impact would have on future discussions. I think we would be completely lost if we launch an institute which is not first rate.

Mrs. REID. It was against your recommendation when the Institute was created?

Dr. MARSTON. Against our strong recommenation.

RESPONSIBILITY FOR GIVING PRIORITY TO EYE INSTITUTE

Mr. NATCHER. Dr. Marston, you have explained to the committee the change with regard to the National Eye Institute and the recommendations that were made. Who made the decision to put this much of the total NIH allowance in the Institute?

Dr. MARSTON. I would have to review the details of this, but in essence it was the NIH recommendation that this amount of additional funds go into the Eye Institute.

Mr. CARDWELL. If you were to examine the history of this budget, and we should do this to answer the question, it would show that NIH proposed increases for all the Institutes; and as the budget was tightened through its evolution the increase for the Eye Institute was left in—but at the recommendation of Dr. Marston.

The budget did not start out from NIH on the basis that would favor this Institute over all others. It ended up that way as the budget evolved. Some budgetary increases were deleted—this one was not hit as hard. That would be my estimate of what happened.

MYOPIA

Mr. NATCHER. Dr. MacNichol, we have a public witness on myopia every year for several years. One or more witnesses will appear again this year.

Wha are you doing and what progress is being made so far as myopia is concerned? Is there anything else you would like to say to the committee on this particular subject?

Dr. MACNICHOL. We have had the Vision Subcommittee of the National Advisory Council report on refractive anomalies which investigated myopia among various other refractive anomalies. I would be glad to make that report available to you.

Mr. NATCHER. Please do that.

(The committee was furnished a copy of "Vision and its disorders" (NINDB Monograph No. 4–225 pages); and Refractive Anomalies of the Eye (NINDB Monograph No. 5–57 pages)).

GLAUCOMA

Mr. NATCHER. You have discussed with us glaucoma. Can we say at this time that glaucoma can be controlled?

Dr. MACNICHOL. To a large extent by surgery and drug therapy. One of the big problems is identifying it early enough and instituting treatment early enough.

Mr. NATCHER. Can you give us some approximate estimate of the number of people who lose their vision simply because they do not have glaucoma treated in time?

Dr. MACNICHOL. It is reported that more than a million persons have glaucoma, that half of them are unaware of the problem, and that every year 3,500 people are blinded by the disorder. If the 500,000 who do not know they have glaucoma went to their doctors and were examined, the deterioration of the eyesight could be arrested. It is estimated that over 2 percent of the population over 40 has glaucoma.

Mr. NATCHER. Mr. Michel?

DEFINITION OF EYE AND BLINDNESS

Mr. MICHEL. Since we are now breaking out research on the eye into a special institute, I looked in Dorland's Illustrated Medical Dictionary for a definition of the eye, and then following this long explanation of the composition of the eye I find a great number of adjectives which indicate the maladies of the eye, such as bleareye, Bright's eye, pinkeye, et cetera.

Then I turned to blindness and I found a number of reasons here.

I do not know whether or not it would be worthwhile placing the dictionary's definition of both the eye and blindness at this point in the record, but to me it points up the many, many areas of trouble spots which I suppose will be areas for your investigation and inquiry on how to remedy them. Maybe we might have that in the record at this point.

(Information requested follows:)

EYE AND BLINDNESS DEFINITIONS

(From the American Illustrated Medical Dictionary 22d Edition, Dr. W. A. Newman Dorland, publisher: W. B. Saunders Co.)

EYE

The organ of vision. In shape the eye consists of a large sphere, with the segment of a smaller sphere, the cornea, in front. It is composed of three coats—the sclerotic and cornea, the choroid, and the retina—each coat being divided into several layers. Within the three coats are the refracting media—namely, the aqueous humor, the crystalline lens, and the vitreous humor. The sclerotic, or external coat, is white and fibrous. Posteriourly the fibers of the optic nerve enter through small perforations in the lamina cribrosa. The inner surface is attached to the choroid by delicate connective tissue, the lamina fusca. The cornea is composed of five layers, the internal layer being a serous membrane, and sometimes called Descemet's membrane. The choroid, or middle coat, is chiefly composed of blood vessels and pigment. Anteriorly, it terminates near the periphery of the lens in folds called the ciliary processes. The retina, or internal coat, is chiefly composed of nerve tissue, and is made up of three principal layers. The external layer, or Jacob's membrane, is composed of terminal nerve cells, which, from their shape, are called the rods and cones.

The iris is a curtain with a central perforation, the pupil, and is composed of smooth muscular fibers arranged both in a circular and in a radiating manner. It varies in color, and is suspended in the aqueous humor in front of the lens. The ciliary ligament is a ring of connective tissue fibers surrounding the iris. The ciliary muscle surrounds the periphery of the iris and controls the convexity of the lens during accommodation. The aqueous humor fills the cavity between the cornea in front of the lens behind. The vitreous humor fills the space back of the lens, and is a clear, jelly-like substance containing mucin. It is surrounded by the hyaloid membrane. The lens, or crystalline humor, is a double convex lens between the vitreous and aqueous humors, and is held in place by an elastic capsule and suspensory ligament. The arteries of the eye are the short ciliary,

the long ciliary, the anterior ciliary, and the central artery of the retina. The nerves are the optic and the long and short ciliary nerves. Blear e., marginal blepharitis. Bright's e., the eye as affected in chronic disease of the kidney. Cinema e., See Kleig e. Crab's e's, concretions from the stomach of the crawfish. Cystic e., distention of the eyelids by a large thin-walled sac. Dark-adapted e., an eye that has undergone the changes produced by adequate exposure to darkness.

It is more sensitive to very weak light, Epiphysial e. See parietal e. Exciting e., in sympathetic ophthalmia, the eye that is injured or wounded and from which the sympathogenic influences start. Fixing e., in strabismus, the eye which is directed toward the object of vision. Hare's e., lagophthalmos. Hop e., conjunctivitis in hop pickers caused by irritation from the spinelike hairs of the hop plant. Klieg e., a condition marked by conjunctivtis, edema of the eyelids, lacrimation, and photophobia due to exposure to the intense lights (Klieg lights) which are used in making moving pictures. Called also cinema e. Light adapted e., an eye that has undergone the changes produced by adequate exposure to light. Monochromatic e., an eye which can perceive only one color. Nairobi e., a form of conjunctivitis in East Africa produced by the juice of crushed blister beetles. Parietal e., in some lower vertebrates a modification of the pineal body to form a dorsal median eye; called also parietal organ, pineal e., epiphysial e. Pheasant's e., Adonis, Pineal e. See parietal e. Pink e., acute epidimic conjunctivitis produced by Hemophilus of Koch-Weeks. Primary e.

Same as Exciting e. Reduced e., schematic e., an apparatus with two refracting elements, one representing the cornea and illustrating, but not exactly representing, the structure of the eye. Secondary e., same as sympathizing e. Shipyard e. See epidemic keratoconjunctivitis, under keratoconjunctivitis. Snellen's reform e., an artificial eye composed of two concavoconex plates with an empty space between squinting e., the affected eye in strabismus, sympathetic ophthalmia, the uninjured eye which subsequently becomes involved. Trichromatic e. The normal eye: one in which the red, green, and blue end-organs are in a normal state. Trolley e., conjunctivitis in motormen of trolley cars attributed to brass poisoning produced by rubbing the eyes after constant handling of the brass trolley brake.

BLINDNESS

Lack of or loss of sight; inability to see. Amnesic color b., inability to recognize or to name a color, although it is correctly perceived. Blue b., color blindness as to blue tints. Blue-yellow b., tritanopia with blindness for blue and yellow. Bright's b., dimness or complete loss of sight without lesion of the retina or optic disk: seen in uremia. Color b., inability to distinguish differences of color: usually partial, and seldom or never complete. Concussion b., functional blindness due to violent explosions caused by high explosive shells, bombs, etc. Cortica b., blindness due to lesion of the cortical visual center. Cortical psychic b., loss of optic memory image and of spatial orientation due to lesion of the optic lobe. Day b., vision which is better by night than by day; hemeralopia. Eclipse b., blindness due to viewing a partial eclipse of the sun and caused by a thermal lesion of the retina. Economic b., inability to do any kind of work for which sight is essential. Educational b., impairment of vision which makes it impossible or difficult to learn by the usual school methods. Flight b., amaurosis fugax. Functional b., inability to see, even though the eyes and their nervous mechanism are intact; usually hysterical. Green b., color blindness for green; deuteranopia. Lactation b., loss of sight in the mother during the suckling period. Letter b., a state resembling word blindness, in which individual letters, though seen, convey no meaning in the mind. Mind b., same as psychic b. Moon b., retinal anesthesia, said to be caused by exposure to rays of moon during sleep. Night b., a defect of the vision more marked by night or in a subdued light, than by musical notes, due to a central lesion. Object b., a condition in which objects seen make no impression on the mind.

See also apraxia. Psychic b., sight without recognition, due to some brain lesion. Red b., blindness to red tints. Red-green b., inability to distinguish red and green. Show b., dimness of vision, usually temporary, due to the glare of the sun upon snow; niphablepsia. Soul B., same as psychic b. Syllabic b., inability to form syllables. Taste b., a condition in which some substances which ordinarily cause a bitter taste, produce no sensation of taste at all. Total b., inability to perceive light; absence of light perception. Twilight b. see aknephascopia. Vocational b., impairment of vision which renders a person unable to do work at which he has previously earned a living. Work b., inability to recognize written words as the symbols of ideas.

Dr. MacNichol. I think there are two serious and direct problems which have to do with eye research. One is research directed toward the prevention of eye disease and effective treatment of eye diseases. The other is the problem of using most effectively what little vision the patient may have left or being able to have a totally blind person get around by other means.

The preservation of vision and rehabilitation of the blind seems to be two very distinct facets of the problem which require quite different solutions.

Mr. Michel. I must say that when this matter was debated on the floor I had some real serious reservations about our breaking research on the eye out into a separate entity.

What, as a broad application, does the area of neurology encompass? It includes the eye, does it not?

Dr. MacNichol. It certainly includes the retina and the visual pathways. I would not think it would include the parts of the eye used for nourishing the retina or focusing light on it. This is separate from neurology.

The retina is of common interest to both neurology and ophthalmology since it is both a mosaic of light-sensitive cells and also part of the brain which does processing of this visual data and compresses it into a form where it can be sent up the optic nerve into the brain.

This happens to be my own research interest. I started out with an interest in the nervous system. Coming from a physical scientists's background, I wanted to put first things first and begin the study of the nervous system with its input. Therefore, I got into research on the retina and never have really gotten out of it.

Mr. Michel. Is it possible as you go down the road in the area of research with respect to the eye that some of that research will spill over into the other areas which tend to affect the nose, the ears, and so on? I am reminded of the problem when we wanted to move ahead with a more targeted area such as cystic fibrosis.

Those who are experts in the area of metabolic diseases brought out the fact that some of the research was already going on and that you could not necessarily target it as being aimed only at this one malady but that there were a variety of things which were affected. I imagine this would be the case with respect to the eye. Is that correct?

Dr. MacNichol. My own research interests have been guided by the fact that the retina is a piece of central nervous tissue and has many of the properties of tissue in the brain. It is a very good place to study some of the fundamental properties of the central nervous system because it is so directly accessible and can be stimulated naturally. It has many advantages for this purpose. I would hope that the benefits of research on the retina can be applied to the brain as well as the eye and to the other senses.

VISION CLINICAL RESEARCH CENTERS

Mr. MICHEL. In your testimony regarding resources for research, you said "as the new Institute develops its program it will be building on the many resources developed by NINDS over the years. These will include an outstanding intramural research branch in ophthalmology," and you mention the nine clinical research centers, and so on.

Are these in being now?

Dr. MACNICHOL. Yes, sir; these will be transferred to the Eye Institute as soon as it is in business.

Mr. MICHEL. Can we have those nine clinical research centers by name listed in the record at this point along with the amount of support you are furnishing?

Dr. MACNICHOL. Yes, sir.

(Information requested follows:)

VISION CLINICAL RESEARCH CENTERS

[Amounts in thousands]

	Fiscal year 1969 amounts	*Fiscal year 1970 amounts*
Retina Foundation, Boston, Mass	$279	$291
Columbia University, New York, N.Y	346	355
Massachusetts Eye and Ear, Boston, Mass	475	511
Smith-Kettlewell Institute Visual Sciences, San Francisco, Calif	234	376
University of California, San Francisco, Calif	360	360
UCLA, Los Angeles, Calif	355	388
Washington University, St. Louis, Mo	259	268
Columbia University, New York, N.Y	128	142
University of Florida, Gainesville, Fla	277	290
University of Washington, Seattle, Wash	206	130

Mr. MICHEL. Would these research centers be supported solely by money from your shop?

Dr. MACNICHOL. They are university centers.

VISION OUTPATIENT CLINICAL RESEARCH CENTERS

Mr. MICHEL. Then the 14 outpatient clinical research units are also in existence?

Dr. MACNICHOL. Yes, sir.

Mr. MICHEL. Would you supply the same information, where they are, and the amount of Federal moneys for 1969 and projected for 1970?

Dr. MACNICHOL. Yes, sir.

(Information requested follows:)

VISION OUTPATIENT CLINICAL RESEARCH PROJECTS

[Amounts in thousands]

	Fiscal year 1969 amounts	*Fiscal year 1970 amounts*
Duke University, Durham, N.C	$63	$49
New England Medical Center Hospital, New York, N.Y	18	17
University of Miami, Coral Gables, Fla	148	154
Wills Eye Hosp., Philadelphia, Pa	29	29
Boston University, Boston, Mass	47	71
Mt. Sinai Hosp., New York, N.Y	141	100
Jefferson Medical College, Philadelphia, Pa	26	45
University of Wisconsin, Madison, Wis	68	71
Columbia University, New York, N.Y	0	90
State University of Iowa, Iowa City, Iowa	0	95
State University of Iowa, Iowa City, Iowa	68	75
Johns Hopkins, Baltimore, Md	47	58
University of Calif., San Francisco, Calif	51	57
Stein Eye Inst., UCLA, Los Angeles, Calif	57	72
Tulane University, New Orleans, La	--	64

TRAINING OF OPHTHALMOLOGY RESEARCHERS

Mr. MICHEL. Referring to these 4,000 persons who have been trained in investigative ophthalmology and related sciences for the past 15 years, where are most of those people now?

Dr. MACNICHOL. The majority of them are in our medical schools.

Mr. MICHEL. Teaching?

Dr. MACNICHOL. Teaching and doing research.

Mr. MICHEL. How many years of schooling are required to become an eye doctor?

Dr. MACNICHOL. It requires the regular medical education plus residency for 3 years.

Mr. MICHEL. You get your degree—what else is necessary to be a recognized eye doctor?

Dr. MACNICHOL. The Board certification in ophthalmology.

Mr. MICHEL. Then what are the steps over and above that when you want to become even more of a specialist?

Dr. MACNICHOL. There is no further academic degree involved. On the other hand one might take post-doctoral and postresidency training, and some of the fellowships which we give are directed to that end so that one can spend 2 or 3 years after he has had his residency in a research laboratory studying how to do a specific kind of research. Many people doing research in vision, myself included, are not medically trained but have received the Ph. D. from nonmedical university departments. Naturally, we are not permitted to treat patients.

Or he might get one of these career development awards which gives him 5 to 8 years of getting started toward becoming senior investigators in some particular area which he decided to concentrate on.

STIMULATION OF INTEREST IN EYE RESEARCH

Mr. MICHEL. Doctor, I know that you are in the process of getting a director for the Institute. I must say that we have some real problems recruiting for many high Federal Government positions because of the sacrifices many people have to make. I am reminded of one of our sub-Cabinet positions chosen from one of the biggest industries at home in my district who had to make such a tremendous financial sacrifice to get into the service.

It prompts me to think that in some respects, regarding his particular case, our requirement for entering service and divesting yourself of stock is a factor and whether or not you may run afoul a conflict of interest. In the medical area we have had some very fine people who have been motivated to come into the Federal service because, if I might use an expression, this is where a lot of the action is—in this volatile research area.

Many of the formerly established institutes have been well publicized. There is a lot of interest in them. I imagine that attracts people to them.

Here we are for the first time setting up an eye institute as a separate entity. I suspect that once having been esablished and ongoing and the emphasis then is placed on it you would find more people naturally attracted to participating more actively in this research activity.

Dr. MacNichol. I should think so. I believe there is really a tremendous opportunity for the top staff of this Institute to provide the leadership and to point the direction which vision and blindness research will take during the next 20 years or so. They really have a chance to establish the policies and the areas of research that are going to be pursued most actively. Also, they will have an intramural program which will be far larger and has more opportunities than any university department could possibly afford.

Mr. Michel. Doctor, I appreciate that your first responsibility would be to get at the problem of eye diseases and all those things that tend to lead to blindness or loss of sight. Do you envision that you would get in the field of what kind of glasses I ought to have or ought not to have? I am rather concerned in my own case. It has only been in the past 2 years that I have turned to glasses, going over these miniscule figures day after day. I am now to the point that I cannot read a dinner menu in a dimly lit restaurant any more without them, and this is about the third upgrading of glasses I have had over a 3-year period. I am asking myself, what can I do to strengthen my eyes? Conceivably in the next 10 years I will not be able to see at all. Will this sort of thing be looked into?

Dr. MacNichol. I think a good deal is understood about this and from what you describe, I hate to say this, but it is just a part of the aging process.

Mr. Michel. This is very distressing.

Dr. MacNichol. When you were a kid you could read up to the end of your nose, and then it got out here [indicating], and pretty soon you go to the ophthalmologist and say, "Doc, my eyes are all right but my arms are not long enough." The next step is bifocals like I wear.

Mr. Michel. That is all.

Mr. Natcher. Mr. Casey.

GLAUCOMA TEST

Mr. Casey. Doctor, on glaucoma, the test that is now used is very simple, is it not? I guess it is where they put a few drops in your eye and use a pressure gage.

Dr. MacNichol. A tonometer, yes.

Mr. Casey. When was that developed? I mean, when was it discovered that was the way to test for glaucoma?

Dr. MacNichol. I could not tell you. It was a long time ago.

Mr. CASEY. It did not become well publicized until recently, did it?

Dr. MACNICHOL. Yes, I believe so. I can remember having a tonometer used on me when I was a kid, about 1930.

Mr. CASEY. You can?

Dr. MACNICHOL. Yes. It was very unpleasant. That is why I never forgot it.

Mr. CASEY. Are there other developments along this line?

Dr. MACNICHOL. Yes, there are electronic tonometers which are pleasanter to use and which will record rapid changes in the pressure inside the eye so that the effects of drugs can be evaluated right after they are used.

Mr. CASEY. If this kind of test has been known for sometime why do we still have 2 percent of the population over 40 with glaucoma and they don't know it?

Dr. MACNICHOL. They do not get routine tests.

Mr. CASEY. They do not go to an eye doctor until it is too late?

Dr. MACNICHOL. Until the damage has started; yes.

Mr. CASEY. And then it is too late; is that right?

Dr. MACNICHOL. Yes, sir; too late to correct the vision loss that has already occurred, but not too late to prevent further loss.

Mr. CASEY. I would appreciate it if you would put something more in the record on tonometry.

(The additional information follows:)

HISTORY OF TONOMETRY

An outstanding contribution to ophthalmology, particularly to glaucoma, was the invention of the ophthalmoscope by Hermann Helmholtz in December 1850. This made possible the detection of glaucoma by observing an excavation in the disk, and has enabled the surgeon to watch the pathologic changes in the papilla caused by pressure within the eyes.

Adolf Von Weber, 1856, was the first to demonstrate the cupping of the disk in glaucoma, and also demonstrate the different depths of the papilla in the various stages of glaucoma by the parallactic movement which occurs when the examiner changes the ophthalmoscope in different directions.

In 1858, Heinrich Muller observed excavation of the disk in enucleated glaucomatous eyes. He ascribed the excavation to increased intraocular pressure.

Adolf Von Weber also proposed the measurement of ocular tension by tactile examination introducing digital tonometry, the system which is still used today.

In 1862, Sir William Bowman graded the tension as +1, +2, +3; −1, −2, which is the same way that it is suggested that it be graded today.

In 1862, Albrecht Von Graefe (Berlin) built the world's first mechanical tonometer. It was applied over the lid since topical anesthesia was unknown at that time.

In 1905, Dr. Hjalmar August Schiotz of Norway presented the first impression tonometer which, with minor improvements, is still the most widely used throughout Western Europe and America. This tonometer, which measures the indentation produced by a predetermined force, gives readings which depend not only on the intraocular pressure but also upon ocular rigidity. It measures the depth to which the cornea sinks when a weighted plunger is applied lightly to the surface of the eye. The variability of globe rigidity and sclera distensibility has made accurate calibration of this tonometer very difficult. It requires local anesthesia. Only an electrical adaptation of this tonometer can produce a permanent record.

In Schiotz tonometry, only the amount of the force is known. The distribution of this force, as between the footplate and the plunger, is subject to conjecture and varies from eye to eye. The shape of the indentation, too, depends upon the properties of the cornea; not only on its size, curvature and thickness, but also on the molecular constitution of its tissue. These biophysical characteristics determine the visco-elastic properties of the cornea, properties which must be considered before one can attempt to predict the response of the cornea to any applied stress. These problems are not eliminated but certainly are simplified in applanation tonometry where only one force is applied and where the shape

of the deformation is at least approximately known. Many difficulties have been encountered in interpreting the measurement obtained with the Schiotz tonometer. Many uncertainties still exist.

Schiotz based his first conversion graphs on open manometer measurements of enucleated human eyes. These graphs, published in 1909, set the upper limit of normal intraocular pressure at 24 millimeter Hg (or 3 scale divisions with the 5.5 g. load). In 1924, he published a revised graph in which the values were 5 to 6 mm. Hg higher.

William McLean, who claimed that his method of calibration was more valid than Schiotz' since it was conducted on intact human eyes, found that the upper limit of normal to be 40 mm. Hg.

J. S. Friedenwald in 1948 published a conversion table essentially similar to Schiotz' 1924 table, but which lowered the upper limit of normal from 30 to 28 mm. Hg. This conversion table was revised in 1955. The 1955 table, which is the one currently in use, approximates closely the original conversion table published by Schiotz in 1909. In fact, the average normal value, which today is believed to be about 16 mm. Hg corresponds to 5.5 scale divisions on both the 1955 and the 1909 scales. Today, following Goldmann's determinations with the use of the applanation method, we accept 15 to 16 as the average normal intraocular pressure.

Obviously, the manometric calibration of a tonometer can be grossly misleading. This means that the Schiotz tonometer—or any indentation tonometer—can be calibrated only empirically, with little if any help from physical or mathematical theory. Applanation tonometers have at least a basis in mathematical and physical principles which can be used as a starting point in their calibration. Clinical evaluation and statistical analysis are obviously prerequisites to the use of any tonometer that lays claim to clinical validity.

The Goldmann applanation tonometer uses what is known as the uncorrected Inbert-Fick formula to convert force applied into intraocular pressure; so does the recently introduced Draeger hand applanation tonometer. Applanation tonometers such as the Applanometer and the Tonomat use conversion tables based on the Inbert-Fick formula, but corrected to take into account the changes in scleral rigidity with increasing intraocular pressure and tonometer weight. These conversion tables can also be used with the Maklakov-Kalfa tonometer.

Goldmann's applanation tonometer has been used with increasing frequency since 1958 as part of the initial screening examination because it has given the most accurate measure of intraocular pressure to be obtained clinically. It is sensitive and causes very little disturbance of the intraocular pressure, plus practically eliminating error from abnormality of the elastic properties of the eye. This tonometer is now a clinical standard reference, though the Schiotz tonometer is still used to perform more routine clinical examinations.

In 1964, the development of the pneumatic applanation tonometer, which gives accurate measurement of intraocular pressure and eliminates the disadvantages of instruments currently in use, was announced by E. I. du Pont de Nemours & Co. Engineering Physics Laboratory.

This new tonometer evolved from an industrial pressure sensor based on a pneumatic system. Reputedly easy to use, it is alleged to be ruggedly built; it can be gas sterilized, and retains accurate calibration over long periods of time. Unlike other tonometers now in use, it provides a permanent record which can be easily interpreted and permanently filed. It has several advantages over the Schiotz and Goldmann tonometers, which must be applied to the cornea and necessitate local anesthesia. Because of its greater sensitivity, the pneumatic tonometer can be used on the sclera as well as the cornea with equal accuracy. It can be used without anesthesia and with only a minimum amount of training before accurate readings may be obtained.

The pneumatic applanation tonometer has four major components: (1) an air pump which supplies compressed air to operate the sensor; (2) the sensor which is applied to the eye and produces a pneumatic signal; and (3) a transducer which converts the pneumatic signal to an electrical signal and provides a visual pattern of intraocular pressure. The sensor directly measures the intraocular pressure when the contacted surface of the eye is flattened or applanated.

There are two other newly developed tonometers, referred to as applanation tonometers, which do not use the Inbert-Fick formula at all. These are the Mackay-Marg electronic tonometer, and the Tonair pneumatic tonometer. With these tonometers, the measurement is also obtained the instant the applicator probe has applanted the surface of the cornea. The force required to accomplish this is known, but the area flattened is not measured—thus the Inbert-Fick formula is not used.

Mr. NATCHER. Mrs. Reid.

ESTABLISHMENT OF NEW INSTITUTES

Mrs. REID. Dr. Marston, you stated that you did not recommend that there be a separate institute for eye research, and I would certainly hope that during this time when we must watch expenditures so closely that this is not setting a precedent so that there will be other institutes created, because, to quote Dr. MacNichol, separate institutes require both separate funds and separate personnel. Would you care to comment on that?

Dr. MARSTON. Yes. First, I would like to agree with you. We have estimated that the cost of a new institue, the administrative overhead, is about $500,000 and minimally another 50-plus people. This means that when you do have tight budgets that you have to really rob some other areas by giving a high priority to these areas.

The second thing we have run into in trying to establish an institute under these conditions is that after we made a very vigorous effort to get a director for the institute, the first thing he wants to know is how many people he will have and how many dollars he will have. And it is hard for him to get excited if we tell him we are under unusual constraints.

In general we had the same problem in recruiting people for this job in talking to them of the salary differential, particularly in one of sub-specialities like ophthalmology. I might just add that I have recruited at the top level in the last year in the various jobs as I have been shifting around a number of people, and it almost always requires that an individual be excited about the job and be excited about the opportunity, because he usually takes a pay cut when he comes in and this has been very substantial. Therefore, the particular problem in starting up a new institute with dollars and personnel slots as tight as they are now, it is hard to sell the enthusiasm to the person who will provide the leadership if he knows that the probability for the immediate future is that he might have difficulty in getting the resources to establish the institute.

DETECTION OF GLAUCOMA

Mrs. REID. In your discussion with Mr. Casey, did you say that you can detect glaucoma through regular eye examinations, or do you have to have a special examination? For instance, if a child would have an ordinary eye examination, could glaucoma be detected?

Dr. MACNICHOL. I think tonometry is not used routinely, though it should be and is being used increasingly.

Mrs. REID. I should think when you say that 2 percent of the population over 40 have the disease and do not know it that this should be a part of the regular eye examination.

Dr. MACNICHOL. It certainly should be.

Mrs. REID. Would you have any idea how long a person could have glaucoma without being aware of it?

Dr. MACNICHOL. No, I do not.

Mrs. REID. But it could be many years?

Dr. MacNichol. Presumably if he had a much elevated intraocular pressure for very long it would start to show up.

Mr. Michel. Will you yield? Yesterday we heard testimony that 50 percent of the population never see a dentist. Do you have any statistics to show what percentage of our people never have an eye examination of any kind?

Dr. MacNichol. Yes. In 1964, 16.2 million or 8.7 percent of the noninstitutionalized civilian population of the United States were seen by optometrists.

I believe schoolchildren get some kind of an eye examination in school. I am not sure of this.

Mr. Michel. But it is not a requirement, only in selected cases, I believe.

Dr. Marston. You are talking about an examination by a physician?

Mr. Michel. Well, someone competent, for instance in the detection of glaucoma. If you have some generally accepted cursory examination for school children, would glaucoma show up?

Dr. MacNichol. Probably not.

Mr. Michel. Then you will find just a miniscule number of people who will be examined by a competent enough person to detect this. Here we are talking about one person in 50 over 40, are we not?

Dr. MacNichol. Yes.

Mr. Michel. For people with cancer we say they should do this or that for cancer detection, and yet one in 50 people over 40 have glaucoma and do not know about it.

Dr. MacNichol. The other trouble is that glaucoma is a disease that can come on at any age. Even if children were all given a good eye examination, since glacoma mostly develops later in life, it would not have been picked up in childhood. Obviously the answer is to have everybody have a regular eye check-up. The trouble with that is there just are not enough ophthalmologists to do it and they are too busy.

Dr. Marston. Is it not true, Doctor, that one area that shows promise is the use of cortisone-like drugs to identify the prone person before he has any symptoms of glaucoma, and this is fairly far along at present as a potential test.

Dr. MacNichol. I don't know how close this procedure is to routine practice. It also requires the use of an expensive electronic tonometer.

Mrs. Reid. What is uveitis?

Dr. MacNichol. It is an inflammation of the iris and the tissues surrounding the retina. It is a very serious disease. It is an infection which destroys sight.

Mrs. Reid. Thank you very much. That is all.

Mr. Natcher. Dr. MacNichol, we want to thank you for an excellent presentation on the budgets for the National Institutes of Neurological Diseases and Stroke and the National Eye Institute.

Dr. Marston, it is always a pleasure to sit on this side of the table and hear your people testify, and I say that frankly. It is a distinct privilege. We certainly enjoy and profit from the testimony not only of Dr. MacNichol, but Dr. Cooper yesterday made a very masterful presentation. I think you will agree with that.

Dr. Marston. Yes, sir.

Mr. Natcher. The committee will adjourn until 10 o'clock Monday morning.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation

	1969	1970
Appropriation	$ 0	$ 25,778
Comparative transfers from the National Institute of Neurological Diseases and Stroke	22,303	
Comparative transfer to "Salaries and Expenses, Office of the Director"	- 63	
Total currently authorized for obligations	22,240	25,778
Total obligations	22,240	25,778

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
122	Research		$16,206,000		$19,660,000		$+3,454,000
	General research support grants		(1,612,000)		(1,912,000)		(+300,000)
	Scientific evaluation and planning		(25,000)		(25,000)		---
	Categorical clinical research centers		(734,000)		(734,000)		---
	Specialized research centers		---		---		---
126	Fellowships		676,000		650,000		- 26,000
128	Training		3,603,000		3,462,000		-141,000
	Direct Operations:						
129	Laboratory and clinical research	40	737,000	40	754,000	--	+17,000
130	Collaborative research and development	--	349,000	--	349,000	--	---
131	Biometry, epidemiology and field studies	15	303,000	15	317,000	--	+14,000
132	Review and approval of grants	8	366,000	15	466,000	7	+100,000
133	Program direction	--	---	8	120,000	8	+120,000
	Total obligations	63	22,240,000	78	25,778,000	15	+3,538,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decreases
Total number of permanent positions	63	78	+15
Full-time equivalent of all other positions	5	6	+ 1
Average number of all employees	60	76	+16
Personnel compensation:			
Permanent positions	$ 587,000	$ 777,000	$ +190,000
Other personnel compensation	21,000	28,000	+ 7,000
Total personnel compensation	608,000	805,000	+197,000
Personnel benefits	35,000	58,000	+ 23,000
Travel and transportation of persons	51,000	51,000	---
Transportation of things	12,000	12,000	---
Rent, communications, and utilities	34,000	34,000	---
Printing & reproduction	16,000	16,000	---
Other services	928,000	942,000	+ 14,000
Supplies and materials	30,000	47,000	+ 17,000
Equipment	41,000	41,000	---
Grants, subsidies, and contributions	20,485,000	23,772,000	+3,287,000
Total obligations by object	22,240,000	25,778,000	+3,538,000

Summary of Changes

1969 estimated obligations	$22,240,000
1970 estimated obligations	25,778,000
Net Change	+3,538,000

Increases	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
A. Program				
1. Research Grants	--	$16,206,000	--	$3,454,000
2. Review and Approval	8	80,000	7	147,000
3. Program Direction	--	--	8	109,000
Total Program Increases			15	$3,710,000
Decreases				
A. Program				
1. Fellowships	--	676,000	--	26,000
2. Training	--	3,603,000	--	141,000
B. Payment to "National Institutes of Health Management Funds" for centrally furnished services:	--	429,000	--	5,000
Total decreases	--	---	--	172,000
Total net change requested	--	---	+15	+3,538,000

Explanation of Changes

Research Grants — The program increase of $3,454,000 will support new research essential for the development of improved methods of prevention, diagnosis, and treatment of blinding eye diseases and visual disorders, focusing particularly on the problems of glaucoma, disorders of the cornea, infections of the eye, disturbances of eye movements and refractive errors of vision.

Current plans are to have 355 research projects, ten clinical research centers and 13 vision outpatient clinical research centers in 1969. It is planned in 1970 to support 85 additional research projects.

Fellowships — The decrease of $26,000 from 1969 will provide $650,000 to support 35 fellowships in 1970.

Training — The decrease of $141,000 from 1969 will provide $3,462,000 to support 80 training grant awards in 1970.

Review and Approval — The program increase of $147,000 will provide support for seven new positions in program planning efforts of this new institute. Of these new positions, five are required to staff the extramural office and two positions (scientist administrator and secretary) will be used to establish the program analysis office. These positions will support the establishment and coordination of planning and programming activities in the visual sciences.

Program Direction — The increase of $109,000 and eight positions will provide for the initial staffing required in the Office of the Director, i.e., Director, Assistant Director, Executive Officer, and two administrative staff. Also included are three positions for the establishment of an information office.

Significant Items in House and Senate Appropriations Committee Reports

ITEMS	Action taken or to be taken
1969 House Report	
(1) The Committee wished to see increased emphasis in research on refractive errors, the causes and management of near-sightedness, and the pharmacology and toxicology of new drugs in the treatment of diseases of the eye. (Page 23 of the House Report).	(1) The creation of the NEI, with its increased new funds in F.Y. 1970, will permit this increased emphasis. In 1969 advances have been made in ability to correct errors of refraction, such as myopia. Also broadly based epidemiological and genetic studies are underway to assist in solving the problems of refraction anomalies.
1969 Senate Report	
(1) The Committee wished to see increased emphasis in research on refractive errors, the causes and management of near-sightedness, and the pharmacology and toxicology of new drugs in the treatment of diseases of the eye. (Page 46 of the Senate Report).	(1) In 1969 a symposium of diabetic retinopathy was held in October at which a number of the controversial views on treatment were discussed, particularly hypophysectomy as opposed to coagulation.

Legislation	1970 Authorization
Public Health Service Act Section 301--Research and Investigations in General.....	Indefinite
Title IV, Part F--National Eye Institute	Indefinite

PUBLIC HEALTH SERVICE ACT

Authorizing Legislation

The legislative authority which provides for the award of grants for research, research training and fellowships is included in section 301 of the Public Health Service Act.

Public Law 90-489
90th Congress, H.R. 12843
August 16, 1968

"Sec. 451. The Secretary is authorized to establish in the Public Health Service an institute for the conduct and support of research for new treatment and cures and training relating to blinding eye diseases and visual disorders, including research and training in the special health problems and requirements of the blind and in the basic and clinical sciences relating to the mechanism of the visual function and preservation of sight. The Secretary is also authorized to plan for research and training, especially against the main causes of blindness and loss of visual function."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer from:			
"The National Institute of Neurological Diseases and Stroke".....	$22,303,000	---	To provide funds for the establishment of the National Eye Institute.
Comparative transfer to:			
"Salaries and expenses, Office of Director".....	63,000	---	To provide funds covering expenses for the Office of Director, NIH, which were previously funded through the NIH Management Fund.

National Eye Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$25,778,000			

National Eye Institute

Year	Estimate to Bureau of Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$32,029,000	$25,778,000			

Justification

National Eye Institute

	1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
Personnel compensation and benefits.....	63	$ 643,000	78	$ 863,000	+15	$ 220,000
Other expenses.....		21,597,000		24,915,000		+3,318,000
Total.....	63	22,240,000	78	25,778,000	+15	+3,538,000

General Statement

The eye research and training programs of this Institute include research at the Bethesda laboratories, research grants of individual scientists in academic institutions throughout the country, and training grants to aid universities and other centers in educating more ophthalmologists and research scientists.

Notable achievements have included major contributions to the solution of the problem of retrolental fibroplasia, fundamental advances in the knowledge of structure and function of the eye, and important technical advances in the surgical treatment of cataract and retinal detachments. In the last few years, a significant advance was the discovery of a specific antiviral agent to cure a common cause of corneal ulcers. Other more recent advances have included better diagnosis and treatment of glaucoma, more effective grafting of corneal transplants, tests to find harmful side effects of such drugs as chloroquine, and new methods of detecting and treating ocular tumors.

Establishment of 10 clinical eye research centers and 13 outpatient clinical research units for vision and blindness have resulted in continually strengthening the program.

The research programs of the Institute are focused on some particular area of the vision problem. These programs now include:

Cataract
Glaucoma
Retinopath and Neurological Mechanism of Vision
Inflammatory and Parastic
Metabolic and Degenerative
Strabismus and Neuromuscular
Injuries and other Disorders Including Tumors
General Eye Disorders

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research Projects.....	$13,835,000	$16,989,000	+$3,154,000
Special Programs.....	2,371,000	2,671,000	+300,000
Total.....	16,206,000	19,660,000	+ 3,454,000

Introduction

A major part of the extramural research program of the new National Eye Institute will consist of on-going research activities transferred from the National Institute of Neurological Diseases and Stroke. The research grant programs include research projects, research program projects, eye outpatient clinical research projects, and eye clinical research centers. The primary purpose of these grants is the identification, stimulation and support of essential research on problems related to the diagnosis, treatment and prevention of diseases of the eye and its supporting structures and musculature. This includes basic, clinical, comparative, and epidemiological research on: the development, structure and function of the eye; disorders of the eye; and genetic, metabolic, vascular, infectious, and neurological factors directly related to primary disorders of the eye. The importance of a major research effort on eye disorders is indicated by the fact that in the United States over 400,000 people are legally blind; one million have visual impairment so severe they cannot read a newspaper; 300,000 are handicapped to the extent they cannot work; and about 3,500,000 have only partial vision. As a result of on-going training and research grant programs, the research technology, the highly skilled manpower, and the necessary instrumentation are available for a Nation-wide effort against this major cause of disability.

Program Plans for 1969 and 1970

In 1969, approximately 355 regular research projects totalling $13,835,000 will be awarded for studies of eye disorders. The funds proposed for 1970 will provide for approximately 440 regular research projects totalling $16,989,000.

The budgets for 1969 and 1970 must be considered in the light of the generally increasing costs of doing research. In addition to increased costs for personnel, supplies, and hospitalization of research subjects, modern research often requires much more sophisticated and usually more expensive equipment. The grant budgets continue to reflect the need for additional funds as a result of a cost sharing arrangement which considers the full direct and indirect costs of the project in determining the federal and non-federal portion of support.

These funds will continue to support research on disorders of the eye in areas such as glaucoma, cataract, macular degeneration, retrolental fibroplasia, diabetic retinopathy, trachoma, and tumors of the eye. Areas of emphasis and new program needs are described below.

Regular Research Projects

Some 440 regular research projects constitute the major part of the extramural research program. They represent the ideas of independent scientists in laboratories throughout the Nation; some are largely clinical projects; others are effective combinations of clinical and basic research. Many are fundamental studies, not only on the causes, treatment and prevention of eye disorders, but also on the highly important basic mechanisms by which cells, genes, living membranes, protein molecules, and other fundamental biological entities reproduce

and function. Through basic disciplines such as biochemistry, biophysics, electronics, and physiology, the fundamental mechanisms by which the eye maintains itself, the physiochemical means by which light energy is converted to nerve impulses, and many similar problems vitally important to an understanding of the eye are studied. Building upon this broad base of independent research, the Institute will establish special projects and programs directed toward specific categorical objectives. Through this arrangement, the broad attack on disorders of the eye will be most effective.

Eye Clinical Research Centers

In addition to the program of regular research projects, support is being provided for 10 clinical research centers for blindness and eye disorders, each concentrating on special clinical problems such as glaucoma, cataract, macular degeneration, corneal disease, infections of the eye, and disturbances of eye movements. Even though highly specialized, each center maintains a broad approach to the overall problem of blindness. For example, as a basis for approaching the problem of the sensory and perceptual disorders, several centers are developing needed information about fundamental mechanisms by which light impulses are converted to nervous energy and transmitted to the brain for interpretation.

The program of eye outpatient clinical research grants, initiated on a pilot basis in 1967 and 1968, has been successful and now includes support for 13 such units. These programs have made outpatient populations with eye disorders available for essential research studies.

Diabetic Retinopathy

The eye complication of diabetes, diabetic retinopathy, is among the leading causes of blindness in the United States. In patients who have had diabetes for 15 years approximately 70 percent will show retinopathy, the presence of aneurysms in the capillaries supplying blood to the retina. Although several types of treatments are reported to produce improvement in some patients, the results in general are most discouraging. As a result of these considerations, the National Advisory Council has recommended this problem as one that needs special immediate attention. Therefore, special efforts are being made to stimulate research in this area and to search for new approaches to the problem. The first steps have already been taken and through the organization of workshops and planning conferences a pilot project will be available to test the protocol for a National cooperative evaluation of the effect of pituitary ablation on the progress of diabetic retinopathy. Until this study is done, the true role of this dire procedure in arresting the progression of the disease will not be understood. In addition, several newly developed approaches to the problem of diabetic retinopathy and its causes are being explored and need to be supported without delay.

Retrolental Fibroplasia

Retrolental fibroplasia (RLF), usually resulting in blindness, develops through much the same mechanism that produces the later stages of diabetic retinopathy. At one time it was the leading cause of blindness in the United States, until it was discovered through a study supported by NINDS that the disorder was due to exposing premature infants to oxygen in excess of usual atmospheric levels. With this knowledge the incidence of RLF was dramatically reduced until it was nearly an unknown disease in the United States.

Recently, however, a new problem has arisen leading to a resurgence of RLF because of the treatment of the respiratory distress syndrome such as hyaline membrane disease; this disease of prematures may cause the newborn to suffocate. About the only available treatment for this syndrome is an increase in the incubator oxygen concentration. Thus, the choice facing the physician is to try to prevent the infant from suffocating at the risk of inducing RLF and blindness. A standard must be established which will provide sufficient oxygen for metabolism

but yet not stimulate retinal vessel proliferation. New tools must be developed which will aid the physician in maintaining this delicate standard in the premature. The approaches to this highly important problem are under evaluation and support will be necessary for a series of workshops and for rather in-depth studies of this problem, and then for the development and evaluation of the required clinical tools.

Glaucoma

The seriousness of glaucoma is illustrated by the fact that about 14 percent of all newly blind persons in the United States have lost their vision because of glaucoma. It is estimated that about two percent of the population over 40 years of age have the disease and about four percent of the population have a genetic predisposition to it. Although glaucoma occurs in children, it usually develops in adults at the height of their earning capacity. The loss to the individual, his family, and the community is enormous. Since it is initially symptomless in most cases, irreparable damage may occur before the disease is even discovered.

Carefully conducted epidemiological studies are needed to identify the early stages, describe the natural history, and indicate which patients are likely to lose vision. The ongoing Collaborative Glaucoma Study is designed to answer some of these questions. It is especially important to develop better instrumentation to measure intraocular pressure and to elucidate the mechanisms that control it. More effort is needed to breed strains of animals that spontaneously develop glaucoma. Animal studies and new methods are essential for the evaluation of new drugs and for new approaches to treatment. Additional clinical research centers need to be established so new laboratory research developments can be promptly evaluated in patients. Recent studies of the intraocular pressure response to topical corticosteroids have opened a whole new approach to the study of glaucoma. It may be possible to identify the "genetic glaucoma" patient many years before the disease develops. Immediate and urgent research needs include 1) long-term studies of steroid-tested patients, 2) analyses of the mechanisms of response to corticosteroids and, 3) development of experimental animals whose eyes respond like those of the human.

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Cataract.....	$1,151,000	$1,414,000	$+263,000
Glaucoma.....	1,373,000	1,691,000	+318,000
Retinopathy & Neurological Mechanisms of Vision.....	4,478,000	5,745,000	+1,267,000
Inflammatory & Parastic....	2,358,000	2,597,000	+239,000
Metabolic & Degenerative...	847,000	1,034,000	+187,000
Strabismus & Neuromuscular.	785,000	1,006,000	+221,000
Injuries & Other Disorders Including Tumors.....	681,000	826,000	+145,000
General.....	2,162,000	2,676,000	+514,000
Total Regular Research Grants.....	13,835,000	16,989,000	+3,154,000

Distribution of Research Grants

	1969 Estimated		1970 Estimated		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Non-competing.....	241	$9,671,000	243	$9,775,000	+2	$+104,000
2. Competing.....	114	3,839,000	197	6,714,000	+83	+2,875,000
3. Supplementals.....	(30)	325,000	(45)	500,000	(+15)	+175,000
4. Subtotal Regular Program.....	355	13,835,000	440	16,989,000	+85	+3,154,000
5. General Research Support Grants.....	--	1,612,000	--	1,912,000	--	+300,000
6. Scientific Evaluation....	--	25,000	--	25,000	--	---
7. Categorical Clinical Research Centers.....	--	734,000	--	734,000	--	---
8. Total Research Grants....	355	16,206,000	440	19,660,000	+85	+3,454,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Fellowships.....	$676,000	$650,000	-$26,000

Introduction

The research fellowship programs of the National Eye Institute are designed to encourage advanced, specialized research training by providing the financial support necessary for clinical and laboratory scientists to become qualified for research on problems relating to diseases of the eye. For advances in solving these problems, it is essential that there be substantial numbers of scientists highly skilled in the diversified research disciplines related to diseases of the eye; for example, ophthalmic anatomy, pathology, physiology, virology, pharmacology, physiological optics, biophysics, biochemistry. These scientists must be skilled in the most up-to-date techniques and instrumentation applicable to study of the eye. Past NIH experience has demonstrated that the fellowship programs are a most effective means of providing this training and of encouraging individuals to enter research careers.

Postdoctoral Fellowships

Postdoctoral fellowships provide financial support during the three years of research training immediately following the doctoral degree.

During 1970, training will be emphasized in scientific fields relating to research on problems of glaucoma, cataract, uveitis, macular degeneration, and other important diseases of the eye. The funds available in fiscal year 1970 will lead to a reduction in the number of promising young scientists whose training can be supported in 1970 as compared with 1969, despite an increase in the number of qualified applicants.

Career Development Awards

Career Development Awards assure support over five to eight year periods for selected scientists who have completed formal research training, and are by this means provided with an opportunity to become established as independent investigators in a chosen line of research. The success of this program over the relatively short time it has existed is demonstrated by the number of Career Development Awards which are terminated before their expiration due to the appointment of awardees to career posts in departments of ophthalmology, physiology, anatomy, and the like.

Funds available during fiscal year 1969 funded approximately one fourth of the approved applications; the funds requested in fiscal year 1970 will fund approximately the same level of activity.

Funds requested for 1970 will provide for 35 awards, compared to 40 in 1969, a decrease of five. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	18	$435,000	17	$444,000	-1	$+9,000
b. Competing.....	11	133,000	11	137,000	--	+4,000
2. Supplementals.....	(13)	12,000	(11)	11,000	(-2)	-1,000
3. New Grants.....	11	96,000	7	58,000	-4	-38,000
4. Total Fellowships.....	40	676,000	35	650,000	-5	-26,000

Fellowhips (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral.....	17	$145,000	13	$104,000	--	-$41,000
2. Development Awards.....	21	489,000	20	502,000	--	+13,000
3. Career Awards.....	1	33,000	1	34,000	--	+1,000
4. Foreign Scholarships.....	1	9,000	1	10,000	--	+1,000
5. Total Fellowships.....	40	676,000	35	650,000	--	-26,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Training Grants.....	$3,603,000	$3,462,000	-$141,000

Introduction

The training grants program of the National Eye Institute provides support to institutions for establishing, improving, or expanding training programs to prepare clinical and laboratory scientists for careers in research and academic medicine in the biomedical and medical disciplines relating to research on the eye.

The scientists trained under these programs can be expected to assume the responsibility for future advances in knowledge leading to the prevention and successful treatment of eye disorders and for training of the next generations of eye scientists. These programs have been growing steadily in number and quality, thus beginning to increase the pool of well-trained scientists available to fill the many vacant positions of leadership as researchers and teachers.

In 1970, the training grant appropriation will require further reductions in both the number of trainees who can be supported and in the facilities and professional staff necessary to provide a high quality training environment.

Funds requested for 1970 will provide 80 awards, compared to 87 in 1969, a decrease of seven. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	38	$2,331,000	38	$2,331,000	--	$ ---
b. Competing.....	28	885,000	28	860,000	--	-25,000
2. Supplementals.....	(8)	73,000	(8)	73,000	-7	---
3. New Grants.....	21	274,000	14	158,000	--	-116,000
4. Scientific Evaluation & Planning.....	(1)	40,000	(1)	40,000	--	---
5. Total Training Grants.....	87	3,603,000	80	3,462,000	-7	-141,000

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Graduate.....	55	$3,187,000	49	$3,059,000	-6	-$128,000
2. Traineeships.....	32	376,000	31	363,000	-1	-13,000
3. Scientific Evaluation & Planning.....	(1)	40,000	(1)	40,000	--	---
4. Total Training Grants.....	87	3,603,000	80	3,462,000	-7	-141,000

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	40	$474,000	40	$474,000	--	----
Other expenses	--	263,000	--	280,000	--	+$17,000
Total	40	737,000	40	754,000	--	+ 17,000

CLINICAL RESEARCH

The present ophthalmology research effort is being carried out as part of the Intramural Research program of the NINDS. Organizationally, it will continue to be part of NINDS until a new Director of the NEI is selected.

Ophthalmology

This Branch is studying the mechanisms through which the visual image is converted to coded messages within the eye and then interpreted within the central nervous system. Investigations of the electrical responses of the eye (electroretinogram and electro-oculogram) have been undertaken for the diagnosis of diseases leading to blindness, for the early recognition of degeneration of the retina produced by drugs, and for the differentiation of various forms of night blindness.

Glaucoma investigations underway are concentrated on the mechanisms producing increased intraocular pressure as well as the development, animal testing, and clinical evaluation of new drugs.

The treatment of inflammations of the eye is being studied with particular attention to compounds suppressing toxoplasma infection and the use of antimetabolites in diseases in which an immunologic mechanism is suspected.

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Other expenses (total).....	--	$349,000	--	$349,000	--	$ --

MEDICAL INFORMATION NETWORK

The NEI participates in the NINDS Neurological Information Network. This Network facilitates the prompt exchange of information within the medical and scientific community through the establishment of information centers in four universities having outstanding library facilities: 1) Columbia University—Parkinsonism and Related Neurological Diseases; 2) The Johns Hopkins University—Hearing, Speech and Disorders of Human Communication; 3) University of California at Los Angeles—Basic Neuroscience; and 4) Harvard University—Vision and Diseases of the Eye. The Harvard University center will be financed in 1970 from NEI funds.

The Network is coordinated by the Office of Program Analysis, NINDS, and operates in close collaboration with the National Library of Medicine. It is engaged in a review of scientific reports, indexing for the MEDLARS system, publication of bibliographies, special reviews, symposia, and a review of articles on topics of special interest.

This Network has now developed to the point where there is a steady output of special service bulletins in a variety of areas such as Parkinson's disease, sleep physiology, electroencephalographic literature, enzyme chemistry of the brain, and communications disorders. Some of the special reviews which have been produced are now the standard works on the subject. The Vision Information Data Bank is computerized and will serve anyone who wants to rent a terminal and pay the line costs to search it. Indexing in the area of neurological diseases and in visual sciences is being done for the Index Medicus of the MEDLARS system of the National Library of Medicine. These special indexing thesauri are being examined and incorporated into the new augmented indexing system for the second generation MEDLARS.

MANPOWER STUDY OF VISUAL SCIENCES

This study is concerned with the evaluation of individuals training in the field of ophthalmology; it was begun in 1968 and will last three or four years. The study includes a survey of the current and projected needs for ophthalmic research and training, professional services and the ophthalmological and optometric manpower necessary to meet the needs for treatment of visual disorders in the United States and evaluate the status of training, both basic and clinical, in the visual sciences in the United States.

Biometry, Epidemiology and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	15	$104,000	15	$104,000	--	$ ---
Other expenses.....	--	199,000	--	213,000	--	+14,000
Total.....	15	303,000	15	317,000	--	+14,000

MODEL REPORTING AREA

Blindness Statistics

The Section on Blindness Statistics conducts a continuing program of collecting, analyzing, and publishing statistical data on blindness disabilities. This Section has encouraged and supported the establishment of registers for the blind in 16 states, and as a result, data is presently being compiled on about 90,000 cases involving vision impairment. The ultimate objective of the program is to develop a national reporting system for all states which will standardize pertinent information on severe visual impairment cases.

The Section will continue its efforts in this direction by encouraging additional states to participate in this program so that more complete and reliable data can be made available to NIH scientists and other organizations involved in health programs and clinical research seeking ways of preventing and treating blindness. The Section has been, and will continue to be, active in working with official, volunteer agencies, or individuals by providing statistical methodology and technical support to their research activities.

EPIDEMIOLOGY

Intensive investigations of eye disease among twins are currently in progress. These studies utilize a registry of over 450 pairs of twins all located in the Washington, D.C. area. The screening phase of these studies continue as new twins are enlisted and specialized studies using this twin population are underway. These studies of identical and non-identical twins will provide important information regarding the role of inheritance in glaucoma, myopia, and other eye disorders.

Observations of the visible blood vessels and other structures in the fundus of the eye have a great value in studies of cerebral arteriosclerosis and degenerative disorders of the ocular nerve and the retina. However, for such observations to be meaningful, precise methods of evaluating and measuring these vessels must be developed. The use of television scanning devices and advanced television technology presents a promising avenue of research and development in this area. In collaboration with the National Center for Health Services Research and Development of the Health Services and Mental Health Administration, a workable television ophthalmoscope and techniques for its employment are being developed.

Collection of data for study of malignant tumors of the eye among residents of the United States has been completed. These data, based on the review of death certificates, provide the first description of mortality in the United States due to specific ocular tumors. These data will be analyzed and reported in the near future.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and Benefits	8	$ 65,000	15	$190,000	+ 7	+ $125,000
Other expenses	-	301,000	--	276,000	-	- 25,000
Total	8	366,000	15	466,000	+ 7	+ 100,000

EXTRAMURAL PROGRAMS

The extramural programs of the NEI will assume its program development and grants administrative responsibilities in 1970. Six positions of the NINDS will be transferred to extramural programs along with associated expenses. Seven new positions are requested to make the transition to a separate organization. The additional staff will provide program leadership necessary to effect the transfer of the NEI major responsibilities for program decisions for its grants and awards programs.

Included in the net increase of $100,000 is $125,000 for support of seven new positions and $22,000 for travel, supplies and equipment of this new office. There is an offsetting decrease of $47,000 for the National Institutes of Health Management Fund.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	--	--	8	$ 95,000	+ 8	+ $ 95,000
Other expenses	--	--	-	25,000	-	+ 25,000
Total	--	--	8	120,000	+ 8	+ 120,000

This activity supports professional and administrative direction of the Institute's activities. The Office of the Director provides for the centralized supervision, coordination and review of these programs, as well as for the direction of the administrative functions of finance, personnel, supply, travel, space utilization and management analysis.

The increase includes $95,000 and eight positions which includes the Director and his administrative staff. An amount of $14,000 is included for administrative support cost and $11,000 for centrally furnished services of the National Institute of Health Management Fund.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Review and Approval			
Associate Director	GS-16		$22,835
Scientific Admin.(Bio. Science)	GS-13		14,409
Physiologist	GS-13		14,409
Administrative Officer	GS-12		12,174
Secretary	GS- 7		6,981
(2) Secretary	GS- 5		11,464
		(7)	82,272
Program Direction			
Director	208 g		28,000
Executive Officer	GS-14		16,946
Information Officer	GS-14		16,946
Budget Officer	GS-12		12,174
Secretary	GS- 8		7,699
Secretary	GS- 5		5,732
Clerk-Steno	GS- 5		5,732
Clerk-Typist	GS- 5		5,732
		(8)	98,961
Total new positions, all activities		(15)	181,233

TUESDAY, APRIL 1, 1969.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

WITNESSES

DR. DORLAND J. DAVIS, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JOHN R. SEAL, DIRECTOR, INTRAMURAL RESEARCH, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
WALTER H. MAGRUDER, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
MARTIN J. FULLER, JR., FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	6,347	6,901	6,979
Positions other than permanent	80	95	95
Other personnel compensation	121	126	126
Total personnel compensation	6,548	7,122	7,200
Personnel benefits: Civilian employees	704	783	791
Travel and transportation of persons	295	320	320
Transportation of things	83	100	100
Rent, communications, and utilities	266	303	303
Printing and reproduction	56	60	60
Other services	15,994	18,065	18,872
Supplies and materials	1,745	1,900	1,900
Equipment	1,267	500	500
Grants, subsidies, and contributions	71,287	74,035	73,891
Subtotal	98,245	103,188	103,937
Quarters and subsistence charges	−15	−15	−15
Total obligations	98,230	103,173	103,922

PERSONNEL SUMMARY

Total number of permanent positions	768	718	737
Full-time equivalent of other positions	7	10	10
Average number of all employees	697	713	720
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	58,520	60,185	60,582
(b) Fellowships	3,911	4,362	4,191
(c) Training	8,856	9,488	9,118
Total grants	71,287	74,035	73,891
2. Direct operations:			
(a) Laboratory and clinical research	13,530	14,581	15,182
(b) Collaborative research and development	9,677	12,630	12,855
(c) Training activities	154	165	155
(d) Review and approval of grants	1,394	1,438	1,531
(e) Program direction	269	324	308
Total direct operations	25,024	29,138	30,031
Total program costs, funded [1]	96,311	103,173	103,922
Change in selected resources [2]	1,919		
Total obligations	98,230	103,173	103,922
Financing:			
Comparative transfers to other accounts	—7,800	—9,783	
Unobligated balance lapsing	3,812	3,450	
Budget authority	94,242	96,840	103,922
Budget authority:			
Appropriation	94,422	96,840	103,922
Transferred to other accounts	—180		
Appropriation (adjusted)	94,242	96,840	103,922
Relation of obligations to outlays:			
Obligations incurred, net	90,430	93,390	103,922
Obligated balance, start of year	56,489	54,334	62,651
Obligated balance, end of year	—54,334	—62,651	—71,144
Adjustments in expired accounts	—2,053		
Outlays	90,532	85,073	95,429

[1] Includes capital outlay as follows: 1968, $815,000; 1969, $500,000; 1970, $500,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $11,061,000; (1968 adjustments $35,000) 1968, $13,015,000; 1969, $13,015,000; 1970, $13,015,000.

Mr. FLOOD. Now we have the National Institute of Allergy and Infectious Diseases.

We have with us Dr. Dorland Davis, the Director. I see you have a statement, Doctor. How do you wish to proceed?

Dr. DAVIS. With your permission, I would like to read it.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Mr. FLOOD. Your biographical statement will be included in the record at this point and you may proceed.

(The biographical sketch follows:)

Name: Dorland J. Davis, M.D.

Position: Director, National Institute of Allergy and Infectious Diseases.

Birthplace and date: Chicago, Ill., July 2, 1911.

Education: 1933 University of Illinois, B.S.; 1937 Johns Hopkins University, M.D.; 1940 Johns Hopkins University, Dr. P. H. (epidemiology); and 1949 certified by the American Board of Preventive Medicine and Public Health.

Experience: 1964 to present, Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; 1956, associate director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; 1954, Chief, Laboratory of Infectious Diseases, National Microbiological Institute (now National Institute of Allergy and Infectious Diseases) NIH; and 1939, Commissioned Officer on duty at National Institutes of Health (1943–1844 on

duty in North Africa for the State Department) advanced through grades to Assistant Surgeon General, 1968.

Association memberships: Fellow, American Academy of Microbiology; Fellow, American College of Preventive Medicine; American Association of Immunologists; American Epidemiological Society; American Society of Tropical Medicine and Hygiene; World Health Organization Panel on Virus Diseases; board of directors, Gorgas Memorial Institute of Tropical, and Preventive Medicine, Inc.; Member National Research Council, Division of Medical Sciences (executive committee).

Special awards, citations, or publications: Edward Rhodes Stitt Award, Association of Military Surgeons of the U.S., 1955; Pih Beta Kappa; Meritorious Service Medal, Commissioned Corps, USPHS, 1967; and publication of 43 papers on infectious diseases.

General Statement

Mr. Davis. Mr. Chairman and members of the committee, we now know how to control some infectious diseases through sanitation, vector control and the use of antibiotics. Vaccines prevent other infectious illnesses, such as poliomyelitis and measles. And yet, the battle continues since more than 100,000 Americans still die each year from infectious diseases. Influenza and pneumonia influenza deaths account for about 70,000 of these deaths in an ordinary year. In years of influenza epidemics, such as the current one, the number of deaths always increases. For example, the latest information is that approximately 15,000 to 20,000 more deaths have occurred this past winter than would normally be expected.

Mr. Flood. I notice in the original statement you presented to the committee for advance reading this statement:

"For example, approximately 7,000 more deaths have occurred this past winter than would normally be expected."

You just stated, "15,000 to 20,000." When did you arrive at the 7,000 figure? How long ago?

Dr. Davis. That was made in January of this year.

Mr. Flood. What is your source of information? Where do you get the information?

Dr. Davis. These figures come from the National Communicable Disease Center, largely, and——

Mr. Flood. How could they make such a glaring error?

Dr. Davis. In January there were only about 7,000 deaths. The epidemic has continued into January and February, and also the records showing excess deaths have continued to come in during February and March and as of the present time our estimated—this is an updated figure—our estimate is——

Mr. Flood. This is not an error; it is just reporting the latest statistics?

Dr. Davis. Yes.

Mr. Flood. That makes me feel better because that is a shocking difference.

Hong Kong Influenza

Dr. Davis. Everyone is familiar with the story that epidemic influenza began in Asia last summer. The causative virus was quickly characterized in the laboratory as different from the previous Asian influenza viruses.

Mr. FLOOD. Do you mean it came from the hinterland into Hong Kong, from the Interior of China, perhaps?

Dr. DAVIS. We don't know actually what the origin was this year. It was first recognized in Hong Kong. It could very well have come from the interior of China.

Mr. FLOOD. It just wouldn't spring up in Hong Kong like Topsy, would it?

Dr. DAVIS. It is interesting that in 1957 there is good evidence that the new strain did originate in South China and then spread to other parts of the world. This presents some very interesting problems of why South China seems to be the origin of at least two and possibly more new strains of influenza virus. We don't have an answer to that.

For this reason, we expected that a worldwide epidemic might occur and that the usual vaccine would not be effective. The new Hong Kong virus was studied in many U.S. laboratories and sent to licensed manufacturers for vaccine production. Mobilization of the Institute's existing resources both intramurally and in the Vaccine Development Branch followed promptly for the study of new vaccines. For example, the Oak Ridge National Laboratory (AEC) has developed a high-speed, high-capacity zonal centrifuge for the production of concentrated or purified vaccine with NIAID contract support.

Mr. FLOOD. What is a zonal centrifuge?

Dr. DAVIS. It separates the different particles out into different zones. This is done by putting the material into what we call a gradient, either a sucrose gradient or another kind of gradient.

Mr. FLOOD. What material?

Dr. DAVIS. The virus-containing material. By use of this device—particles of different sizes can be distributed into different sections of the centrifuge cup and then withdrawn in such a manner as to give the separation. It is a very useful and new instrument for separating particles.

Mr. FLOOD. That may have contributed, I suppose, to the speed with which a vaccine was developed to attack the so-called Hong Kong flu?

Dr. DAVIS. Yes, it did help. At least in providing vaccine for evaluation studies.

Actually the preliminary results show that the zonal centrifuged vaccine has produced fewer side reactions than older types and this is the advantage of the zonal centrifuge. The vaccine is more purified, more concentrated, and the usual unpleasant reactions that one often associates with influenza vaccine seem to be not present.

Preliminary results show that the zonal centrifuge vaccine has produced fewer side reactions than older types. We await the end of the influenza season and laboratory reports to assess the precise effectiveness of this vaccine in preventing illness.

PNEUMONIA

Pneumococcal pneumonia often follows influenza. In fact, this bacterial complication is the major killer during influenza epidemics. Even in years when the incidence of influenza is low, pneumococcal pneumonia is reported to cause from 25,000 to 40,000 deaths annually.

Mr. FLOOD. Is that because the influenza has reduced resistance in the patient?

Dr. DAVIS. Yes, that is a good explanation. The patients become ill and organisms present in the respiratory tract then have a chance to take over and grow.

The goal of the Institute's pneumonia vaccine program is the development of a polyvalent vaccine effective against the types of bacteria which cause the most pneumonia. As I reported last year, the Institute undertook a survey to identify specifically the most prevalent types of pneumococcal bacteria and the population groups at highest risk of infection. Production of experimental vaccines against the 12 most common types of pneumococci is now underway. After preliminary tests in humans demonstrate safety and efficacy, mass vaccination trials will begin. We estimate that an effective vaccine given to high-risk groups should prolong the lives of 15,000 to 25,000 persons per year and save $50 to $100 millions in hospitalization and medicare costs.

Mr. FLOOD. Several years ago we were told, and the public generally thought—apparently erroneously—that the incidence of pneumonia of all types and kinds had gone down dramatically and it was no longer the great infectious killer that it had been all through history.

Now all of a sudden I find out that isn't true, that the incidence of pneumonia has gone back up and it really is a big killer. Are you aware of that story in the last 8 or 10 years?

Dr. DAVIS. Yes.

Mr. FLOOD. Was the story wrong or what happened?

Dr. DAVIS. Following the introduction of penicillin, particularly, the number of deaths was dramatically reduced. Now, looking back after 20 years and examining the experience with treatment by penicillin, which is often administered in the home rather than in hospitals—this is another reason why the incidence appeared to be reduced—studies by the University of Pennsylvania, which we have supported, indicate that, as you say, the number of cases is actually about the same or even increased. The death rate is reduced from pre-penicillin totals, but there are still a large number of deaths due to pneumococcal infection. These are usually in people who die early in the course of the disease, that is within a few days too soon for the penicillin to be effective. We would like to have a good vaccine so they need not get ill at all.

INFECTIONS ACQUIRED IN HOSPITALS

Mr. FLOOD. Why is it that sometimes a person will go to the hospital with a comparatively minor ailment and get pneumonia and die 3 or 4 days later? There are too many such cases of pneumonia being contracted in the hospital, unrelated to the original condition for entry. You go there and get pneumonia in the hospital. Why? An awful lot of people do.

Dr. DAVIS. Many of these, of course, are individuals who contracted the disease before going to the hospital.

Mr. FLOOD. Do you mean it is a coincidence that the timing was such?

Dr. DAVIS. Many of them are——

Mr. FLOOD. Oh, now, Doctor. I am talking about actual acquisition of the infection in the hospital. There is a high incidence of that, isn't there?

Dr. DAVIS. I don't know of any specific studies which would indicate this for pneumonia.

Dr. MARSTON. Mr. Flood, I think the hospital problem is particularly that of drug resistance related to a staphylococcal problem which has concerned people so much in recent years. There are two concerns about that: One, there was an increased incidence in the occurrence of penicillin-resistant staphylococcal pneumonia of patients in the hospital, more because you have a more susceptible population and you have the organism which was there, and this has led to a recurrence——

Mr. FLOOD. That doesn't account for the dramatic increase in the infection. The population has always been susceptible but why are they now more susceptible and why are there more cases?

Dr. MARSTON. The specific problem with hospital-acquired pneumonia has been the *Staphylococcus*. The *Staphylococcus* in the hospitals has tended to be resistant to drugs. A bacterium not sensitive to penicillin, for instance, makes an enzyme—a pencillinase—which actually breaks down the penicillin.

Mr. FLOOD. A new strain of the bug has developed that uses the antibiotic for dessert and thrives on it?

Dr. MARSTON. Yes, sir. In the very early days, following the discovery and production of penicillin, it was found that the *Staphylococcus* particularly could develop an ability to produce an enzyme which would break down the penicillin and would make it ineffective in the treatment of diseases. This has been the problem particularly in hospital pneumonia. It hasn't been a problem with increased pneumonia due to pneumococcus and some other organisms, but it has been the specific problem with the *Staphylococcus*.

Now, the reason that this particular penicillin-resistant *Staphylococcus* has a higher incidence in the hospital is probably because there is more use of antibiotics there and, therefore, more selection of the organisms.

There have been studies that Dr. Davis would be able to speak to better than I could of actual carriers of penicillin-resistant *Staphylococci* in the nose of hospital personnel. It has led us back, in recent years, to the type of isolation techniques we had begun to be lax about following the discovery of the antibiotics because——

Mr. FLOOD. Isn't there also an administrative problem, lack of soap and water and elbow grease, just plain uncleanliness?

Dr. MARSTON. Most hospitals now have staphylococcal committees who are monitoring the prevalence of the penicillin-resistant *Staphylococci* all the time and are reintroducing the kind of management techniques you are talking about. Whenever they see any evidence of an increased incidence, they put out plates, dishes, in the environment to check to see if these organisms are present.

Mr. FLOOD. You may proceed, Doctor.

RUBELLA

Dr. DAVIS. Rubella, or German measles, a mild disease in children, can deform the unborn child of a mother who has no immunity to the

virus. The tragedy of rubella was emphasized during 1964–65, when an epidemic in the United States left in its wake an estimated 30,000 abnormal children.

The rubella research story illustrates what can happen when we have the essential information and congressional support for getting a job done. The rubella virus was isolated 7 years ago. Since then (1) the virus has been attenuated to the point where it can produce immunity without causing disease, (2) tests have been developed for precisely measuring immunity to rubella, and (3) candidate vaccines have been employed in clinical trials. This rapid progress amply demonstrates the value of collaborative research, as administered by the Institute's Vaccine Development Branch. After Drs. Meyer and Parkman, Division of Biologics Standards, developed their HPV–77 attenuated rubella virus strain, the efforts of a number of pharmaceutical companies under contract to NIAID were quickly channeled into new programs of production, using the HPV–77 strain. Attenuated vaccines were prepared in three tissue culture systems, were carefully studied in laboratories, were evaluated in closed populations, and are now undergoing extensive field trials. One field trial was conducted on Taiwan involving 9,900 schoolboys during a rubella epidemic. Among those boys vaccinated prior to exposure, more than 90 percent showed effective protection against the natural disease. Studies of these and other vaccines were reported at the recent International Conference on Rubella Immunization held at NIH. We expect that the accumulated evidence will justify licensing one or more candidate vaccines for commercial production before the next rubella epidemic predicted for the early 1970's.

Mr. FLOOD. How can you predict an epidemic?

Dr. DAVIS. On the basis of past experience. Rubella epidemics have occurred about every 8 or 9 years in the last several decades. The one in 1964 and 1965 was unusually severe.

Mr. FLOOD. Why? Why an epidemic every 9 years?

Dr. DAVIS. The usually accepted explanation is that it takes about this long for youngsters who are susceptible to come into the population and build up enough susceptible children so that the virus then will spread in a natural way. This is the explanation with regard to measles and many other epidemics. The new youngsters coming into the population.

THE NEXT DECADE

Developments in the production of vaccines are but a part of the battle against infectious diseases. As we look ahead to the decade of the 1970's, several ecological factors directly affect diseases within the purview of this Institute. Our cities with their influx of the unskilled, slum housing, air pollution, and excessive crowding, present us with some of our most urgent health problems. Urban populations are particularly subject to diseases such as infantile diarrhea, pneumonia, tuberculosis, and the venereal diseases, largely because of economic and social conditions.

A more mobile society and jet-age travel will undoubtedly contribute to the speed with which certain infections, such as influenza, are spread. Air and water pollution will increase the potential for microchemical as well as microbiological insults to healthy individuals. And

as the average life span is extended, a larger proportion of our population will be aged citizens with impaired health who are at greater risk to infectious diseases.

Present research gives us reason to hope that specific vaccines will be available during the next decade against: *Mycoplasma pneumoniae*, now known to be a cause of primary atypical pneumonia in young adults; *respiratory syncytial virus*, incriminated only 5 years ago by NIAID scientists as a major cause of infant pneumonia; and the *parainfluenza viruses, the* major causes of upper respiratory disease in younger children and of the well known croup. We are confident that NIAID-supported research will contribute to the goal of reducing the Nation's infant death toll by 50 percent in 1976.

We are also committed to the objective of conquering such health problems as respiratory diseases of children, hepatitis and infectious mononucleosis. In addition, we will want to learn more about the immune mechanisms of the body in order to understand clinical allergies such as asthma, autoimmune diseases such as glomerulonephritis, and the rejection phenomena so important to organ transplantation.

Mr. FLOOD. What is croup? I though that was obsolete and an old-fashioned term. I haven't heard it for years.

Dr. DAVIS. Croup refers to the particular kind of cough which accompanies a severe respiratory infection in children. We now know that the parainfluenza viruses——

Mr. FLOOD. The condition is not obsolete and neither is the term. The use of it is, but it still exists as such?

Dr. DAVIS. Croup is an old term. Nowadays they use longer words.

Mr. FLOOD. Yes, I notice. So do you.

INTERFERON

Dr. DAVIS. Although many viral diseases can be *prevented* by vaccines, none can be cured by drugs. A somewhat mysterious substance known as *interferon* helps the body throw off viral infections. Interferon also has such desirable properties as being active against all viruses so far tested—over 100—and some other microbes and as having no toxicity. However, interferon is species specific, and adequate quantities of the human variety are impossible to obtain. Scientists have turned their efforts to the study of inducers that stimulate the body to make extra amounts of its own interferon. A recent laboratory study on the effectiveness of induced or applied interferon in assisting recovery from viral infections was conducted jointly by investigators from our institute and from New York Medical College. These scientists demonstrated that interferon induced by a chemical known as polyI:C cured eye infection in rabbits as late as 3 days after deliberate exposure of the animals to the herpes virus, a cause of eye disease in man. Most of the untreated rabbits lost their sight and about one-third died.

Another NIAID investigator has shown that polyI:C can inhibit growth of tumors in experimental animals and extend their life. Whether the antitumor effect is specifically attributable to the action of interferon or yet another unknown compound remains to be determined. Our institute, the National Cancer Institute and the Division of Biologics Standards are collaborating on toxicity studies to deter-

mine the practicability of using polyI:C to stimulate interferon against human viral diseases and cancer.

Mr. FLOOD. I have before me an article from the Washington Post, Monday, January 13, 1969. It says "New Compound Fights Tumors."

"A manmade compound that stimulates the body's production of interferon, naturally-produced virus-fighter, has been found effective against virus-produced tumors in test animals."

"In his report, Dr. Levy, of the National Institute of Allergy and Infectious Diseases, disclosed that PolyI:C was effective in reducing, sometimes obliterating a variety of virus-caused tumors in test animals. No one has yet proved that viruses cause human cancers—but scientists are working on that theory."

What about the use of the product interferon? Can you create interferon chemically?

Dr. DAVIS. Interferon is a protein which is produced by the cells within the tissues as a defense against invasion by virus. When viruses attack the cells, this is their response, to produce interferon.

What the inducers do, is to kind of fool the cells into thinking that they are being attacked because the chemical constituent of the inducers is similar to some of the chemicals in a virus.

Mr. FLOOD. What the interferon does, as I understand it, is to prevent the reproduction in the cells of the virus, is that it?

Dr. DAVIS. It prevents the reproduction of the viruses within the cell. The inducers stimulate the production of this interferon before the cell is actually attacked by the virus and so it can protect iself.

Mr. FLOOD. If you could produce interferon artificially, or if you could, by this inducer, develop a thousand times more interferon than normally exists within the body, this would be the most stupendous thing that has happened in the history of medicine. You would have one thing within the body itself to destroy and fight all infections and all viruses, instead of having vaccines pointed against one. You would eliminate the need for vaccines.

Mr. DAVIS. This is essentially the way it is, Mr. Flood.

Mr. FLOOD. That is really out of this world, that concept, isn't it?

Dr. DAVIS. The interferon prevents invasion of cells by viruses primarily, but also some other microbes such as the parasites. Many of the bacteria, however, do not necessarily invade the cell, but just do their damage outside the cell within the tissues.

Mr. FLOOD. But the fact still remains, if you could create interferon. artificially, or if you could, by induction, cause the body to produce a hundred or a thousand times greater quantity of interferon than now exists, you would in effect have made a breakthrough probably never equaled in medical history since the beginning of time.

Dr. DAVIS. We think this is an extremely significant advance. It should be understood this work is still in the animal stages. It has not been used extensively in man.

Mr. FLOOD. I understand the Russians did use it.

Dr. DAVIS. There have been a few trials.

Mr. FLOOD. Aren't we about to use it this year?

Dr. DAVIS. Yes, and there are plans for the proper controlled use of these inducers. One of the problems is the toxicity of these inducers and this is what the chemists and the scientists are attacking now, to be sure that——

Mr. FLOOD. So that is the problem. The toxicity?

Dr. DAVIS. That is the major problem at the moment. The potential toxicity of the inducers.

Mr. FLOOD. So much a problem this may never come about?

Dr. DAVIS. For topical application such as in eye infections and perhaps for skin infections——

Mr. FLOOD. How about the common cold?

Dr. DAVIS. The common cold, it might be effective by topical application into the respiratory tract.

Mr. FLOOD. This might be the answer to the attack on the common cold. We have no other.

Dr. DAVIS. This might very well be. We are really very encouraged about this.

Mr. FLOOD. I have before me an article from the Wall Street Journal of February 17, 1969. The headline is "Scientists See Promise in New Line of Attack on Infectious Diseases. Aim Is To Employ Interferon, a Natural Defense: Use on Colds, Cancer Studied."

We will place that and the Washington Post article on this subject of interferon in the record.

(The articles follow:)

[From the Washington Post, Jan. 13, 1969]

NEW COMPOUND FIGHTS TUMORS

(By Nate Haseltine)

A manmade compound that stimulates the body's production of interferon, naturally produced virus-fighter, has been found effective against virus-produced tumors in test animals.

The finding was reported in Lyons, France, by a Bethesda, Md., virologist, Dr. Hilton Levy. It may have far-ranging results for mankind, particularly if it is ever proved that viruses cause human cancers.

When existence of interferon was first reported by British scientists Isaacs and Lindenmann in 1957, it was generally scoffed at. Since then vast research has been conducted to show that all living things, including plants, produce their own anti-viral substance, interferon.

The trouble is that nature produces interferon too slowly to provide protection against most viruses, particularly flu "bugs." And each living thing, including plants, produces its own special type of interferon.

A race began to find ways to stimulate the body's production of interferon.

A breakthrough was made in 1968 when scientists at Merck, Sharpe & Dohme Laboratories produced a chemical combination—a double-stranded ribonucleic acid called Poly–I–C—to trigger the release of interferon in rabbit corneal eye cells.

Dr. Ralph Pollikoff, virologist at Temple University Health Sciences Center, Philadelphia, reported that use of Poly–I–C helped combat two different viruses which normally cause ulcerations of rabbit eyes. Interferon, triggered by Poly–I–C, he reported hastened the healings and prevented blindness even when the stimulant was used three days after infections.

In his report, Dr. Levy, of the National Institute of Allergy and Infectious Diseases, disclosed the Poly–I–C was effective in reducing, sometimes obliterating, a variety of virus-caused tumors in test animals. No no has yet proved that viruses cause human cancers—but scientists are working on that theory.

In a press conference here, Dr. Samuel Baron, a research colleague, said study had shown that an animal's body, including man's, naturally produces "only one one-hundredth to one one-thousandth enough interferon to effectively protect against viral invasions."

Dr. Levy, in his Lyons report, said he had quelled leukemias (blood cancer) in mice with Poly–I–C, and that the compound showed "a definite effect" on a variety of fast-growing hard tumors.

All the animals were purposefully infected either by virus injection or by tumor transplants of virus-caused tumors.

About 30 percent of the RNA-treated animals have survived, he stated. In contrast, all animals used as controls died of their cancers.

Virologists said that at this stage there are no plans to use Poly-I-C on humans, although Dr. Levy said the animal tests may justify an application with the Food and Drug Administration for an IND (investigational new drug) permit for human trials.

[From the Wall Street Journal, Feb. 17, 1969]

FIGHTING VIRUSES—SCIENTISTS SEE PROMISE IN NEW LINE OF ATTACK ON INFECTIOUS DISEASES—AIM IS TO EMPLOY INTERERON, A NATURAL DEFENSE; USE ON COLDS, CANCER STUDIED—MUCH RESEARCH STILL NEEDED

(By Jonathan Spivak)

WASHINGTON.—Medical men are probing the mysteries of a virus-fighting protein molecule, known as interferon, that may hold the key to protection against a host of diseases.

Many experts believe interferon could prevent the common cold, as well as aid in treatment of more serious viral diseases, such as hepatitis and smallpox. The substance works by triggering the body's own defense mechanisms against infection.

"It's very, very promising," declares Merck & Co.'s Maurice Hilleman, one of the nation's leading interferon researchers.

"We hope to begin clinical tests this year," says Dr. Thomas C. Merigan of the Stanford University school of medicine, adding that the first studies are encouraging. Experiments on animals have indicated that interferon can cure viral pneumonia and eye infections and can halt some cancerous growths in animals.

Many months, perhaps years, of laboratory and human trials will be needed before interferon's practical potential is fully explored. And problems of safety and efficacy could prevent its application to human disease, doctors warn. But if obstacles do not arise, the substance could supply medical men with an entirely new strategy against viral infection—a single chemical compound effective against scores of viruses rather than a variety of vaccines each aimed at a single bug.

ATTACKING THE COLD

If interferon lives up to its promise, one of the first targets will be the common cold, because of its prevalence and the need for effective, inexpensive protection. Industry loses billions of dollars annually through employee absenteeism and disability caused by sniffles and sore throats. Vaccination for colds appears impractical despite diligent efforts by drug-company researchers; separate immunizing agents would be required for each of the 50 or more cold-causing viruses.

But interferon, a complex protein manufactured by the body in response to infection, appears effective against most respiratory viruses. Some scientists envision the development of an easy-to-use interferon spray that could ward off scores of troublesome cold viruses. "When epidemics break out, absenteeism in schools and factories could be cut down," says Dr. Samuel Baron, a researcher at the Government's National Institutes of Health.

Scientists say interferon could also be used to combat other respiratory infections, such as influenza. Vaccines are available against these diseases, but they are not completely effective. While interferon treatment of more severe diseases such as hepatitis and smallpox is also possible, it might pose greater difficulties; these viruses spread widely through the body and would be less accessible to interferon's action than the respiratory invaders.

PLANS FOR CLINICAL TRIALS

Interferon does not attack viruses directly but enables besieged cells to block the viruses' ability to reproduce; chemicals can be used to stimulate interferon's production by the body. Most experiments so far have been with animals, but major U.S. clinical trials in human beings are likely to start later this year or next year. They'll be conducted under the auspices of the National Institutes

of Health at a number of U.S. medical centers. In addition, researchers at Stanford hope to sponsor interferon trials abroad.

NIH's Institute of Allergy and Infectious Diseases will spend almost $1 million this year for basic research on interferon. Many drug companies are actively pursuing possible applications. Among them are Merck, Chas, Pfizer & Co., Smith Kline & French Laboratories, Eli Lilly & Co. and Schering Corp.

U.S. scientists are reluctant to undertake interferon tests in humans until they have resolved all questions about safety, but the Russians have already reported successful use of the substance in human trials against influenza and a virus-caused eye infection. Some American experts are skeptical about the findings, however, because of sketchy Soviet data.

Though the body produces interferon as a natural defense against infections, often it's not available rapidly enough or in large enough quantities to halt the spread of disease.

STIMULATING PRODUCTION

At first, researchers hoped that interferon itself could be produced and administered as a drug. But the substance has proved costly and impractical to produce in the desired quantities; it must be extracted from the blood of human volunteers. Manufacture of a synthetic form is impossible, because interferon's precise chemical composition remains unknown.

Instead, scientists are using natural or synthetic chemicals to prime the body's production of interferon. "The studies in our laboratory during the past several years have been directly especially to the discovery of a highly active interferon-inducer which would be worthy of clinical evaluation," reports Merck's Mr. Hilleman.

A number of possible interferon-stimulating substances have been examined, including plastics, molds, harmless viruses and bacteria, and synthetic forms of RNA (ribonucleic acid), a genetic material found in living cells. The basic goal is to find a material that is safe and capable of stimulating enough interferon to immediately overwhelm attacking viruses. The ideal substance would also be inexpensive, easily manufactured and convenient for patients to take.

So far, the most promising substance appears to be a synthetic RNA designated I:C (for inosinic-cytidylic acid). It is manufactured for basic research studies by several firms. Merck scientists unexpectedly discovered that I:C stimulated interferon production and that it could cure viral pneumonia in mice. More recently NIH scientists demonstrated that I:C will cure a viral eye infection of rabbits and halt the growth of malignant tumors in mice.

Merck scientists say I:C is far too toxic for use as a cold remedy, and they are not planning to try it out on human beings as a cold fighter. But the safety standards can be less stringent for use of I:C against cancer, because of the disease's far greater health hazards. And so NIH's National Cancer Institute will sponsor the first major U.S. trials, expected to start this year. The institute is now performing preliminary safety tests that could require several months. Scientists in the cancer field warn against undue optimism about interferon-inducers; many initially promising anticancer compounds have turned out to be valueless.

If all doubts about safety can be resolved I:C's effectiveness will be assayed in more than 100 cancer patients. They will be treated at NIH's clinical center in Bethesda, Md., and other institutions, including Veterans' Administration hospitals in Washington, D.C., and New York City, the Mayo Clinic in Rochester, Minn., and M. D. Anderson Hospital in Houston.

What most excites the Government researchers is the possibility that I:C could be useful against solid, slow-growing tumors, like lung and colon cancer, against which drugs have proved least effective. "If we have activity (effectiveness), I'd think we'd know before the year is out in some key diseases," says Dr. Gordon Zubrod, the National Cancer Institute's scientific director for chemotherapy.

SEVERE REACTIONS

Another interferon-stimulating substance, a plastic known as pyran, is already under NIH-sponsored test as an anticancer drug. It's more toxic than I:C, however, and causes severe reactions, such as internal bleeding. Dr. Bruce Shnider of Georgetown University, chairman of a group of participating scientists, says preliminary results show some promise, but it is far too early to reach any conclusions.

Even if I:C and pyran prove useless against cancer, the effort won't be wasted. NIH scientists hope the cancer tests will be the first step in a broader effort to use interferon stimulation for treatment of other diseases. The knowledge acquired could help scientists develop more effective, less toxic stimulators.

Some specialists think variations of synthetic RNA substances may ultimately provide the answer. But Merck scientists believe naturally occurring RNA may work better and more safely. They are currently working to extract RNA from a harmless bacterial virus for testing as an interferon stimulator.

Interferon was discovered by British scientists in 1957, but it has taken researchers years to unravel its mode of action. Experts at NIH's Institute of Allergy and Infectious Diseases, Stanford University, the Medical College of Virginia and Merck's Institute for Therapeutic Research at West Point, Pa., have played leading roles. Much of their research has dealt with subtle, subcellular biological processes.

HOW VIRUSES WORK

Viruses are stealthy invaders that do their damage by taking over the productive machinery of cells and directing them to produce thousands of identical infectious virus particles. Interferon acts, in effect, to warn cells of imminent viral attack and enable them to avoid destruction.

The process is complicated. Interferon stimulates cells to make a second substance, called antiviral protein. This material permits cells to recognize a virus as a foreign invader and refuse to follow its "wrong" manufacturing instructions. As a result, multiplication of the virus and spread of the disease are halted.

A major uncertainty is whether interferon stimulator will work quickly enough to cure disease; if not, its application could be limited to prevention. Another problem is making certain interferon is available precisely where needed; the substance works only when it comes in direct contact with threatened cells. Thus, massive amounts might be needed to reverse viral infections such as smallpox that afflict the whole body.

Mr. FLOOD. We will also place in the record your special report on this subject.

(The report follows:)

SPECIAL REPORT: INTERFERON RESEARCH AT NIAID [1]

Control of the many diseases caused by viruses is a major segment of the mission of the National Institute of Allergy and Infectious Diseases.

This goal—long sought by medical research—has been partially reached through immunization by vaccines which are preparations of killed or weakened viruses. But each vaccine is only protective against a specific virus. A time can scarcely be visualized when vaccines will, or should, be produced that protect man from all the hundreds of known viruses.

More than 10 years ago, English scientists reported the discovery of a substance produced by the body's cells in response to a viral infection. They named this substance "interferon" beause its presence in the influenza-infected chick cells with which they were working protected the cells from infection by a second virus.

Since then, research has yielded considerable information about interferon. It is now known that though interferon is not virus-specific (as are vaccines) it is species specific. That is, chick interferon is not very effective in mice, nor is human interferon effective, in general, in chickens. But regardless of origin, all interferons are proteins produced by host cells following stimulation by certain foreign substances, such as viruses.

Accumulated evidence suggests that interferon plays an important role in the natural history of many viral infections. An animal's recovery from viral disease can often be related to the concentration of interferon in its tissues, and its resistance or degree of susceptibility to infection can be measured according to the ability of its cells to make interferon. In either cell cultures or animals, interferon definitely limits the growth or multiplication of viruses.

Recent research has indicated that interferon may also play a role in recovery from diseases caused by organisms other than viruses. These include bacteria, rickettsia, and protozoa.

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[1] Prepared January 1969 as background information for the Director of the National Institute of Allergy and Infectious Diseases, Public Health Service, U.S. Department of Health, Education, and Welfare, in connection with fiscal year 1970 appropriations hearings.

During the past year, two exciting research projects by NIAID scientists have contributed to this growing body of knowledge. Both sets of experiments have made use of previous findings that cells can be induced to produce extra amounts of interferon by several nonviral—and, in some cases, synthetic—substances.

VIRAL INFECTIONS

Using one of these nonviral substances, a chemical known as polyI:C, Dr. Samuel Baron of this Institute and a colleague at New York Medical College cured a serious virus-caused eye infection in rabbits. Interferon induced by polyI:C applied as late as 3 days after onset of infection was 100 percent effective—a startling finding when one considers that most viral infections in animals or man are impervious to presently known drugs. This research has now been extended—with similar good results—to other viral infections of laboratory animals.

PolyI:C is a synthetic chemical formed by mixing two commercially available materials. Dr. Maurice R. Hilleman and his associates at Merck Laboratories were the first to show that polyI:C has marked interferon-inducing ability. It is now widely synthesized and used experimentally.

TUMOR STUDIES

Since polyI:C induces interferon which, in turn, is believed to profoundly affect the control of genetic expression in the cell, Dr. Hilton Levy of this Institute decided to try out the chemical's effect on tumors—a prime example of cellular genetic control gone awry. In cooperation with Drs. Lloyd Law and Alan Rabson of the National Cancer Institute, Dr. Levy inoculated mice and rats with a variety of malignant tissues. A series of experiments were carried out to determine the effect, if any, of polyI:C on these "transplanted" tumors. In all studies, treatment with polyI:C was found to decrease the rate of tumor growth and increase survival of the anmals.

In one experiment, when the scientists delayed treatment until tumors were of moderate size, massive tissue destruction took place. However, after a few weeks, these tumors again increased in size, despite continued treatment.

The effect of polyI:C on survival of animals was most marked in experiments using a strain of black mice known as C57. In one such study, all animals treated with polyI:C were alive 41 days later; all untreated animals were dead. In another, 30 percent of the treated animals were alive and with no signs of tumor, 2 months after injections of polyI:C were stopped. In still other studies, polyI:C treatment caused a virtual disappearance of tumor growth.

An interesting twist to this research is evidence that leads the investigators to believe that the antitumor effect of polyI:C may not be attributable to any antiviral action of induced interferon. Other possible antitumor actions of polyI:C are being studied.

At present, studies are underway to determine the toxicity of polyI:C in animals before venturing into testing its effectiveness in treating viral or malignant disease in man. Carefully controlled studies are needed to provide answers to such questions as how much inducer is needed to produce protective amounts of human interferon.

OTHER RESEARCH ON INTERFERON INDUCERS

NIAID-supported scientists and others are engaged in a continuing search for new nonviral inducers of interferon. For example, a synthetic plastic, pyran copolymer, has been found to be a potent stimulator of interferon production in man and experimental animals.

Scientists are eager, too, to find ways of enhancing the activity of interferon-inducers. Cell culture studies have shown that the amount of interferon produced can be increased 100-fold when a chemical—diethylaminoethyl ether of dextran—is added to the culture along with the inducer. If this should prove true in man, less of an inducer could be used and its toxic potential thus reduced.

TRANSPLANTATION IMMUNOLOGY

Mr. DAVIS. The present decade has witnessed the birth of what might be termed a new scientific discipline: transplant science. Today, it is surgically possible to transplant many organs of the human body.

More than 2,300 kidneys, 110 hearts, and 20 livers have been transplanted. Surgeons have also transplanted the lungs, pancreas, spleen and thymus, but with poor results. And within the last 6 months, there have been encouraging reports of successful transplantation of bone marrow. It is generally agreed that there are two immunological keys to making organ transplantation a successful routine: (1) scientists must define, and match as closely as possible, those antigenic substances which determine whether the body recognizezs a graft as compatable or foreign, and (2) the natural immune reaction which cannot be eliminated by matching must be suppressed usually with drugs.

Although tissue matching is still in its infancy, rapid advances have been made in large part through the Institute's collaborative transplantation immunology program. In only 4 years, we have obtained the kind of information in tissue matching that took 25 years to get for blood typing.

A relatively smal number of so-called histocompatibility antigens have been identified in the body's white blood cells which appear to be shared by the body's tissues generally, and which appear to be important in determing the immunological acceptance or rejection of a graft or transplant. Simplified and reliable techniques for tissue matching have been developed using white blood cells and two basic phenomena—cytotoxicity and cell agglutination. The applicability of these methods to the whole complex of patient and donor selection, surgery, pre- and post-operative care is being evaluated by tissue matching facilities established in nine medical centers. In addition, the Institute is providing typing reagents to more than 100 transplantation research centers throughout the world.

Although tissue matching will reduce the body's rejection response, a "perfect" matc hwhich would eliminate all conflict between donor and recipient tissues is very unlikely. Thus, research on methods of suppressing the immune response are very important. Immunosuppressive drugs are generally toxic to the tissues and tend to suppress the body's reaction to infection, so attention has turned to biologic immunosuppressives, such as antilymphocyte serum (ALS). The Institute has launched a major effort to develop better ways of making and testing ALS.

SUMMARY OF BUDGET

In conclusion, Mr. Chairman, the 1970 request for the National Institute of Allergy and Infectious Diseases is $103,922,000, including up to $700,000 for the Gorgas Memorial Laboratory, an increase of $748,500 over 1969 of $103,173,500. The 1970 request provides for increases of $396,500 for research grants; $601,000 for laboratory and clinical research; $225,000 for collaborative research and development; $93,000 for review and approval of grants, and decreases of $171,000 for fellowship; $370,000 for training grants, $10,000 for training activities, and $16,000 for program direction.

I shall be happy to answer any questions.

GORGAS MEMORIAL LABORATORY

Mr. FLOOD. I notice in the requested language on page 2, you ask us to increase the amount earmarked for the Gorgas Memorial Laboratory to $700,000 from $500,000. What is the justification for that?

Dr. DAVIS. The reason for the language as it is listed is that the Congress authorized an increase to a million for the appropriation for the Gorgas Memorial Laboratory.

Mr. FLOOD. That is the maximum amount authorized?

Dr. DAVIS. $1 million, as provided by the act of Congress of last year. When we made up our budget we felt we should recognize this increase in the request of up to $700,000. Yet when we came to the final display and assignment of funds the actual budget proposes only $500,000, which is shown on page 5, I believe, of our obligations by activity, which is the same as last year.

Mr. FLOOD. You know, Doctor, on the books today—I don't know whether it will startle you or not—on the books today there are about $40 billion authorized by Congress for public works, for which Congress has never appropriated a dime over a period of some 25 or 30 years; $40 billion is upstairs there waiting for the money to start these public works projects. So there they are. Just because Congress put a ceiling of a million dollars on this doesn't mean that is the amount to be spent.

Dr. DAVIS. Our proposal is to activate $500,000 of the total budget.

Mr. FLOOD. Then why do you want to go up to $700,000 in the language?

Dr. DAVIS. We don't propose to use $700,000. We propose to use $500,000.

Mr. FLOOD. You have language on page 2, "Not to exceed $700,000." You know what that means. When one of you fellows downtown tells me you are not going to exceed $700,000, that means you are going to spend $700,000, period, unless the rules have changed overnight. That "not to exceed $700,000" is old legal hocus-pocus as far as we are concerned. Why do you want that language? Why not just plain "$500,000"?

Mr. MAGRUDER. We requested this language up to or not to exceed $700,000 specifically for the purpose of having some say on what amount of money would go to Gorgas.

We felt in prior years it was pretty much a limit of $500,000 that had to be put in. This sort of makes it an open thing.

Mr. FLOOD. Indeed it does. That is the point—wide open.

Mr. MAGRUDER. It could be $400,000, too.

Mr. FLOOD. But it is not, it is $700,000. You have gone from five to seven.

Mr. MAGRUDER. We did not have much to do with setting of the million dollar limitation.

Mr. FLOOD. I just told you that. What difference does that make? Just because it is set, do you have to use it?

Mr. MAGRUDER. No.

Mr. FLOOD. That is what the Appropriations Committee is for.

Mr. CARDWELL. The language was put in at this amount in order to give this Institute the option to spend up to $700,000. Under this language, they could not spend more than that. The budget plan at the moment says they will not spend more than $500,000 of the appropriation. If you held the language to $500,000, that is the maximum they could spend even if events later in the year showed a need for a larger amount. I think, simply stated, that is the issue.

CENTRALIZATION OF INTERNATIONAL PROGRAMS IN THE JOHN E. FOGARTY CENTER

Mr. FLOOD. Talking about the Gorgas Memorial and the International Centers for Medical Research and Training, which are under this Institute, what about the Fogarty International Center created by this committee, and in which we have a great interest? We expected that practically all of the international health and medical activities would be transferred to the Fogarty Center. We were led to believe by some in high places in the Department that, under this tremendous reorganization, that is what was going to happen. What about it?

Dr. DAVIS. The Gorgas Memorial Laboratory is an operating agency in which there is required a certain degree of program evaluation and judgment. This is also true of the International Centers for Medical Research and Training. It is my understanding that it was believed that these could be better administered within an operating Institute than they could through the Fogarty Center, which directs its attention to other matters.

Mr. FLOOD. What do you mean, "other matters"? The matters the Fogarty Center will deal with are those matters assigned to it. Why weren't these so assigned?

Dr. MARSTON. Mr. Flood, the total activity of the Office of International Research, which had been in the Director's Office, was transferred to the Fogarty Center. There are some other areas in which the direct program responsibilities, the operational activities, seemed to fit better into the existing Institutes. I am thinking of some of the activities in the United States-Japan program, which is the one I have been reviewing recently, which is focused on the control of infectious diseases as its major activity. So it almost has to be managed by this Institute because it has all of the resources and expertise that is actually needed for this work.

Mr. FLOOD. Do you know that we were certainly led to believe—of course, that is our fault—that in this last dramatic reorganization all international health activities, with perhaps a few minor exceptions would be placed under the Fogarty Center. Are you aware of that?

Dr. MARSTON. I know there was discussion of the whole area of international health activities in the Department as a whole and its relationship to the Fogarty Center.

I think we would have to say that at this time the Fogarty Center is still evolving. The entire Office of International Research, that was a part of the Director's Office, has been transferred in toto to the Fogarty Center. There are other activities both within NIH and within the Department which, as you are quite right, have not been transferred to the Fogarty Center at present.

Mr. FLOOD. Why not?

Dr. MARSTON. In some of the instances that I have had to deal with directly, it has been a matter of where we have the competence for the actual program management. It would not be possible to build up all of the expertise in the area of infectious disease in the Fogarty Center that is required to carry out some of the specific programs.

Mr. FLOOD. Just keep in mind that we intend that the Fogarty Center be given the benefit of the doubt when there is a question as to where activities in the international area are to be placed.

Dr. MARSTON. Yes, sir.

IMMUNOTHERAPY OF SKIN CANCER

Mr. FLOOD. There has been a small but active group, Doctor, interested in immunotherapy of skin cancer. Last year we put language in the report which urged and encouraged that something be done in this field. Have you started anything yet?

Dr. DAVIS. Yes, the Institute has just awarded a research grant to Dr. Klein of the State University of New York in Buffalo. This is for a 3 year period, totaling $190,000. Dr. Klein requested this through the usual research grant channels. It was reviewed in the normal process and he now has his funds and can continue work in this area of immunotherapy of skin cancer.

Mr. FLOOD. You mean the curtain is going up or what?

Dr. DAVIS. He is being supported to investigate the usefulness of this form of therapy.

Mr. FLOOD. You do not seem very enthusiastic about it.

Dr. DAVIS. There are many, many competing needs.

Mr. NATCHER. If the Chairman would yield at that point, Doctor, you say he is being supported. Who is this?

Dr. DAVIS. Dr. Edmund Klein of the State University of New York in Buffalo.

Mr. MICHEL. To what extent is Dr. Klein being supported, moneywise?

Dr. DAVIS. He has just been awarded a grant of $190,000 over a period of three years.

Mr. FLOOD. Is this worthy of very strong support? We would like to know.

Dr. DAVIS. Yes, we think this is an appropriate support for his work. He is a very hard-working, energetic clinician who wants to investigate and further the observations he has made on the use of various chemicals, particularly for the treatment of disseminated skin cancers. He needs to have support for laboratory studies, immunologic studies, which will provide an explanation for it and rationale and perhaps extend it even further. We think this is worthy of support at this level.

U.S.-JAPAN COOPERATIVE PROGRAM

Mr. FLOOD. The U.S.-Japan Cooperative Medical Sciences program has been somewhat controversial. What have you done since we talked about this last year?

Dr. DAVIS. We think that the U.S.-Japan program has been extremely productive in encouraging and accelerating the research activities in a number of important diseases. These are not only diseases which occur in Southeast Asia, to which the program was directed, but also here in the United States, such as tuberculosis. Under the U.S.-Japan program, the number of grants and the number of funds going into research in tuberculosis has just about doubled. We are also concerned with malnutrition, certain virus diseases.

Mr. FLOOD. How much are we putting into this program and how much are the Japanese putting into it?

Dr. DAVIS. We are putting about $6.5 million into the support of research. This is divided about $5 million in grants, about $1.5 million

in contracts. It is very difficult to determine how much the Japanese are devoting to this.

Mr. FLOOD. Why? Did you ever ask them?

Dr. DAVIS. I have not asked them.

Mr. FLOOD. Have somebody ask them and put it in the record. We would like to know.

Dr. DAVIS. The Japanese report their funding in quite a different way than we do. It is much more indirect. Much of their work comes through the Department of Education. The support of research comes through the Department of Education instead of the normal health departments.

Mr. FLOOD. Have somebody try to analyze that and have the record show how much they put into this operation. We would like to know, within reason, what we put in and what the Japanese put in.

(The information follows:)

FINANCIAL SUPPORT OF THE UNITED STATES-JAPAN COOPERATIVE MEDICAL SCIENCE PROGRAM

The United States-Japan Cooperative medical science program is funded with each country paying the costs of research by its own scientists on diseases included in the program. For instance, no U.S. funds are provided for support of research or travel of Japanese scientists. Cooperation consists of agreement by joint panels of scientists on the research objectives for the diseases under investigation and conferences between United States and Japanese scientists at regular intervals.

A comparison of financial support for the programs by each country cannot be precise because of the relative size of national budgets and the fact that much support for the Japanese effort comes from unidentifiable general research funds. The following information has been supplied by the NIH Pacific Office in Tokyo.

Japanese support comes not only from the Ministry of Health and Welfare but also from research grants of the Ministry of Education which is the major funding agency of nationally supported universities and medical schools. In 1967 the total budget for the Ministry of Health and Welfare was $1,778,000 of which $247,000 or 14 percent was for the United States-Japanese program. The Ministry of Education alloted in the same year only $635,000 for all grants for biomedical research. In 1967 U.S. support for biomedical research in the Department of Health, Education, and Welfare (including NIH) was $1,050 million. The Japanese national budget in 1967 provided only $466 million for all science and technology including atomic energy and space.

This is only 3.4 percent of the Japanese budget of $13.750 billion compared to U.S. expenditure of 14.3 percent for science and technology of its 1967 budget of $158.413 billion.

Other differences in the distribution of research funds between the two countries are in the size of grant awards and the cost per research worker. Japanese grants average about $2,600 annually and research costs amount to $8,440 per worker. In the United States the average present size of the NIH grant is $42,571 and the cost per principal investigator is $31,000. The Japanese provide travel funds only for foreign travel while the U.S. program pays all necessary travel whether domestic or foreign. Direct grants from the Japanese Ministry for research do not normally include personnel costs which form 50 to 70 percent of the costs of NIH grants in the United States. Japanese grants for all medical research including United States-Japan program do not provide for total costs of the project and therefore are not comparable to U.S. figures. Necessary additional funding comes indirectly through institutional budgets.

An accepted way of judging the capabilities of different countries to participate is to use as a common denominator a factor derived from the gross national product (GNP) times total population. In 1967 the Japanese GNP and population were $115 billion and 100 million, and those of the United States were $811 billion and 199 million. This results in a U.S. capability 14 times that of Japan.

The following table summarizes available data on funds accounted for by the government support. Although these figures appear to indicate a significant difference in level of effort, they should be interpreted in the light of differences in

total governmental funding of biomedical sciences in the two countries and by the capabilities as indicated by the gross national product.

Purpose	U.S. segment		Japanese segment	
	Fiscal year 1967	Fiscal year 1968	Fiscal year 1967	Fiscal year 1968
Support of research	$3,703,000	$5,283,000	$156,600	$156,600
Conferences and meetings	223,000	242,000	61,500	(1)
Fellowships	0	0	17,800	12,300
Program management	211,000	258,000	10,000	10,000
Total	4,137,000	5,781,000	245,900	178,900

[1] Meetings held in Japan in 1968.

A more meaningful measure would be the contributions of Japanese scientists to new knowledge of the diseases under study and their participation in conferences of the United States-Japan program. In the judgment of the U.S. Delegation of the Joint Committee and the panel chairman, Japanese scientists have made new and significant contributions to our knowledge of disease and to techniques for study. For example, the Japanese reported at the Joint Tuberculosis Panel meeting in Tokyo, August 1968, on the ultrastructure of the tuberculosis bacillus using the electron microscope and the relation of this structure to enzyme activity. In a Joint Panel on Leprosy, the Japanese reported that a specific antibody to the leprosy bacillus could now be identified with the technique of immunofluorescence. Such information is important and new to American or European scientists. Joint conferences are well attended by Japanese scientists. For instance, at the "Conference on the Biology of the Mycobacterioses" in New York, October 1967, 23 Japanese and 44 United States scientists attended. At a Joint Conference on Parasitic Diseases in Japan, May 1968, 70 Japanese and 14 United States scientists attended. Under the aegis of the program the Japanese have formed informal "working groups" of various sizes that stimulate progress but the costs are not reflected in the Japan Ministry of Health and Welfare figures.

Mr. FLOOD. If this thing is as good as you indicate it is, why don't we have a United States-English program, United States-French program, a United States-Brazilian program. Why not?

Dr. DAVIS. This program actually has funds authorized for research. There are agreements between the United States and other countries, for instance, Iran, for cooperative research in the sciences. But these have no funds appropriated to them. I think it would be a very good thing to have a formal research program between scientists of different countries, whether or not they have funds supporting them or not, because this should improve the communications between the scientists of the involved countries, and should accelerate our knowledge of the diseases which are being under consideration.

I would like to say, Mr. Chairman, that we believe that the Japanese scientists are making an equal contribution to the American scientists from the standpoint of their research productivity. We have really been very pleasantly surprised at how much work was going on there. I speak particularly about immunology of tuberculosis. In many areas they were in advance of the United States scientists. The U.S. scientists have learned a great deal by the frequent communications with the Japanese. Incidentally, these are all in English so that there is no problem of communication.

The same is true in leprosy where they have a great deal of experience which our scientists do not always have, and virus diseases, including such things as rabies and Japanese B encephalitis.

Mr. FLOOD. Do they have a high TB incidence in Japan?

Dr. DAVIS. Not very high. This program is directed toward the problems of Southeast Asia.

Mr. FLOOD. I was thinking of Japan itself.

Dr. DAVIS. No, they do not have a particularly high one. It is about the same as this country.

AUTOIMMUNE DISEASES

Mr. FLOOD. On page 14 you refer to the growing list of autoimmune diseases.

What are you talking about specifically? First of all, what do you mean, and then what are you doing?

Dr. DAVIS. Autoimmune diseases are diseases which occur when the body reacts by forming antibodies against some substance which is already present in the body. One of the most important of these, is glomerulonephritis.

There is a fine distinction medically which differentiates an immune response to an antigen, a substance in the body, and formation of scar tissue in certain areas of the body.

Mr. FLOOD. What are you doing about the autoimmunization?

Dr. DAVIS. At the present time the studies are investigating the identification of these substances which can cause the autoimmune response. For instance, in glomerulonephritis there is good evidence that this is caused by an antigen antibody complex which is deposited in the basement membrane of the glomerulus of the kidney and produces a disease with resultant dysfunction of the kidney.

We are supporting a large study on this at Scripps Clinic and Research Foundation in California under the general direction of Dr. Frank Dixon which is leading to a much better understanding of what the process is.

TRANSPLANTATION IMMUNOLOGY

Mr. FLOOD. It is our opinion there is more interest in your activities regarding transplantation immunology than any single group of activities in your entire institute. I do not think there is any doubt about that. What recent advances, if any, can you report on that?

Dr. DAVIS. I would like to mention two things; one is the general area of basic research leading to new knowledge, that is, the identification and isolation of tissue antigens—pure antigens, in a soluble form. This has been done in animals and also in man.

So we now have a tool which can be used to actually desensitize individuals.

Mr. FLOOD. Are you talking about the skin matching program?

Dr. DAVIS. No. The second point I would like to refer to is the improved techniques for tissue typing. This is the matching of these antigens that are found in the white blood cells as representative of the cells of the body, the matching of these antigens between a donor and a recipient prior to the time of transplantation.

This has been going ahead at a very rapid pace. The number of matchings and the number of transplants has increased very rapidly.

In fact, I think that probably no transplants are being made without the tissue matching which is found so necessary.

Mr. FLOOD. Actually that is about the only thing you can get Brownie points for in this whole business of transplantation. As a matter of fact, now that the first dramatac impact of transplantation is wearing off and only a small handful of the patients have survived, you can probably say that any skilled team of surgeons can do the transplant. That is not the trick anymore. While it is a tremendous accomplishment and achievement in surgery, it is no longer world shattering when you transplant an organ. Any topflight surgical team trained to do it can do it, period. It is the body's immune response, the resistance, that is the problem, and you have gotten no place with that.

Dr. DAVIS. I think we have made very marked progress.

Mr. FLOOD. Outside of the tissue matching, what else have you done?

Dr. DAVIS. We have learned to use immunosuppressive drugs much more effectively. Not only immunosuppressive drugs, but as I mentioned earlier, actually a serum, antilymphocyte serum, which is a serum made in horses specifically directed against the cells that cause the rejection phenomenon. This has been used much more widely this last year and with much more effective results than in the past. I would like to point out that we have heard a lot this last year about heart transplants, but in the meantime the work on kidney transplants has been going extremely well, although we have not heard very much about it in the country. For instance, last year within the United States alone there were 600 patients that were given kidney transplants. The results of these, when they are examined, are turning out to be very good.

The recent reports we have, which come from the best clinical centers, where typing is done, where if ALS is needed it is used, where immunosuppressive drugs are needed, they are used. They show that in transplants from siblings or parents 85 percent of the kidneys remain functioning for 2 years. If the transplants are from cadavers—matched cadavers—60 percent of the kidneys survive for 2 years. The patient record is even better than this, because a kidney can be removed when it begins to reject or break down and another one implanted, or the patient can be put back on the dialysis machine. So the record of survival of patients is really very good and very encouraging and it is getting better all the time.

Mr. FLOOD. I have before me a letter from Dennis W. Watson, president of the American Society for Microbiology. I quote a sentence from that letter:

> Beyond the technical skill of the surgeons there has been no breakthrough in the transplantation field and any major advance will require continued basic research into the immunology of tissue rejection.

That part of the sentence which I direct your attention to is this:

> There has been no breakthrough in the transplantation field beyond the technical skill of the surgeon.

Dr. DAVIS. I think he must not have been referring to very recent work because I think no one could doubt that the concept of tissue matching, the development of techniques for the use of immunosuppressive drugs which was started many years ago had a very significant effect. I think the hopes for the use of soluble antigens as a

desensitization procedure specifically is something which we can look forward to.

Dr. MARSTON. Mr. Flood, if I may add something here, the fact that one is seeing the type of success with kidney transplants at present means that this is going to be a problem that is going to be before us and before this committee for many years. Dr. Watson's point that to be able to move further is going to require a better understanding of the basic mechanisms of immunology is one that I think Dr. Davis and I would both back strongly. The problem of transplantation now seems to be one that very clearly is going to be with us for some time.

Mr. FLOOD. We are a long way from home.

Dr. MARSTON. We are a long way from home, and we need to understand much, much better the basic processes of immunology to be able to handle this over the period of the next few years.

Mr. FLOOD. Mr. Michel.

COST OF KIDNEY TRANSPLANTS

Mr. MICHEL. Doctor, you mentioned the 600 kidney transplants. What was the average cost to the patient of those transplants?

Dr. DAVIS. $16,000 per patient.

Dr. BERLINER. I think that is the total cost of the transplant, not necessarily the cost to the patient.

Dr. DAVIS. That is right. The procedure.

Mr. MICHEL. How many of those 600 patients would you say have participated with little or no cost to themselves by just volunteering to participate in a research project as against those who had the means and wherewithal to pay the full freight? Do you have any idea?

Dr. DAVIS. I do not have a way of getting at that information.

Mr. MICHEL. The very citing of this figure suggests that in addition to all the other things that would stand in the way, we have a real problem here of just economics, do we not?

Dr. DAVIS. That is correct.

INCREASE FOR LABORATORY AND CLINICAL RESEARCH

Mr. MICHEL. This $610,000 increase for laboratory and clinical research, calling for 15 additional positions what are we talking about here specifically?

Dr. DAVIS. We are requesting 15 new positions to extend the work in two areas. We are proposing nine new positions for clinical studies on allergy and infectious diseases in the clinical center. Two years ago under a new clinical director we determined that we should develop our work on allergy much more extensively than it has been done. We now have, and I should mention, a new Chief of the Laboratory of Immunology, Dr. Benacerraf, who joined our staff last fall and brings a tremendous talent to the Medical Center. We are building our clinical program in that direction.

Several years ago we actually reduced the number of staff in this work when we had a change of clinical directors and also a change in the direction of the work. We want to build that now into an area which we think is really ripe for full exploitation. The other six positions we will use at the Rocky Mountain Laboratory in Hamilton,

Mont., where we have some new facilities for the study of slow virus diseases. These are diseases of animals, such as Aleutian mink disease, which have many similarities to human disease and can best be studied under the conditions of the Rocky Mountain Laboratory.

Mr. MICHEL. On that latter point what kind of cooperation is there between that operation and the animal disease laboratory we fund under our agriculture appropriation bill? Is there a free exchange of communication?

Dr. DAVIS. There is constant communication. Actually, the people who are doing most of the work at Rocky Mountain Laboratory are trained as veterinarians. They feel free and easy in the circles of the Agriculture Administration. There are a number of workshops which have occurred from time to time. They go to essentially the same meetings. I have been concerned about that question myself and also with other work going on along this line supported by other parts of the Public Health Service and NIH. I am satisfied that there is good communication on this problem. The problem is interesting. There are relatively a small number of scientists who are interested in it. So it is exciting to them and has great import for basic knowledge which eventually should provide us with much better understanding of some of these mysterious diseases.

ALLERGIES

Mr. MICHEL. How do we distinguish between an allergy and an infectious disease?

Dr. DAVIS. An infection is caused by a living organism which actually invades and multiplies. An allergy is also a foreign invader, but it is a substance usually a protein, which comes into the body but does not multiply.

Actually, the body reacts in somewhat the same way to it, the formation of antibodies and cellular response.

Mr. MICHEL. Allergies can be fatal.

Dr. DAVIS. Yes.

Mr. MICHEL. What are the most striking and critical allergies and the most dangerous ones? If you have set any priorities in that area, what are we aiming for first?

Dr. DAVIS. Of course, the most striking clinical condition is the anaphylactoid shock where the body is exposed to an allergen to which it has a very high responsiveness. When the reaction takes place, there is a tremendous release of histamine which results in the constriction of the blood vessels, with swelling of the throat.

Mr. FLOOD. What was that term you used?

Dr. DAVIS. Anaphylaxis.

Mr. FLOOD. What is that?

Dr. DAVIS. Anaphylaxis is the medical term referring to the immediate massive response of the body to an allergen which is life threatening and in many cases actually is fatal. However, I suppose one of the major problems in allergic diseases in terms of death is asthma. Asthma we know causes some 5,000 to 6,000 deaths a year. This is based on a long history of exposure to allergens and a buildup of the body's response.

Mr. MICHEL. Is the best treatment for asthma still to go to Arizona if you live in a State like mine?

Dr. DAVIS. Very often this helps for a time, but not necessarily.

Mr. FLOOD. It would not help much with miners' asthma, would it?

Dr. DAVIS. No, sir.

Dr. MARSTON. This anaphylactoid reaction is a problem in the use of antitoxin against tetanus in which there has to be a careful testing to be sure that a patient is not sensitive to horse serum. This has been one of the most worrisome areas in terms of causing either sudden death or major reactions when people have gotten a cut and they have not had the regular immunizations and one starts using horse serum. If they had it before, one can get really very dramatic and dangerous reactions.

Dr. DAVIS. Another example is a bee sting or wasp sting. One reads about this frequently in the newspapers. It is simply a massive reaction to an allergen to which an individual is sensitive.

INCREASES REQUESTED

Mr. MICHEL. On page 6 there is an increase of $807,000 for "Other services." That along with several other increases is offset by a reduction in grants, subsidies, and contributions, but it is nevertheless an increase of nearly a million dollars. What are we talking about?

Mr. MAGRUDER. That is specific to contracts and includes the amounts of money that are in there for the management fund.

Mr. MICHEL. How much of that is in the management fund?

Mr. MAGRUDER. $547,000.

Mr. MICHEL. The balance is an increase in what—contracts?

Dr. BERLINER. If you add the increase in the contracts to the $547,000 it becomes $807,000.

Mr. MICHEL. You have an item under research grants of $396,000 to provide for approximately 11 additional project grants. What are these? Are these new ones or renegotiated old ones?

Dr. DAVIS. These are old ones continuing. Actually this next year we expect to have 11 more than we did last year which would be continued.

We are requesting funds for the same number of new projects as we did last year.

Mr. MICHEL. Do you want to break out for the record specifically what these 11 are going to be by name?

Dr. DAVIS. We are now supporting 1,400 grants. It would be rather difficult to identify at this time specifically what those 11 would be, because those would be out of 1,111.

Mr. MICHEL. Then they are not actually new ones.

Dr. DAVIS. No, they are not new ones. These are on the basis of Council actions.

Mr. MICHEL. In other words, there are no new ones which you have entered into. How do you get 11 additional ones if you have no new ones?

Dr. DAVIS. We already have commitments to many grantees and this year we expect to carry over 11 more than we had last year.

Dr. MARSTON. Mr. Michel, I think this is the additional number needed to implement the noncompeting research grants for next year.

Dr. DAVIS. That is right.

Dr. MARSTON. We will have the same number of competing research grants as this year.

Dr. DAVIS. That is right.

Dr. MARSTON. In making the budget estimates we looked at what our responsibilities were for those noncompeting grants next year and it turned out to be 11 more this year than last year.

Mr. MICHEL. The competing ones total how many?

Dr. DAVIS. 276. We expect to fund 276 competing new grants in 1970, which is just the number we had planned for.

Dr. MARSTON. This is a combination of actual new grants and those that have run out of their moral commitment period of 3 or 5 years and therefore must compete for continuation.

CONTINUATION GRANTS

Mr. MICHEL. What is the longest length of time any grant has run over a period of years?

Dr. DAVIS. Counting continuations, renewals?

Mr. MICHEL. Yes.

Dr. DAVIS. Our Institute makes a commitment for no longer than 5 years, but then the renewals can occur. I believe we have some that are going for 14 or 15 years.

Mr. MICHEL. Give me an example of what amounts are involved. I am curious to know whether or not we are really getting our money's worth. These things go on for 5 years and you continue them for another 5. If it gets to be so easily obtainable, I wonder if these people are being pushed to the limit they ought to be to get some results.

You say something runs for 14 years. What kind of renewal grant do we have that runs 14 years? The inclination is to think you have a pretty good thing going.

Dr. DAVIS. These of course come up for renewal at least every 5 years and sometimes 3. They are then reviewed by the study section which asks the question, is this research doing what we said it would? Has it been productive? And on the basis of the quality of research, recommendations are made many of them are disapproved.

Actually, I think the disapproval rate on competing renewals is something like 20 percent.

These, after the Study Section review and recommendation go to the Advisory Council of our Institute, which then examines them again and makes recommendations, and, insofar as our funds are available, we will pay them on the basis of priority. The grants which extend for that long are individuals who are extremely productive leaders in the field, who started out some years ago to be productive, make good contributions, and have continued to do so.

I myself am perfectly satisfied with the review process and that these grants, even of such long terms as that, are good.

Mr. MICHEL. To satisfy myself, please give me one that runs as long as 14 years and tell me the amount, to whom it was granted, and what the results were. I hope there will be some significant ones.

Dr. DAVIS. I will be glad to.

(The information follows:)

Summary of 20 years of research grant support to Dr. Maxwell Finland, director, Thorndike Laboratory, Boston City Hospital.

The applicant for a research grant is free to request as many years of support (up to a maximum of 7) as he thinks reasonable. Our Advisory Council, conscious of the perennial shortage of funds has very rarely recommended funding for

over 5 years and, indeed, the average award has been for only 3 to 4 years. This meant that the awardee would have to make a completely new and detailed application, generally during the last year of his current award. Such a "competing renewal" application would be judged by a study section in exactly the same way, and at the same time, as new applications competing with it for funds. In fact, the study section would be in a better position to make a judgment on a competing renewal application than it was on the original. The study section, for example, would have the written record of the reasons for its initial judgment and, because of the turnover of personnel built into the study section system, most of its members would be new—tending to counter-balance any unconscious initial bias. Also, the applicant would have had a chance to prove himself in his profession by publication of the results of his previously supported work in professional journals and by presentations at scientific meetings. It is in this arena of peers that an academic scientist proves his competency, productivity, and creativity.

A recent review of the nearly 1,500 active research grants supported by NIAID revealed 43 grants that had been supported for 14 years or more. One of these has been selected for detailed review. This research grant—AI00023, entitled "Infectious Diseases and Antimicrobial Therapy"—is now in its 20th year. It was awarded to Harvard University with Dr. Maxwell Finland of the Boston City Hospital as its principal investigator, and has provided well over half of his research grant support, at least during the past 10 years.

Dr. Finland was born in 1902, educated at Harvard College, and received his M.D. from Harvard Medical School in 1926. He has been on the staff of Boston City Hospital since 1927, and on the faculty of Harvard Medical School since 1928. Since 1950, he has been associate director, or director, of the Thorndike Memorial Laboratory of the Boston City Hospital, a post from which he retired in August 1968. Dr. Finland is a member of a number of professional societies and has been a consultant to the Department of Defense, the Veterans' Administration, and the National Research Council. Although he served on the Bacteriology and Mycology Study Section of the National Institutes of Health from 1958 to 1962, he has not been on an established NIH advisory group since. Dr. Finland devotes a goodly portion of time (from 25 to 35 percent over the last 7 years, in which time and effort reporting has been required) from his busy schedule to the activities of this research grant; although no part of his salary has ever come from the grant funds. Six times in the past 20 years, even such a distinguished physician as Dr. Finland has had to present his research proposals for review and judgment by his peers. A brief recapitulation of the study sections' judgments follows:

Date of review	Study section	Priority score	Number of years recommended for award	Study section remarks (see below)
May 1965	Chemotherapy	113	5 (17–21)	(1)
January 1960	Pharmacology and experimental therapeutics.	100	5 (12–16)	(2)
April 1955	do	112	5 (7–11)	(3)
January 1952	do	125	3 (4–6)	(4)
May 1950	Experimental therapeutics.	145	[5] 2 (3 and 4)	(5)
May 1949	Antibiotics		[5] 2 (1 and 2)	

[1] The distinguished record of Dr. Finland, and the superb resources and environment, enable him to attract able assistants. The group has published 89 papers that serve as a source of important information on hospital infections, the methods for use or improved applications of antibiotics, both new and old.

[2] The extensive work of this group has resulted in 77 publications that are a fountainhead of information on mechanism of action and clinical efficacy of antibiotics.

[3] These are highly competent workers, with admirable facilities. They should have assurance of long-term support.

[4] Highly qualified to carry on this work of importance to the whole field of therapy of infectious diseases. 10 publications listed.

[5] There was an administrative action that adjusted the 4 years of awards to 3 years.

[6] Outstanding qualifications and experience—profound potential significance of the study. 31 publications listed.

To portray the work of 20 years faithfully and briefly is not easy; but, mention of a few highlights may suffice. One theme has been central to Dr. Finland's investigations. He "lives" in a large metropolitan public hospital. The problems of those patients are his problems, and if the emphasis changes than it is because

the urgency and significance of the problems has changed. The conquest of infectious disease has moved through several great eras. In the last 30 years, and particularly the last 20, there has been the truly remarkable and sophisticated development of a host of chemotherapeutic agents, both snythetic and natural—the antibiotics. Probably every American beyond childhood, and certainly any one who has ever been admitted to a hospital, has received some sort of antibiotic therapy.

The pharmaceutical industry discovered many antibiotics, and the availability of these and others owe much to commercial development programs aimed at increased production, more efficient isolation and purification, and chemical manipulation of the molecular structure or synthesis of related compounds with more desirable properties. However, antibiotics are a two-edged sword and it is only in the hands of clinical researchers, like Dr. Finland's group, that the usefulness and the hazards of therapy are mapped out.

Given a compound that shows activity in the test tube against some laboratory strains of bacteria, or seems to cure infections in laboratory animals, much remains to be studied in humans. Primary, naturally, to human studies is a determination of safety. With that established, studies of efficacy and limitation of use can begin, both in normal volunteers and in selected patients. The list is long, and includes questions of the following type:

What dose can be given, how frequently, by what route?

What blood levels of antibiotic must be attained? Can specific quantitative assays be developed to determine these levels?

What species of bacteria are sensitive and what relatively resistant? Is there significant variation between strains of the same species? How can sensitivity and resistance be estimated by laboratory tests?

How and where is the antibiotic absorbed or concentrated or broken down and excreted? How are these processes modified in patients with specific diseases such as renal failure, liver disorder, gastrointestinal complications?

Are combinations of antibiotics more or less effective against specific species of bacteria, in specific diseases? If administered orally, what derangement of the body, especially in the gastrointestinal tract, may occur—change of intestinal bacteria, overgrowth by pathogens, interference with absorption of vitamins or amino acids?

If administered by any route, what complications may occur—particularly development of resistance, development of an infection with a different (and resistant) type of bacterium?

If resistance develops in a particular species of bacterium, does that resistant strain show any resistance to other antibiotics?

Why does resistance develop, is it due to particular enzymes of the bacteria, is it inherited by the offspring of the bacteria?

Dr. Finland and his colleagues have published over 200 papers on all these subjects for well over 30 different kinds of antibiotics. His group has been particularly interested in the organisms that cause so much trouble in hospital infections—staphylococcus, and the so-called Gram negative rods (salmonella, aerobacteria, klebsiella, pseudomonas) and in the types of infections that are such a problem in hospitals—pneumonia, urinary tract infections, ear infections, meningitis, and complications of pregnancy.

The relative importance of these organisms changed from the pre-antibotic era. For example, in a continuing study of hospital infections, Dr. Finland found that: "Pneumococci and beta hemolytic streptococci in 1935 accounted for more than ½ the cases and ⅔ the deaths; while in 1957 they were responsible for only ⅛ the cases and ⅛ the deaths. Staphylococci on the other hand which accounted for more than ⅕ the cases and ⅕ the deaths in 1935 had figured in ⅖ the cases and ⅖ the deaths in 1957. Klebsiella, pseudomonas, proteus and coli were relatively infrequent as causes of cases or deaths in 1935 but accounted for ⅛ the cases and ½ the deaths in 1957." The diseases still important in the general population, such as rheumatic fever, gonorrhea, and influenza, figure prominently in his investigations. In the early years of the grant, he devoted much time to investigating the effects of steroid hormones, such as cortisone, on resistance to infection with or without antibiotic treatment.

In addition to the scientific aspects of a grant, there is a fiscal, or administrative, aspect. People unfamiliar with the process might suppose that once the Council has recommended award the Government simply hands out the money each year for the life of the grant. Nothing could be further from the truth. Before each year's award is made, the Extramural staff has reviewed the rate

and total amount of expenditures, compared it with the detailed budget proposed for the new award year, and sought to find some "savings." Savings might result from such circumstances as generally reduced level of activity, temporarily understaffing, or overbudgeting for items such as equipment or travel. Negotiation with the principal investigator follows to reach an equitable decision. Our scientist administrators have become very adept at this. For example, in fiscal year 1968 they "saved" about $5 million (9.6 percent of $52 million budget) and used this money to fund other approved applications of good priority that otherwise would have had nothing.

The following table summarizes the fiscal story on Dr. Finland's grant, with some detail given for the past 4 years:

Year of grant	Direct costs: Requested	Direct costs: Awarded	Adjustments by staff	Total awarded
20	49,800	37,664	−6,163, 12 percent cut − 450 cut	$206,316
19	49,459	38,962	−10,047 carryover −500 cut	
18	57,316	45,183	−5,039 carryover	
17	51,378	49,678	−1,700 cut	
			Renewal application for 7 years reviewed by Chemotherapy Study Section. Recommended for award for 5 years. Priority 113.	
16–12			Renewal application reviewed by Pharmacology and Experimental Therapeutics Study Section. Recommended for award for 5 years. Priority 100	182,153
11–7			Renewal application reviewed by Pharmacology and Experimental Therapeutics Study Section. Recommended for award for 5 years. Priority 112.	
6–4			Renewal application reviewed by Experimental Therapeutics Study Section. Recommended for award for 3 years. Priority 125	369,550
3–1			Renewal application reviewed by Experimental Therapeutics Study Section. Recommended for award for 3 years. Priority 145	
			Grand total	758,019

The work of Dr. Finland and his colleagues has had effect far beyond the environs of Boston—touching, in a very real way, the life of any citizen who has been saved from death by treatment with antibiotics.

RESEARCH FELLOWSHIPS

Mr. MICHEL. Now these fellowships. They are going to be below the level for 1969 according to your justifications, but there will be some 240 awards. These will go principally to whom?

Dr. DAVIS. A large proportion of these will go to what we call the research career development awards. These are young men or women who are 4 to 5 years beyond their doctorate degree, who have gotten a fairly good start into the career of research, but they are not really fully established.

And some years ago the Institute established this program which provides them support and a salary commensurate with what they could be earning outside or in a university, and provides this to them to work in a research setting within a university. These are now made for a period of 5 years, and they might be renewed for a year or two.

Mr. MICHEL. What are the basic qualifications for one of these fellowships?

Dr. DAVIS. I would say already having accomplished some research project, having demonstrated competence, somebody has promise to be one of the scientific leaders of the country in the future. These are more advanced than the postdoctoral fellowships, which is the largest number, and these are awarded to individuals who have just completed their doctorate degree, usually a Ph. D., but it can be a medical degree. They have not been fully experienced in the techniques and the philos-

ophy and research, and under an experienced preceptor they are awarded a chance to get 1 or 2 or even 3 more years of experience.

Mr. MICHEL. In that earlier category, could you qualify with just a bachelor's degree?

Dr. DAVIS. No.

Mr. MICHEL. What would you need?

Dr. DAVIS. The research career development?

Mr. MICHEL. Yes.

Dr. DAVIS. You would have to have an M.D., these are primarily for medical people, but they could also be Ph. D.'s. You would have to have 4 to 5 years post M.D. at least.

Mr. MICHEL. Is that in the latter category you were talking about or the earlier group we were talking about?

Dr. DAVIS. The research career development awardees must have 5 or 6 or more years after they get their doctor's degree, and perhaps a few more years than that.

Mr. MICHEL. What is the other category?

Dr. DAVIS. These come immediately after receiving the doctors' degrees.

Mr. MICHEL. What fellowships are awarded for receiving a doctor's degree?

Dr. DAVIS. They are awarded for predoctoral.

Mr. MICHEL. What do you need to qualify in that category?

Dr. DAVIS. Our Institute does not award any of these in the predoctoral degree. I believe these are done by the National Institute of General Medical Sciences.

Mr. MICHEL. But none in your shop?

Dr. DAVIS. No.

TRAINING GRANTS

Mr. MICHEL. Training grants principally are going to be a little below the level of 1969, but these are for what, principally?

Dr. DAVIS. These are awarded to individuals in university or medical school departments who can provide an atmosphere and environment for training research workers. These young men come in and are awarded stipends and work within the department, under the direction of experienced scientist investigators in order that they can acquire these skills and knowledge that are necessary for development of a fully rounded and trained investigator.

Mr. MICHEL. How many more applications than awards do we have roughly in that area?

In other words, what percentage of those who express an interest and are so motivated actually have those ambitions satisfied by being awarded a training grant?

Dr. DAVIS. I do not have the specific figure of the number of applications. I would be glad to supply that for the record.

(The information follows:)

During fiscal year 1968 (the latest year for which complete figures are available, because of forward financing), 53 applications of all types were received for training grant support. Of these, 36 (68 percent) were recommended for award by the Institute's Training Grant Committee and the Council, but funds were available to pay only 28 of the recommended applications (78 percent).

The following table gives a more detailed breakdown:

TYPE OF APPLICATION

	New	Competing continuation	Supplemental	Total
Received	21	29	3	53
Disapproved	9	6	2	17
Approved	12	23	1	36
Funded	9	19	0	28

REVIEW AND APPROVAL OF RESEARCH GRANT APPLICATIONS

Mr. MICHEL. One quick question on that award of $190,000 to Dr. Klein up in New York on immunotherapy of skin cancer.

Why would that not be awarded over in the Cancer Institute rather than in your shop?

Dr. DAVIS. Dr. Klein wanted to investigate whether or not there was an immunologic mechanism which was present in this reaction, which he found when he applied the drugs, so that he requested funds. When the application came in it was so worded it was assigned to our Institute. There was also, as I recall, dual assignment to the Cancer Institute.

Mr. MICHEL. Has he had prior awards from the Cancer Institute?

Dr. DAVIS. Yes, he has had.

Mr. MICHEL. Was he denied a grant from the Cancer Institute to pursue this same line?

Dr. DAVIS. I cannot answer that question. We would be glad to provide that information.

Mr. MICHEL. The thought occurs to me in the wording of an application we might be dealing in sematics here, and you do not qualify in one Institute so you change the phraseology around a little bit and qualify in another.

Do the same people make a decision as to whether or not a grant is made in the Cancer Institute or in your particular shop, or is there a different group?

Dr. DAVIS. Usually a different reviewing group. My memory is his application was reviewed by the Immunobiology Study Section.

Mr. MICHEL. Is it possible you could come in and be turned down by one group, turn it around a little bit and get it before a different group and get a favorable nod?

Dr. DAVIS. I think it depends on what the application proposes to do.

If the review group judges the proposal worthy and the resources adequate to the job then the application is recommended for approval. But if an investigator, for instance, wants to do something for which he does not have the background, staff, or the facilities, it might very easily be turned down. It is not the same proposal to the two groups, but with a different purpose and different resources being available.

Mr. MICHEL. I think that is all, Doctor.

The other thing I had in mind was with respect to one of those paragraphs on page 23 of the justifications, which had to do with work out at the laboratory in Montana. I think we have pretty well explored that.

You have been satisfied you are working closely with these people in the Animal Disease Laboratory, and obviously there is a connection

between some of those animal diseases and similar diseases that affect human beings.

Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Casey?

RESULTS OF INVESTMENT IN RESEARCH

Mr. CASEY. Doctor, the National Institute of Allergy and Infectious Diseases over the past 10 years has had appropriated roughly $675 million in round figures. That is over a half-billion dollars. You pay taxes and I pay taxes, and the taxpayers are screaming now and they look at this—and I am not singling you out particularly because I think they could take any one of the institutes separately and probably ask the same question and probably have the same momentous amount of money facing them.

If a taxpayer asked me what did we get in the way of improvement of my health or the community health for all of this money we have invested, and why should we put another $103 million in this coming year, what do you say?

Dr. DAVIS. I would like to mention three things, Mr. Casey.

RUBELLA VACCINE

One is, the studies which the Institute has supported on rubella and rubella vaccine, which now seems to be just around the corner. This goes back not only to the actual development of the vaccine, but it is the work that has gone on in the last several years on the studies of the virus itself, the ways of growing it, the study of the disease.

Mr. CASEY. You understand, Doctor, that several ahead of you have been claiming rubella as one of their big projects too.

Dr. DAVIS. Yes.

Our Institute has had a special program in the development of the vaccine itself through contracts, but particularly through evaluation of the candidate vaccines.

ORGAN TRANSPLANTATION

The other area I would mention again is that of organ transplantation, where the support of this Institute I am sure has had major impact upon the effectiveness of transplantation through the tissue-typing procedures.

INCREASED KNOWLEDGE OF VIRUSES

A third area, which is more general, is the vast increase of knowledge of viruses and the diseases they cause, which has been supported by this Institute in the last 10 years or so. Viruses are now implicated in many other diseases beside the ones we ordinarily think of as infectious diseases.

We hear about viruses in cancer, we hear about viruses in neurologic diseases, and yet our Institute has been the one which has been primarily responsible for funding and supporting the hard study, the basic studies on viruses—how many are there, what do they do, how do they differ from each other, what kind of reaction do they cause

in man, what leads can we get from this study to either provide a vaccine or else to give some leads toward chemotherapy.

I am sure if we had not invested these funds in the basic study of viruses over the last 10 years we would not be on the threshold as we are now I think of an improved treatment for virus diseases, particularly interferon.

Mr. CASEY. We are on the threshold, you say?

Dr. DAVIS. I believe we are on the threshold of a real advance in the treatment of virus diseases.

Mr. CASEY. You have found the various viruses but so far you have not found the treatment for them, is that right?

Dr. DAVIS. I am referring specifically to interferon, the substance which is produced in the cells of the body when it is invaded and our finding out that this reaction can be accelerated, that interferon can be induced by some chemicals, chemical inducers, which has every promise of providing adequate treatment for virus diseases over the years to come. I would not like to predict how soon this would be, it will probably take some time because there are many questions related to its use and particularly the toxicity which has to be answered.

Mr. CASEY. How many viruses have you found?

Dr. DAVIS. There are probably 300 viruses which attack man. Actually, we know there are something like 100 different viruses which can cause the common cold.

Mr. CASEY. You say there are 300. How many of these were found with this money we have appropriated?

Dr. DAVIS. A very large number of these were found in our own laboratories in Bethesda.

Mr. CASEY. That will not do, Doctor, a large number. Have you roughly an idea? I cannot go up on the floor and tell a certain Member I know a large number of viruses were found. He will say, you should have found more than that with $675 million.

Dr. MARSTON. Instead of talking about particular percentages, we should compare the situation today with that of about 10 years ago, in 1959. We have really entered the age of virology in that 10-year period.

Mr. CASEY. My question was, how are we living better or longer or healthier? That is what I want to know.

Dr. MARSTON. One can list diseases that have been cleared up such as polio and measles. I think we could give you a rundown of the vaccines that have been developed.

Mr. CASEY. Was the polio vaccine in this Institute?

Dr. DAVIS. Very little. This was developed back in 1954 and 1955.

RESEARCH ACCOMPLISHMENTS OF LAST DECADE

Mr. FLOOD. Might I suggest that you give us for the record a statement of what you have accomplished over the past 10 years with the $675 million we have appropriated?

Dr. DAVIS. Yes, sir.

(The information follows:)

Over the 10-year period fiscal year 1960 to fiscal year 1969, the obligations of the National Institute of Allergy and Infectious Diseases totaled $675,514,000. This amount was allocated to the major activities of the Institute as follows:

	Millions
Research grants	$394.6
Fellowships and training grants	99.9
Total grants (73.2 percent)	494.5
Intramural research	114.8
*Collaborative research	53.3
Other activities	12.9
Total direct operations (26.8 percent)	181.0

*Most of the funds for collaborative research are used for contracts or grants. However, collaborative projects (as the name implies) also involve the intramural staff of the Institute and collaborative research is therefore customarily shown in the budget as a direct operations item.

During the past decade, the National Institutes of Health have, collectively, provided about 40 percent of the funds expended for medical research in this country. NIH research grants have provided 70 percent of the funds for medical and health-related research conducted in academic institutions, hospitals, and other non-profit research institutions. These proportions hold true for the National Institute of Allergy and Infectious Diseases in its particular fields of interest. It follows that most of the work done in these fields has been to some extent dependent—and in many cases very heavily dependent—on funds made available through the NIAID appropriations. The pervasive role played by research-support provided by the Institute and the complex, inter-locking pattern of many separate research achievements that eventually result in the solution of a disease problem make it very difficult—and rather meaningless—to classify accomplishments by source of support. In most cases, it would not be fair to attribute the accomplishment solely to NIAID support. It is, however, fair to say that the impressive progress made in the fields with which the Institute is concerned would clearly not have been possible without the extensive support provided by the Institute.

The primary concern of the Institute is in the field of infectious diseases, especially the virus diseases, and in the relatively new and promising field of immunology.

The conquest of infectious diseases has made great strides—it is, in fact, the field in which medicine has thus far made its greatest contribution and saved the largest number of lives. Many serious, and often fatal, diseases have been virtually eliminated from the civilized world. Beginning with smallpox more than a century ago, the list includes diphtheria, typhoid fever, cholera, bovine tuberculosis, bubonic plague, typhus fever, malaria, yellow fever and, since World War II, poliomyelitis. The measles vaccines licensed in 1963 and 1964 should shortly eliminate this disease and its sometimes serious aftermath. A rubella vaccine will be available before the end of this year and will, it is hoped, forestall a repetition of the 30,000 defective babies that were born as the result of the last rubella epidemic.

For infectious diseases which can not yet be prevented, there has been the truly remarkable and sophisticated development of a host of chemotherapeutic agents, both synthetic and natural—the antibiotics.

But there are still many infectious diseases that can be neither prevented nor controlled. Some remain stubborn and difficult problems because we cannot yet isolate the cause of the disease (e.g. infectious hepatitis) or prevent its spread (e.g. staphylococcus infections in hospitals, and salmonellosis) or because we are puzzled by failure of natural immunity to develop after disease and therefore do not yet know how to develop a vaccine (e.g. gonorrhea).

Effective action against a disease usually requires reliable information resulting from three basic approaches to the problem:

Discovering the cause of the disease which, in the case of infectious diseases, involves isolating the infective agent, identifying it, and developing a technique for growing it in the laboratory;

An understanding of the course of the disease which, for infectious diseases, includes the ways in which the organisms enter the body, grow, and cause

the damage (i.e. the pathology of the disease), and the signs and symptoms that make precise diagnosis possible;

The study of the epidemiology of the disease—how it is transmitted from person to person, the collection of morbidity and morality statistics with special attention to their variations with age, sex, geography, seasons of the year, etc.

Each of these steps is complicated, time-consuming and—all too frequently—frustrating. Often the solution to a particular problem is long-delayed because one or more pieces of the puzzle are missing. For example, the polio virus was discovered in 1909 but effective work on the development of a vaccine was not possible until the late 1940's because many other problems had first to be solved including the crucial development of a practical technique for growing the virus (which in 1949 proved to be three strains of virus). As is so often the case, the solution to the tissue culture problem was found by a group of scientists who were not working on the polio problem but on cancer. This example is cited only to illustrate the complexities of most medical research and the years of effort by scientists in a wide range of endeavor that usually lies behind each success that comes to the public's attention.

One of the most important developments of the past decade is the growth of the field of virology to which the Institute is deeply committed. The discovery and definition of new viruses was one of the great achievements of the 1950's and early 1960's. As a result, research on virus structure, chemistry, and inheritance of characteristics has been a major preoccupation of the 1960's. Although much still remains to be done in this area, and in the development of instruments of disease control, there has been tremendous progress in the elucidation of the relationship of viruses not only to infectious diseases but to diseases heretofore not suspected of having a viral origin. Virus research has also had a far-reaching influence on our knowledge of the structure and function of DNA, gene action, and cancer production by viruses. These four fields are among the 12 cited by Harvard Historian Donald Fleming as part of the biological revolution of the future. It is now known that there are probably more than 340 viruses capable of infecting man. Scientists on the intramural staff of the Institute have been responsible for discovering and characterizing over 100 of these.

The rapid development of virology during the past decade has given biomedical research a powerful new tool and has opened the way to the eventual solution of many disease problems. However, as is often the case with major advances in the still relatively primitive biological sciences, it has also shown that some of these problems are much more complex than they were thought to be. For example, as recently as 16 years ago the influenza virus was the sole known cause of viral respiratory infection. Now, about 140 immunologically different kinds of viruses are known to be involved in respiratory diseases which, in terms of disability and economic loss, are a major national problem. Even with this knowledge, nearly 50 percent of upper respiratory infections remain of undetermined cause.

A fairly recent development in the study of viruses, which has great potential importance for the solution of major disease problems, is the accumulating evidence that so-called "slow viruses" persist in the body long after exposure and may have serious consequences many years later. "Slow viruses" are now suspected of being causal or predisposing factors in a number of serious diseases that are not infectious in the usual sense.

One of the Institute's major collaborative activities is its vaccine development program which is concerned not only with the development of new vaccines but with enhancing the efficacy and safety of existing vaccines. A recent accomplishment in this field is an improved rabies vaccine which eliminates the risk of allergic brain damage that accompanied the rabies vaccine used heretofore. Much research and developmental work is in progress on vaccines for a variety of respiratory infections. There have also been notable achievements in developing quicker and more accurate diagnostic methods for virus diseases such as, for example, the development of a fluorescent-labeling technique which makes it possible for a laboratory technician to detect rabies virus in the brain of a suspected dog more quickly, cheaply, and accurately than heretofore. This technique, moreover, is a powerful new research tool because it permits an investigator to determine precisely where in the body—indeed, where in the complicated architecture of a single cell—a virus is located.

The field of virology has moved far during the past decade and its frontiers are still expanding. It is safe to predict that major advances in the diagnosis, the treatment, and—most important of all—the prevention of a wide range of diseases will result from the work that is now in progress. Many of the most significant accomplishments to date, however, are in the complex stages of research that are impossible to explain simply and whose full import cannot be fully assessed until long after the work was done.

The second major development during the past decade, in the field with which the National Institute of Allergy and Infectious Diseases is concerned, is the emergence of immunology as an important and productive area of medical research. Immunology, which for many years was a useful but comparatively simple adjunct of infectious-disease research, has now become a full-fledged discipline with important subfields of its own. Some of the most significant advances in biomedical research are now occurring in the field of immunology that are changing basic concepts concerning a broad range of medical problems ranging from allergies to organ transplantation. The bulk of this research is supported by NIAID funds.

Immunology deals with the action of antigens (proteins, complex carbohydrates. and fat-protein combinations) that are capable of stimulating certain cells of the body to produce other complex proteins (called antibodies) that are capable of reacting with antigens of the type that produced them. For example, when bacteria or viruses, acting as antigens, invade the body, blood serum proteins, called antibodies, are produced that combine with or neutralize the invader. The purpose of conventional vaccinations is to produce such antibodies before the bacteria or viruses invade. Immunology is also concerned with the chain of reactions that occurs between antigen-antibody complexes, other substances in the body, and cellular surfaces which results in cellular injury (e.g., inflammation and edema). In other words, it seeks an understanding, in terms of the chemistry of cells, of how the damage of disease occurs.

Traditional immunology, as an adjunct to research on infectious diseases, was mainly focused on the invaders and antibodies of all sorts, although large and complicated molecules, were assumed to be rather similar, chemically. Modern immunology has begun to change these concepts and is mainly concerned with the mechanism of body response. The type of antibody protein molecule (IgE) that triggers the unpleasant response of the body in allergies is now known to be different in structure and rate of production from the common protective antibody (IgG) which acts against infectious agents. And the IgC is known to differ in specific ways from the antibody IgM that appears early in immunization, and from IgA, the antibody that appears in nasal secretions. Resistance to certain viral infections is now known to depend upon IgA levels. Current research on this diversity of antibodies is trying to discover their methods of functioning at the cellular level and the molecular events by whch antigens stimulate cells to produce antibodies. Far afield from infectious disease research, the antigen-antibody reaction now makes possible the quantitative specific determination of a number of very important hormones, such as insulin, angiotensin, and growth hormone, which has clear implications for clinical medicine, therapy, and diagnosis.

An understanding of the phenomenon of immunological tolerance (the failure of the antibody producing mechanism to respond normally to antigen)—and the ability to produce it at will—would provide a practical solution to the problem of rejection of foreign organ grafts. Immunobiology, the study of cellular reactions and mechanisms, not only is important to the problem of tissue graft rejection but may be the key to the whole problem of how the body distinguishes self from nonself tissue and how it continuously monitors itself to detect and destroy cancer cells that arise from genetic modification of self-tissue. Some scientists even feel that in the realm of immunobiology lie the mechanisms that explain aging and the bodily changes characteristic of senility.

Immunopathology advanced during the past decade initially through the development and analysis of a variety of animal models for disease. But what was a laboratory curiosity a few years ago is now beginning to explain a whole series of human diseases—for example, glomerulonephritis (one of the major chronic renal diseases and often a reason for kidney transplant), rheumatoid arthritis, lupus erythematosus, and multiple sclerosis. Understanding of such disease would not only explain their mechanism but pinpoint the cause and permit specific drug therapy to interrupt or modify the sequence of molecular reactions.

It is only within the past 10 years that immunosuppressive drugs have been used clinically to treat and maintain patients with previously hopeless diseases such as lupus erythematosus, rheumatoid arthritis, psoriasis, thrombocytopenic purpura, periarteritis and certain types of granulomas. These practical uses encourage the hope that eventually drugs will be developed to block or modify a particular step in a chain that starts with antigen-antibody combination and continues through the complicated series of reactions that leads to specific tissue damage.

The collaborative programs, which were begun about 1963, are designed to translate the results of laboratory and clinical research into standard clinical technology. The collaborative approach is particularly for the deveopment and evaluation of end products such as vaccines and antibiotics, and new techniques such as tissue matching.

Collaborative programs have the following characteristics:

Formal definition of socially important goals;

Adequate base of scientific and technological knowledge;

A clear understanding of the research and developmental pathways to be followed;

Continuing adaptive coordination of a complex of research contracts, each playing an identifiable role in achieving the goal.

Collaborative programs often work in concert with the Institute's intramural research activities.

The intramural scientific staff of the National Institute of Allergy and Infectious Diseases have made significant contributions in all research areas within the Institute's purview. They have developed vaccines for Colorado tick fever and Q fever. They have been particularly active in the evaluation of amphotericin B and other antibiotics for serious fungal infections, such as cryptococcal meningitis (amphotericin B gives an 80 percent cure rate in this otherwise fatal disease) and coccicioidomycosis, and in the epidemiology and treatment of the lung disorder, histoplasmosis. The intramural investigators are also deeply involved in a study of the usefulness of the semi-synthetic penicillins in the treatment of staphylococcal infection. These penicillins have been chemically modified to give them more desirable properties including resistance to bacterial enzymes and diminished hypersensitivity in penicillin-sensitive patients. The latter property is of considerable practical significance when it is realized that about two millon Americans are already allergic to penicillin.

Intramural investigators have also played a leading part in research on primary atypical pneumonia, a widespread infection by mycoplasmas (a kind of delicate, naked bacterium). It is estimated that there are about 500,000 infections a year many of which go undiagnosed and, hence, untreated. Scientists in the Institute's laboratories at Bethesda were the first to identify this organism as a cultivatible organism, establish the epidemiological importance, and develop effective antibiotic treatment.

Fellowship and training grant funds support postdoctoral training in medicine and biomedical sciences. Trainees and awardees are carefully selected, and from their cadres come teachers, clinicians, and researchers who insure continued high quality education of the practicing physician. The point seems incontroversible that the quality of American medical care and education today has been made possible, in large measure, by Federal support through these mechanisms of NIAID and the other NIH Institutes.

Research grant funds also contribute in a direct, but less easily measurably way, to the quality of teaching and the production of trained personnel. Despite the recurrent debate over the balance between research and teaching and about details of the mechanisms for providing educational support, a vigorous research program is an essential attribute of a first-class medical or graduate school. The training and education of every physician, veterinarian, dentist, public health officer, nurse, and laboratory technician has been strengthened and enriched—directly or indirectly—by the training and research funds.

Mr. FLOOD. Mr. Shriver?

PNEUMONIA VACCINE

Mr. SHRIVER. Doctor, your statement in the justifications mentions the current production of experimental vaccine to control 12 types of

pneumonia. "Experimental vaccines against 12 most common types of pneumonia is now underway."

How many kinds of pneumonia are there?

Dr. DAVIS. In this statement I am referring to the pneumonias caused by pneumococci, of which there are some 50 different types. Twelve of these seem to cause about 80 percent of the pneumonia which occurs in this country anywhere.

The attempt here is to develop a vaccine which would combine something up to 12, maybe eight or 10, in one shot so as to actually prevent the development of pneumococcal diseases so we do not have to treat it when it occurs.

Mr. SHRIVER. How is that experiment coming along?

Dr. DAVIS. It is doing very well.

Mr. SHRIVER. How long will it be before there will be some results, not in the experimental stage?

Dr. DAVIS. We actually have contracts now for 2 million doses of each of these 12 types. The laboratory testing and certification of the trial vaccines will take place during this year and then the following year we expect to have mass trials, large-scale trials in a number of evaluation centers throughout the country, places such as the Indian reservations.

We find, for instance, among such disadvantaged groups as the Indians they have an unusually high attack rate of pneumococcal pneumonia and they will provide an excellent place in which to make an evaluation.

This material is a simple carbohydrate compound which has been studied for some years experimentally, and we just have not put it really into the developmental stage. We have every expectation that this will be a very significant addition for the practicing physician and the public health practitioner.

RUBELLA VACCINE

Mr. SHRIVER. I recall some four or five divisions that we have heard request funds for the rubella vaccine program. Of course, this is a great thing, I am not critical. But what Federal agencies are participating in this program? What is the total program cost? How much is in your Institute?

Dr. DAVIS. Actually, for 1969 we have estimated about $1.5 million for evaluation of rubella vaccine.

For 1970, this will be reduced to about a half a million dollars because we think the job is pretty well done and what we need to do now is to continue the surveillance of groups which will have received the vaccine to be sure there are no adverse effects, and also to continue the search for another kind of vaccine. We anticipate reducing very markedly our funds for rubella next year.

Mr. SHRIVER. In your Institute?

Dr. DAVIS. Yes.

Mr. SHRIVER. What are the other agencies or divisions involved in this?

Dr. DAVIS. The Division of Biologics Standards has a very active and very influential intramural program guided by their own scientists.

Mr. SHRIVER. We heard from them.

Dr. DAVIS. Yes.

Mr. SHRIVER. If you accumulated all of it, how much would it be?

Dr. DAVIS. The National Communicable Disease Center also has a rubella vaccine program dealing not with research but rather with large-scale immunization as a preventive measure.

I would not know what the leveling of funding is.

Dr. MARSTON. Could you guess, Dr. Berliner?

Dr. BERLINER. I would guess it is in the order of half a million.

Most of the money for which you are getting requests for future work in rubella is in the area of supplying vaccine for widespread use rather than for research.

Dr. MARSTON. There have been the three areas involved. The Allergy Institute in really supporting the research through its vaccine program. The Division of Biologics Standards, through its intramural program, as Dr. Murray explained, in the process of preparing to license the vaccine also made a vulnerable discovery. The CDC is responsible for the distribution of the vaccine.

Mr. SHRIVER. You refer to comprehensive planning?

Dr. MARSTON. Yes, in the Health Services and Mental Health Administration.

Mr. SHRIVER. We have heard about it in at least four, maybe five budgets.

Dr. MARSTON. You are having your hearings at the very time that rubella is a very hot subject. It is right in the midst of moving from research to the production of vaccine—to licensure and distribution. You are right in the middle of a very rapidly moving field that does involve coordinated activities across these various agencies.

Mr. SHRIVER. Does your institute have programs in connection with malnutrition? That is another subject we have heard considerably about during these hearings.

Dr. DAVIS. No, we do not have any direct programs per se.

INTERNATIONAL CENTERS FOR MEDICAL RESEARCH AND TRAINING

Mr. SHRIVER. In the justifications on page 18, mention is made of the international centers for medical research and training. Where are those international centers?

Dr. DAVIS. There are five international centers for medical research and training. These are composed of the home university plus arrangement with an institution in an off-site location.

For instance, Johns Hopkins University has an arrangement with the institution in Calcutta, the All-India Institute of Hygiene and Public Health. The University of Maryland has their arrangement with the Institute of Hygiene in Lahore, Pakistan. Tulane University has an association with the Universidad del Valle in Cali, Colombia. University of California works with the Institute for Medical Research

in Kuala Lumpur, Malayasia, and Louisiana State University works with the University of Costa Rica in San Jose, Costa Rica.

Mr. SHRIVER. What amount is included in this request for funds for International Centers for Medical Research and Training?

Dr. DAVIS. $2.3 million.

Mr. SHRIVER. And that is all?

Dr. DAVIS. That is all.

Mr. SHRIVER. And in those countries that you mentioned, their government pays for their part, is that right?

Dr. DAVIS. They make contributions, but the international centers, the universities who have these grants actually send their own staff members down there, for whom they pay.

But you are quite right, local cooperating institutions provide the salaries for their own staff work, working together and cooperating with the scientists and teachers from the other institutions.

Mr. SHRIVER. Is any of this money used for the support of those centers in those countries?

Dr. DAVIS. Yes, in the sense it pays the salary of Americans who are there, and supplies, and the necessary resources to maintain it. It is a cooperative joint arrangement.

Mr. SHRIVER. Do institutions in those other countries receive any funds from any other departments of the Federal Government, for instance, from the Agency for International Development?

Dr. DAVIS. Yes, they may. I cannot answer it specifically by individual cases. But there is nothing to prevent them from receiving support to extend their work and make it more effective. But usually not very extensive because these funds are directed toward training of Americans in doing research on diseases which are not found in the United States but diseases for which it is important to have trained Americans available some time in the future.

This of course is the purpose of it. It is not an aid program in any sense, it is strictly for the benefit of American science.

Mr. SHRIVER. Will you illustrate how it would be beneficial to America in the future even though we do not have that kind of a disease in this country?

Dr. DAVIS. For instance, cholera. Cholera does not occur in this country and yet it is a major problem. And it is important to have American scientists working on cholera, trained in cholera because our commitments, our national interests might require that we have people experienced in this disease.

Malaria is another example.

SEATO CHOLERA RESEARCH PROGRAM

Mr. SHRIVER. How much is our Government contributing to the SEATO cholera research program?

Mr. DAVIS. This Institute contributes six positions and $100,000. It is also supported by AID, which provides, I think, $600,000. Is there any other support? I am talking to Dr. Seal, who is chairman of the NIH Cholera Advisory Committee.

Dr. SEAL. The NCDC contributes two positions and about $30,000 for salaries for those two positions. The United Kingdom about 15,000 pounds a year, the Government of Pakistan somewhere in the order of around 400,000 rupees.

Mr. SHRIVER. How much in dollars?

Dr. SEAL. The last figure I heard on the official conversion rate was about 4.7 rupees per dollar. The NIH puts in out of its special fund currency program about 2 million rupees per year.

Mr. SHRIVER. These are counterpart funds that we have accumulated and can only be used there and by agreement with that country?

Dr. SEAL. Yes, sir. These are Public Law 480 section 104k funds.

Mr. SHRIVER. What about other countries?

Dr. SEAL. They have contributed both scientists and equipment, a number of other countries have had people come to the laboratory and work for a period of 2 to 3 months.

Belgium, France, and the Scandinavian countries, Norway and Sweden, have had scientists at the laboratory. It is one place in the world we can really depend on cholera occurring annually in the poputon and we can evaluate the advances of research in the human situation.

GEOGRAPHIC MEDICINE PROGRAM

Mr. SHRIVER. Would you describe in greater detail the functions and costs of the geographic medicine program?

Dr. DAVIS. Under our program of geographic medicine, we have included the International Centers for Medical Research and Training, which I have just described, the United States-Japan program which was referred to earlier, and also a very small program on international research career awardees.

We have funds for about five or six young men who are offered opportunities to do research in a foreign situation.

The United States-Japan program—would you like more detail?

Mr. SHRIVER. I am interested in this. For one reason, I am on the committee that appropriates money for AID, and they get into all kinds of things, including medicine.

As indicated previously, some of these programs are here, there and the other place and you do not know the full extent unless you inquire about them.

Dr. DAVIS. The United States-Japan program has been going for some 4 years now, and as we indicated earlier, it is funded directly, included in the appropriations. Six different diseases have been selected

by the joint delegation of senior United States and Japanese scientists as being most important in Asia and Southeast Asia, these are, as I mentioned before, tuberculosis, leprosy, certain virus diseases, cholera, certain parasitic diseases, and malnutrition.

The applications for research grants are made to the NIH by American scientists and to some extent by third country scientists, but not by Japanese scientists. They go through the regular granting process, review for scientific excellence and review for program by the Council.

The funds are roughly distributed as follows:

Parasitic diseases we expect for 1970 about $679,000, for virus diseases, $775,000. I am not sure this is what you would like.

For cholera, $1,068,000. Tuberculosis, $1.446 million. Leprosy, $1,055,000. Malnutrition, $1,626,000.

In addition to this, there are some contracts for specific objectives. All this includes about 100 different projects and something less than 10 of these are awarded outside the country, all of the rest are awarded to American scientists to work on these particular problems.

Mr. SHRIVER. Thank you, Mr. Chairman.

Mr. FLOOD. Mrs. Reid?

KURU

Mrs. REID. You speak of "Kuru" disease as a new lethal neurological affliction. What is it and how prevalent is it?

Dr. DAVIS. Kuru is a degenerative, slowly developing, but invariably fatal viral disease of the brain. In nature, it occurs only among the relatively small population of a tribal group in the interior highlands of New Guinea. In that population, it is the most common cause of death, exceeding all other causes combined. The disease is under active investigation by the National Institute of Neurological Diseases and Stroke; although both the NINDS and NIAID have programs of research on other similar human and animal diseases.

INTERNATIONAL RESEARCH CAREER DEVELOPMENT PROGRAM

Mrs. REID. In connection with your international research career development program and foreign research, in what other countries besides Japan do you have programs operating?

Dr. DAVIS. There is a total of seven young physicians receiving training under the international research career development program. They are currently stationed in Malaysia (2—to be terminated about June 30, 1969), Pakistan (2), Taiwan (1), Canal Zone (1), and NIH (1 temporary assignment to be reassigned to Taiwan). We have no awardees to Japan.

Mrs. REID. That is all, Mr. Chairman.

Mr. FLOOD. Thank you, Doctor.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Amounts Available for Obligation

	1969	1970
Appropriation	$96,840,500	$103,922,000
Comparative transfer to Salaries and Expenses, Office of the Director, NIH	-545,000	...
Comparative transfer from General Research and Services, NIH	10,328,000	...
Cutback required by P.L. 90-364	-3,450,000	...
Total obligations	103,173,500	103,922,000
Disposition of cutback:		
To be returned to the Treasury	3,450,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
14	Research		$60,185,500		$60,582,000		+$396,500
	General research support grants		(5,889,000)		(5,871,000)		(-18,000)
	Gorgas Memorial Laboratory		(500,000)		(500,000)		(0)
	Categorical clinical research centers		(1,100,000)		(1,100,000)		(0)
	International centers for medical research and training		(2,300,000)		(2,300,000)		(0)
19	Fellowships		4,362,000		4,191,000		-171,000
20	Training		9,488,000		9,118,000		-370,000
	Direct operations:						
21	Laboratory and clinical research	603	14,581,000	618	15,182,000	+15	+601,000
25	Collaborative research and development	39	12,630,000	42	12,855,000	+3	+225,000
31	Training activities	6	165,000	6	155,000	0	-10,000
32	Review and approval of grants	46	1,438,000	47	1,531,000	+1	+93,000
33	Program direction	24	324,000	24	308,000	0	-16,000
	Total obligations	718	103,173,500	737	103,922,000	+19	+748,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	718	737	+19
Full-time equivalent of other positions	10	10	0
Average number of all employees	713	720	+7
Personnel compensation:			
Permanent positions	6,901,000	6,979,000	+78,000
Positions other than permanent	95,000	95,000	0
Other personnel compensation	126,000	126,000	0
Total personnel compensation	7,122,000	7,200,000	+78,000
Personnel benefits	783,000	791,000	+8,000
Travel and transportation of persons	320,000	320,000	0
Transportation of things	100,000	100,000	0
Rent, communications, and utilities	303,000	303,000	0
Printing and reproduction	60,000	60,000	0
Other services	18,065,000	18,872,000	+807,000
Supplies and materials	1,900,000	1,900,000	0
Equipment	500,000	500,000	0
Grants, subsidies and contributions	74,035,500	73,891,000	-144,500
Subtotal	103,188,500	103,937,000	+748,500
Deduct quarters and subsistance charges	-15,000	-15,000	0
Total obligations by object	103,173,500	103,922,000	+748,500

Summary of Changes

1969 estimated obligations	$103,173,500
1970 estimated obligations	103,922,000
Net change	+748,500

	Base		Changes from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay costs	...	...	...	$9,000
B. Program				
1. Research grants	...	$60,185,500	...	396,500
2. Laboratory and clinical research	603	10,636,000	15	60,000
3. Collaborative research and development	39	12,545,000	3	271,000
4. Review and approval of grants	46	682,000	1	6,000
Total program increases	...	...	19	733,500
C. Payments to the "National Institutes of Health management fund" for centrally furnished services	...	4,839,000	...	547,000
Total increases	...	...	19	1,289,500
Decreases				
A. Program				
1. Fellowships	...	4,362,000	...	-171,000
2. Training grants	...	9,488,000	...	-370,000
Total decreases	...	...	...	-541,000
Total net changes requested	...	...	+19	+748,500

Explanation of Changes

Research grants--The net increase of $396,500 will provide for approximately 11 additional project grants and include a reduction of $18,000 for general research support grants.

Fellowships--The decrease of $171,000 will provide a total of $4,191,000 for about 240 awards, or 31 below the 1969 level.

Training grants--The decrease of $370,000 will provide a total of $9,118,000 for approximately 156 projects or 6 below the 1969 level.

Laboratory and clinical research--The increase of $60,000 and 15 positions will provide for expanded research in clinical allergy and immunology, chronic and degenerative, and viral diseases.

Collaborative research and development--The increase of $271,000 and 3 positions will provide for expanded support in transplantation immunology and the geographic medicine program.

Review and approval of grants--The increase of $6,000 will provide one additional position to support grants management activities.

Significant Items in House and Senate Appropriation Committee Reports

Item	Action Taken or to be Taken
1969 House Report	
(1) At the Committee's recommendation, the Institute is now supporting a multidisciplinary study of the relationship of viruses, bacteria and immunologic processes in the causes and development of emphysema and chronic lung disease. (Page 24)	(1) The Institute is submitting to the Committee a special report involving the problems and recent progress of research in this field. **Pages 15 and 17.**
(2) The Committee last year heard testimony on the Immuno-Therapy of Skin Cancer. It therefore directs that part of the appropriation for the Institute of Allergy and Infectious Diseases be donated to a collaborative research program of Immuno-Therapy and that funding of the program proceed without delay. (Page 25)	(2) The Institute has approved a grant for this research project.
1969 Senate Report	
(1) The Committee recommends an increase of $4,000,000 for accelerating research in the related fields of immunology and immuno-therapy. (Page 49)	(1) No funds appropriated for this research in 1969.

Authorizing Legislation

Legislation	1969 Authorization
Public Health Service Act	
Section 301--Research and Investigation, in general.	Indefinite
Title IV, Part D--National Institute of Allergy and Infectious Diseases.	Indefinite

PUBLIC HEALTH SERVICE ACT

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in section 301 of the Public Health Service Act.

The Public Health Service Act, Title IV, Research Institutes, Part D, National Institute on Arthritis, Rheumatism, and Metabolic Diseases, National Institute on Neurological Diseases and Blindness, and other Institutes.--

"Sec. 431 (b) The Surgeon General is authorized with the approval of the Secretary to establish in the Public Health Service one or more additional institutes to conduct and support scientific research and professional training relating to the cause, prevention, and methods of diagnosis and treatment of other particular diseases or groups of diseases (including poliomyelitis and leprosy) whenever the Surgeon General determines that such action is necessary to effectuate fully the purposes of section 301 with respect to such disease or diseases."

"Sec. 433 (a) Where an institute has been established under this part, the Surgeon General shall carry out the purposes of Section 301 with respect to the conduct and support of research relating to the disease or diseases to which the activities of the institute are directed, through such institute and in cooperation with the national advisory council established or expanded by reason of the establishment of such institute. In addition, the Surgeon General is authorized to provide training and instruction and establish and maintain traineeships and fellowships, in such institute and elsewhere, in matters relating to the diagnosis, prevention, and treatment of such disease or diseases with such stipends and allowances (including travel and subsistence expenses) for trainees and fellows as he may deem necessary, and in addition, provide for such training, instruction, and traineeships and for such fellowships through grants to public and other nonprofit institutions. The provisions of the subsection shall also be applicable to any institute established by any other provision of this Act to the extent that such institute does not already have the authority conferred by this subsection."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and Expenses, Office of the Director, NIH".....	$545,000	...	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH Management Fund.
Comparative transfer from:			
"General Research and Services, NIH".....	10,328,000	...	To transfer programs and functions from the Office of International Research.

National Institute of Allergy and Infectious Diseases

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
1960	24,071,000	30,286,000	41,000,000	34,054,000
1961	34,739,000	38,439,000	48,234,000	44,000,000
1962	48,322,000	52,182,000	60,000,000	56,091,000
1963	59,342,000	62,142,000	68,142,000	66,142,000
1964	69,226,000	68,723,000	69,226,000	68,723,000
1965	68,600,000	70,100,000	70,400,000	70,100,000
1966	74,987,000	74,987,000	77,987,000	77,987,000
1967	85,702,000	88,670,000	90,670,000	90,670,000
1968	94,422,000	94,422,000	98,922,000	94,422,000
1969	98,562,000	95,119,000	99,119,000	96,840,500
1970	103,922,000			

National Institute of Allergy and Infectious Diseases

Year	Estimate to Bureau of Budget	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
1960	25,379,000	24,071,000	30,286,000	41,000,000	34,054,000
1961	35,414,000	34,739,000	38,439,000	48,234,000	44,000,000
1962	50,063,000	48,322,000	52,182,000	60,000,000	56,091,000
1963	64,155,000	59,342,000	62,142,000	68,142,000	66,142,000
1964	69,364,000	69,226,000	68,723,000	69,226,000	68,723,000
1965	69,256,000	68,600,000	70,100,000	70,400,000	70,100,000
1966	76,374,000	74,987,000	74,987,000	77,987,000	77,987,000
1967	94,684,000	85,702,000	88,670,000	90,670,000	90,670,000
1968	102,682,000	94,422,000	94,422,000	98,922,000	94,422,000
1969	106,061,000	98,562,000	95,119,000	99,119,000	96,840,500
1970	106,044,000	103,922,000			

Justification

National Institute of Allergy and Infectious Diseases

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	718	$7,905,000	737	$7,991,000	+19	+$86,000
Other expenses.....	...	95,268,500	...	95,931,000	...	+662,500
Total.....	718	103,173,500	737	103,922,000	+19	+748,500

General Statement

The Institute conducts and supports research on the causes, characteristics, prevention, control, and treatment of diseases believed to be caused by infectious agents including bacteria, fungi, viruses, and parasites--or by abnormalities in the body's immune mechanisms such as allergies. In its attack on infectious and allergic diseases, the Institute is focusing attention primarily on important problems that demand increased research efforts. Two types of programs--nationally organized research programs and special emphasis research programs--have been set up to deal with these problems.

The nationally organized research programs are collaborative, contract-financed, Institute-coordinated efforts carried on by many laboratories to attain a common goal. They are conducted in partnership with industry, university research centers, and other Institutes of NIH. The special emphasis research programs are designed to intensify investigations of critical disease problems in urgent need of increased effort. Special emphasis research programs are also aimed at promoting the exchange of information to help identify and evaluate avenues of research that should be followed. The Institute also supports a large body of free-ranging investigator-inspired research.

The National Institute of Allergy and Infectious Diseases is requesting a total of $103,922,000 for 1970, an increase of $748,500 over 1969. This net increase is to be directed toward research of allergic and infectious diseases in the following areas: (1) research grants +$396,500, fellowships -$171,000, training grants -$370,000 or -$143,500 for extramural activities; (2) +$633,000 for intramural research and (3)-$260,000 for the contract program.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research projects.....	$50,346,500	$50,761,000	+$414,500
Special programs.....	9,839,000	9,821,000	-18,000
Total research grants.....	60,185,500	60,582,000	+396,500

Introduction:

The National Institute of Allergy and Infectious Diseases is continuing its efforts to obtain even more effective National Advisory Council participation in the grant and program review process. The Special Emphasis Research areas, described in last year's budget narrative, are one device for focusing attention on research needs of national importance. In June 1968 the Council subcommittee system was instituted. Each subcommittee is able to devote its time and the expertise of its members to consideration of the problems raised by a much smaller block of grant applications that relate to one disciplinary field. These problems may be concerned with scientific content, with program balance or policy. Particular attention is paid to applications previously singled out by staff as requiring special consideration. The subcommittee recommendations and actions are recorded and made available to all Council members prior to the assembled meeting, during which staff presents the subcommittee action for approval by the entire Council.

In 1969, the National Institute of Allergy and Infectious Diseases plans on supporting approximately 1,376 regular research projects with the amount of $50,346,500. The majority of these projects are ongoing noncompeting continuation grants which were recommended for payment by advisory groups in prior years for project periods of two to five years.

Program plans in 1969 and 1970

Allergy and other Immunologic Disorders:

Transplantation Immunology--Transplantation Immunology is a Special Emphasis Research area and also the subject of a current Special Report. Such emphasis recognizes the practical and intellectual importance of the field. On the practical side the principal barrier to successful organ transplantation is rejection of the transplanted organ. The explanation and control of rejection lies in immunology. Additionally, the field is in a period of great intellectual ferment and accomplishment. Understanding of the mechanisms involved can be expected to have great spillover benefits to the understanding (and possibly control) of neoplastic diseases, the growing list of auto-immune diseases, and to pathology generally. The programming activities of staff reflect this importance, and it is probable that the potential exists for a substantially increased number of meritorious grant applications.

This program area will be funded in 1969 at a level of approximately $2,617,000, and in 1970 at a level of approximately $2,653,000.

Bacterial and Mycotic Diseases:

Drug Resistance--The widespread use of potent antimicrobial agents has resulted in a new responsibility of major proportion to public health. More and

more strains of bacteria are becoming resistant to a greater variety of drugs. The present arsenal of antimicrobial agents will not continue to be adequate even though their judicious use will minimize the development of resistance to some of the antibiotics developed recently. This phenomenon of drug resistance has been dramatically emphasized by severe outbreaks of meningococcal infection, staphylococcal disease, and the continuing presence of chronic bacterial diseases, as demonstrated by chronic pyelonephritis and chronic pulmonary disease.

The program is wide ranging, including: the principal groups of bacteria to which drug resistance has been a problem (so called Gram negative intestinal bacteria, staphylococci, meningococci, bacteria modified (often by antibiotics) to naked or L forms) as well as antibacterial agents and their modes of action.

This program area will be funded in 1969 at a level of approximately $4,909,000, and in 1970 at a level of approximately $4,938,000.

Viral Diseases and Problem Areas:

Emphysema and Chronic Lung Disease--Emphysema is a Special Emphasis Program area and the subject of a current Special Report. The great public health importance of this group of diseases requires no further explanation. Regrettably, there have been no great practical or scientific advances to promise an early understanding of the causes, or an effective means of prevention or treatment. But as a result of Institute effort, there has been a substantial increase in the past three years in both the number of investigators (+270%) and the level of funding (+144%) devoted to discovering the intricate and obscure causes and the true dimensions of this disease complex. Interest is continuing to develop in the multidisciplinary approach of the more exact laboratory sciences, and in the long-term surveillance and epidemiological surveys.

This program area will be funded in 1969 at a level of approximately $1,218,000, and in 1970 at a level of approximately $1,310,000.

Chronic and Degenerative Diseases--This area includes such dread diseases as chronic renal disease, multiple sclerosis, vascular diseases, amyotrophic lateral sclerosis, and connective tissue diseases. The possible infectious and immunologic genesis of these diseases is a research area which, until recent years, received little attention from the scientific community. There is a significant body of information available from both extramural and intramural investigations to warrant a broad-fronted attack on the problems of the infectious and immunologic genesis of the chronic and degenerative diseases in man. Because of the chronic nature of these diseases, both in humans and animal models, observation periods are necessarily long and costly and progress relatively slow.

This program area will be funded in 1969 at a level of approximately $1,959,000 and in 1970 at a level of approximately $1,971,000.

Antiviral Substance--Viral diseases as a single category constitute the largest single cause of morbidity in the United States. In addition, present evidence suggests that many diseases of unknown etiology may eventually be shown to be of viral origin.

The great diversity of virus types necessitates consideration of broadly based alternative approaches in combating virus diseases. Drug screening, largely empirical, has revealed no generally useful antiviral drugs and, with few isolated exceptions, no drugs useful in the treatment of viral diseases.

Recently, however, partly from empiricism, partly from an understanding of the basic molecular biology of nucleic acid, and partly from the knowledge of the antiviral substance--interferon--produced naturally as a result of viral infection of cells, has become a most interesting series of compounds. These synthetic polynucleotides have been shown to cure or prevent virus infections in the intact animal and, additionally, to have anti-tumor activity in animals. This dramatic demonstration of the usefulness of basic knowledge in providing a practical way of disrupting virus growth will continue the demand for increased support of research on all phases of virus-cell interaction.

This program area will be funded in 1969 at a level of approximately $4,928,000, and in 1970 at a level of approximately $4,957,000.

U. S.-Japan Cooperative Medical Sciences Program--This program is a part of a comparative transfer from "Research and Services, NIH," to support research on certain diseases of Asia in cooperation with Japanese scientists and to foster exchange of new knowledge among workers by regularly scheduled symposia. Specific goals, such as, disease prevention through immunization, improved chemotherapy and nutritional improvement have been established by specific advisory committees for tuberculosis, leprosy, parasitic, bacterial and viral diseases which have Japanese counterparts.

This program will be funded in 1969 at a level of approximately $4,969,000, and in 1970 at a level of approximately $5,060,000. This is an increase of $91,000 over 1969.

Special programs:

General Research Support Grants--The decrease of $18,000 represents the Institute's proportionate share of the proposed budget for this program.

Gorgas Memorial Laboratory--The same level of support $500,000 is proposed for 1969 and 1970, for payment to the Gorgas Memorial Institute for maintenance and operation of the laboratory.

Categorical Clinical Research Centers--The same level of support, $1,100,000 is continued from 1969 to 1970, for centers participating in multidisciplinary investigations brought to bear on disease areas of critical need, including transplantation immunology and allergies.

International Centers for Medical Research and Training--The same level of support, $2,300,000 is continued from 1969 to 1970, to promote research and research training of United States scientists in selected foreign settings under the sponsorship and direction of American universities and with cooperating foreign institutions and investigators. The five centers now in operation provide unusual experience and exceptional biomedical research opportunities for American physicians and scientists for the long range interests of the United States. The program is a part of a comparative transfer from "Research and Services, NIH."

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Allergy and other immunologic disorders	$9,279,000	$9,392,000	+$113,000
Transplantation immunology	(2,617,000)	(2,653,000)	(+36,000)
Bacterial and Mycotic Diseases	17,649,000	17,911,000	+262,000
Drug Resistance	(4,909,000)	(4,938,000)	(+29,000)
Parasitic Diseases	6,047,000	6,004,000	-43,000
Malaria	(560,000)	(564,000)	(+4,000)
Viral Diseases and Problem Areas	16,271,500	16,341,000	+69,500
Emphysema and Chronic Lung Diseases	(1,218,000)	(1,310,000)	(+92,000)
Chronic and Degenerative Diseases	(1,959,000)	(1,971,000)	(+12,000)
Antiviral Substance	(4,928,000)	(4,957,000)	(+29,000)
Other Research	1,100,000	1,113,000	+13,000
Subtotal	50,346,500	50,761,000	+414,500
General Research Support	5,889,000	5,871,000	-18,000
Scientific Evaluation	50,000	50,000	0
Gorgas Memorial Laboratory	500,000	500,000	0
Categorical Clinical Research Centers	1,100,000	1,100,000	0
International Centers for Medical Research and Training	2,300,000	2,300,000	0
Total, research grants	60,185,500	60,582,000	+396,500

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting projects	1,100	$38,869,500	1,111	$39,284,000	+11	+$414,500
2. Competing projects	276	10,836,000	276	10,836,000	0	0
3. Supplementals	(67)	641,000	(67)	641,000	0	0
4. Subtotal regular programs	1,376	50,346,500	1,387	50,761,000	+11	+414,500
5. General research support		5,889,000		5,871,000		-18,000
6. Scientific evaluation	(1)	50,000	(1)	50,000		0
7. Gorgas Memorial Laboratory		500,000		500,000		0
8. Clinical research centers	5	1,100,000	5	1,100,000		0
9. International Centers for Medical Research and Training	5	2,300,000	5	2,300,000		0
10. Subtotal special programs	10	9,839,000	10	9,821,000	0	-18,000
11. Total research grants	1,386	60,185,500	1,397	60,582,000	+11	+396,500

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total fellowships.....	$4,362,000	$4,191,000	-$171,000

The primary objective of the Fellowships Program is to increase the availability of trained professional researchers in research areas within the categorical interests of the Institute. The Program is an integral portion of the research grant and training activities which are supported by the Institute.

The postdoctoral fellowships supports postdoctoral training for Ph.D's and those holding other equivalent degrees. Special fellowships are for those who can justify that additional training is needed to increase their value as independent investigators. Research career development awards are for support of young investigators who plan to pursue careers in independent research and teaching and who need further experience and training. Funds requested for 1970 will provide 240 awards compared to 271 in 1969, a decrease of 31. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	144	$2,813,000	141	$2,782,000	-3	-$31,000
b. Competing.....	44	692,000	44	766,000		+74,000
2. Supplementals.....	(7)	9,000	..	...	(-7)	-9,000
3. New.....	83	848,000	55	643,000	-28	-205,000
4. Total, Fellowships...	271	4,362,000	240	4,191,000	-31	-171,000

Fellowships (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral.....	110	$880,000	81	$706,000	-29	-$174,000
2. Special.....	35	420,000	40	527,000	+5	+107,000
3. Research Career						
a. Career.....	23	710,000	21	600,000	-2	-110,000
b. Development.....	103	2,352,000	98	2,358,000	-5	+6,000
4. Total, Fellowships...	271	4,362,000	240	4,191,000	-31	-171,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Training Grants...	$9,488,000	$9,118,000	-$370,000

The Institute's Graduate Training Grant Program is particularly concerned about providing young scientists with essential training and experience to meet manpower requirements in neglected and rapidly expanding areas of prime concern. Properly trained personnel are especially essential to insure continued progress in such areas as immunology and virology.

Funds requested for 1970 will provide for 156 grants, compared to 162 in 1969, a decrease of 6. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting...	151	$8,505,000	141	$8,000,000	-10	-$505,000
b. Competing.....	4	258,000	12	868,000	+8	+610,000
2. Supplementals.....	(17)	326,000	(7)	50,000	(-10)	-276,000
3. New.....	7	349,000	3	150,000	-4	-199,000
4. Scientific Evaluation.....	(1)	50,000	(1)	50,000	..	...
5. Total, Training Grants.....	162	9,488,000	156	9,118,000	-6	-370,000

Training Grants (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Graduate.....	162	$9,438,000	156	$9,068,000	-6	-$370,000
2. Scientific Evaluation.....	(1)	50,000	(1)	50,000	..	...
3. Total, Training Grants.....	162	9,488,000	156	9,118,000	-6	-370,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits....	603	$6,524,000	618	$6,591,000	+15	+$67,000
Other expenses.....		8,057,000		8,591,000		+534,000
Total.....	603	14,581,000	618	15,182,000	+15	+601,000

Introduction

The intramural research program is a broadly based effort of discovery and exploitation of new knowledge leading to improved prevention and treatment of diseases resulting from infection or abnormal immunological mechanisms. The program has a wide scope, embracing both basic and applied research. An effort is being made to give emphasis to those problems which are difficult to accomplish under the research grant mechanism and to take maximum advantage of the wealth of talent that exists in the intramural programs of other institutes by wide collaborations and frequent exchange of information. Infections under active study include those caused by viruses, bacteria, mycoplasma, yeasts, molds, fungi, protozoa, and helminths. New infective agents are discovered, the role of new or previously recognized agents in human disease evaluated, new or improved diagnostic technics developed, and the host-parasite relationship studied including initial tests in human volunteers. Emphasis is given to the discovery and evaluation of antiviral agents which might be useful in prevention or therapy of a wide variety of viral infections. The present work is concentrated on studies of the natural antiviral substance - interferon - and its inducers. Immunological studies are concerned with the problems of allergy, transplanted organ rejection, mechanisms of protection against infections, and prevention of autoimmune disease.

In recent years there has been increasing recognition of the tendency of many viruses to remain in host cells for prolonged periods after the acute infectious episode is over. New technics developed in large part within the Laboratories of Viral Diseases and Biology of Viruses have shown that there may be persistence of the infectious nucleic acid core of the virus in host cells, even though the whole virus is no longer produced, and that this viral genetic material may alter cell morphology and physiology. Such viral persistence may be related to cancer, certain endocrine disorders, genetic birth defects, and to various chronic and debilitating diseases. Other viruses have been categorized as "slow" viruses because of the long interval which elapses between infection and damage to the target tissues. "Kuru" in man, scrapie in sheep, are examples. That these are virus diseases has been amply demonstrated by animal transmission but the actual viruses remain to be isolated and identified in the laboratory and the full scope of such chronic virus infections which may lead to a wide variety of disabling neurological, pulmonary, and other diseases in man will remain unknown until new technics enable virus isolations and serological study. Similar inabilities to identify the viruses which are the cause of hepatitis, epidemic gastroenteritis and many respiratory diseases block effective research toward prevention. Infectious hepatitis is a major problem, with some 40,000 cases per year reported in the United States and perhaps ten times as many unreported or unrecognized cases. Most university scientists have dropped work in this field because of previous unrewarding efforts and the poor possibility that they can make significant progress within a grant period. The intramural program encourages a long range effort to develop the technics needed in the search for such viruses, enlisting a wide variety of scientific talent throughout the scientific

community in the effort.

The Institute continues to maintain field stations in Honolulu, Hawaii; Hamilton, Montana; Atlanta, Georgia; and the Panama Canal Zone. The Pacific Research Unit in Honolulu conducts epidemiological and laboratory studies on viral and parasitic diseases, utilizing the special ecological opportunities of oceanic islands. The Rocky Mountain Laboratory has special facilities for work with a variety of research animals and hazardous agents not possible at Bethesda. Atlanta provides opportunity for therapeutic and immunological studies in malaria-infected volunteers. The Middle America Research Unit in the Canal Zone affords special laboratory and field opportunities to work with a variety of insect transmitted viruses and their animal reservoirs, again impossible at Bethesda. This laboratory is jointly operated with the Walter Reed Army Institute of Research which conducts parasitological research. The Institute also has responsibility for the SEATO Cholera Research Program and the Pakistan-SEATO Cholera Research Laboratory in Dacca, East Pakistan, where significant advances in the testing of new vaccines and treatments have been made. Still other vaccines, including one which may neutralize the toxin responsible for the lethal diarrhea of cholera are under development under the auspices of the SEATO program, funded by the Agency for International Development, and the U. S.-Japan Cooperative Medical Sciences Panel on Cholera, and will be tested in Pakistan when available.

Program plans in 1969 and 1970

Clinical Allergy and Immunology:

With the appointment of a new Clinical Director last year, the Institute began the development of a clinical research program involving allergy and including the role of hypersensitivity to microbial agents as an important element in the development of asthma and chronic bronchitis. The program, designed to take advantage of the unique capabilities of the Clinical Center, to utilize the broad capabilities of other institutes and NIH laboratories, includes studies which because of their prolonged nature are difficult in a more general hospital setting. Allergic disorders affect more than 20,000,000 Americans but, despite the rapid advance of medical science in many areas, are still little understood and are usually treated empirically. The closely related problem of immunological rejection of transplanted organs and tissues has been highly publicized and study of this phenomenon is a necessary part of research on allergy, as is the study of the genetically linked immunological disorders. The importance of these diseases in American medicine, and the difficulty of establishing broad and continuing programs in non-Federal facilities where the investigator must depend on short term grants and competitive use of clinical facilities for care of the sick and for research, make it necessary to undertake the program intramurally.

Paralleling the redirected effort in Clinical Investigation is the program of the Laboratory of Immunology. Under direction of a new Laboratory Chief, who is an internationally recognized leader in immunological research including the problems of hypersensitivity, autoimmunity, and mechanisms of tolerance to antigenic stimuli, the program is expected to be complementary and closely correlated with the efforts on human disease problems in the clinical program.

To expand and implement these research programs 9 positions and $38,000 is requested.

Viral, Mycoplasma and Rickettsial Diseases:

The virological research program was reorganized to provide three major efforts. The Laboratory of Viral Diseases is concerned with the problems of respiratory virus and mycoplasmal diseases. The sections of the Laboratory of Viral Diseases, which have been engaged in studies on the oncogenic properties of respiratory viruses that also have significance for oncogenesis in general, were combined with the sections on viral biology from the Laboratory of Biology of Viruses and undertake the additional responsibility for the program of research on viruses as underlying causes of chronic and degenerative diseases. This effort will relate to the program at the Rocky Mountain Laboratory on slow viruses, but will reduce the need to install a sophisticated virological competence at that laboratory by making it possible to take advantage of the animal models under study on the NIH site. The redirected laboratory effort also relates to the programs of the Laboratory of Clinical Investigation on chronic bronchitis and other chronic infections since the deranged physiological activities induced by chronic viral infections may be an important underlying element. The Laboratory of Biology of Viruses will provide the capability for biochemical and biophysical studies of viruses at the molecular level which is necessary to the understanding of the enzymatic and physiological changes induced by viral infections. Since the 1970 requirements for these reprogrammed efforts will be mostly met by present resources of the two laboratories, no specific increase is requested.

The "slow" virus research program at the Rocky Mountain Laboratory was scheduled for expansion in 1968 to take advantage of the animal facilities which were enlarged in 1967. This expansion was planned because of the importance of rapidly advancing efforts to isolate and identify in vitro this group of viruses which cause chronic progressive fatal diseases in animals as an essential step towards similar studies in man. Cost reductions have postponed this expansion at RML.

With the identification of "Kuru", a lethal neurological disease of man, as a virus disease, the importance of pursuit of studies on "scrapie" in sheep became a great importance since the pathologic process is very similar. Attempts will be made to transmit other chronic, disabling diseases of man from man to animals and to study the diseases and transmissible agents.

The Rocky Mountain Laboratory has had four animal diseases under intensive investigation for the past 7 years, scrapie, and mink encephalopathy, Aleutian mink disease, and a chronic proliferative pulmonary disease of sheep which resembles certain tumors of man. Concurrent efforts are being made to relate the viruses which cause these diseases to diseases of man, to isolate and identify the viruses, and to develop immunological technics which will enable less cumbersome approaches to the investigation of the human problem. To conduct these studies the virology laboratories have been renovated and expanded, and new tissue culture laboratories equipped. A new animal compound was completed last year which will make possible the long term isolation of animals involved in these studies and minimize the risk of cross infections with other agents under study at the Rocky Mountain Laboratory or accidental infection of personnel.

An increase of 6 positions and $22,000 is requested to implement both new facilities and to carry on the work.

Bacterial and Mycotic Diseases:

Work on killed tuberculosis vaccine will be maintained even though costs are increasing rapidly as the studies on immune processes progress through the necessary stages of studies from mice to higher animals before reaching man. Facilities at the Rocky Mountain Laboratory are not adequate for safe challenge of immunized primates with virulent mycobacterium tuberculosis strains, therefore these studies must be done in contract facilities. The increased costs will be met by reprogramming both at RML and elsewhere. No increase in costs are projected.

Still another parameter to the problem of antibiotic resistance of bacteria was added during 1967 when it was reported that genetic factors causing resistance to several antibiotics could be quickly transferred from resistant bacteria to previously susceptible bacteria even of different species. While the initial importance of this finding was directly related to enteric infections caused by gram negative bacteria, the discovery opened new pathways for the study of resistance in other micro-organisms and needs to be fully explored. Since these factors occur at the cellular level and the mechanism of action is so far undetermined, the primary efforts are in the area of bacterial genetics and the determinants of resistance. The work could be highly important to the study of chronic infections such as bronchitis since the unresponsiveness of such infections to antibiotic therapy and because the rapid emergence of resistant strains of bacteria can create serious problems of spreading infections in hospitals.

The involvement of intramural staff in research related to the disease categories identified under the U.S.-Japan program has increased the opportunities in research on such diseases as filariasis, schistosomiasis, tuberculosis and cholera. There are, however, no plans to increase the scope of commitment to research in these areas in 1969 and 1970.

Renovation and updating of laboratories and equipment will continue as funds and opportunities permit. This is a continuation of a program begun in 1966 and directed toward the eventual replacement of obsolete laboratory furnishings and equipment. With the necessary regroupings which accompany shifts in research emphasis as a result of turnover of senior investigators, the continued advancement in equipment and changing technological requirements saves time and expands capability for the scientists. Competing with laboratory equipment needs is the rapid growth of computer technology and the expanding requirements for funds to employ programmers and to obtain computer time.

Other programs of the Institute will continue at about the same levels as in 1969 with major changes being accomplished by reorientation.

Also included in the requested increases is $7,000 for annualization of 1969 pay costs, and $534,000 for centrally furnished services from the National Institutes of Health Management fund.

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	39	$475,000	42	$487,000	+3	+$12,000
Other expenses		12,155,000		12,368,000		+213,000
Total	39	12,630,000	42	12,855,000	+3	+225,000

Introduction

The Collaborative Research and Development Program has as its mission the translation of significant basic research data into practical achievements of clinical applicability in allergy and infectious diseases. These activities are carried out primarily through research contracts with industry, universities, and other Federal and non-Federal institutions. In the planning and evaluation of contract-supported work the Institute is advised by committees comprised of leading scientists in the fields concerned. Each contract is monitored by a scientist project officer, usually an NIH intramural research investigator, who reviews the scientific progress of the work and aids the contractors with special technical problems. In addition, an administrative project officer is assigned to each contract to handle the non-scientific aspects of the project. The research areas encompassed by the Collaborative Research Program are: (1) Transplantation and Immunology; (2) Research Reference Reagents; (3) Virus Vaccine Development; (4) Bacterial Vaccine Development; and (5) Geographic Medicine.

Program Plans in 1969 and 1970

Allergy and other Immunologic Disorders:

The primary mission of the Transplantation Immunology Program is to determine the utility of histocompatibility matching in the selection of tissues for human transplantation. Studies of the tissue types of donors and recipients and the continuing evaluation of recipients of typed tissues indicate the utility of matching and the relative importance of the number of tissue antigens in the organs of transplant donors and recipients.

The Program, initiated in 1965, has placed major emphasis on the production and collection of adequate amounts of sera needed for human histocompatibility testing. Characterisitics of these different sera have been listed in a revised catalog which is available to interested immunologists; good-quality antisera are now being distributed to qualified laboratories in bulk and in special microplates containing 60 different sera to each plate. The microplates make identical sera available to a number of investigators throughout the world permitting more rapid testing and a large-scale evaluation by many laboratories of the efficacy of techniques and reagents. In addition, the accuracy of typing of the various

laboratories can be tested. The use of these reagents has made it possible for a WHO expert committee, comprising a number of the Institute's contractors and other ousiders, to reach an agreement on a system of histocompatibility nomenclature (the HLA system). This standard nomenclature and the recognition of the antigens with sera, provided by the Program, has greatly facilitated the world-wide research in histocompatibility matching. The utility of tissue matching already domonstrated in several small scale programs is now being further studied on a large scale in kidney and also in heart transplantation.

The Institute has established nine regional histocompatibility evaluation centers which participate in a program of prospective matching of donors and recipients. During the one-year period ending June 30, 1968, approximately 15,000 donors and recipients were typed. The activities of these laboratories resulted in organ matching for 1,350 transplantation procedures. Prospective recipients of heart and kidney transplants are typed and form a patient pool awaiting the availability of cadaver organs. Programs are under way for the rapid typing of dying and dead patients utilizing computer matching of histo-compatibility with awaiting recipients. Surgeons are then notified of the availability of requested tissues. On a more modest scale, members of the patient's families are typed and matched for the use in living kidney donor transplant operations. A program is underway to provide immunological studies of patients who have received transplanted organs to determine the presence or recurrence of immunological disorders such as glomerulonephritis, antoimmune disease and incipient graft rejection. Tests are also conducted on the serum of pretransplant patients for the presence of preformed antibodies resulting from previous blood transfusions or other forms of sensitization. The detection of these antibodies is necessary to prevent acute rejection when certain tissues are transplanted into these patients. There continues to be a severe shortage of qualified immunologists and technicians for tissue typing. During the past year over 100 persons have been trained in contractors' laboratories with funds provided by the Program. These courses vary in length from one week to three or more months. The program plans to continue the sponsorship and expansion of these training programs during the next year.

During 1970, the Program will be directed toward a larger scale evaluation of the efficacy of tissue typing in the selection of appropriate donors and recipients utilizing standard sera and techniques in well staffed institutions whose personnel are periodically checked for efficiency. Facilities will be available to type for kidney, heart, bone marrow and other organ transplantation. Emphasis will be placed on quality control of serum and only high-titered, potent material will be obtained and distributed. The development of lyophilization facilities will permit the storage and shipment of serum at room temperature obviating the necessity of freezing as a method of serum preservation. No new regional typing facilities will be funded. The Program will provide high-quality reagents in micro-trays to all qualified laboratories that are willing to report the results of their testing. This conditional gift will permit the correlation of data from a number of laboratories and a more expeditious evaluation of new sera. Studies will be continued in delineating the pathophysiological changes taking place in kidneys during storage with the aim of producing more efficient methods for the preservation of these tissues. Short-term methods of storage (less than three weeks) will be explored as a means of facilitating the rapid

distribution of viable cadaver organs between cities for transplantation. Long-term techniques for frozen storage of kidneys will also continue to be developed. These will permit true banking of available cadaver organs which can be used many months later for transplantation and which can be shipped long distances. Typing evaluation centers will continue to be closely integrated with existing dialysis and surgical programs and organ procurement and storage activities.

During 1970, studies directed at achieving more efficient immunosuppression will be instituted. A number of new anti-cancer drugs have been tested for immunosuppressive activity. Contract supported research has led to the short term successful use of one of these agents in the transplantation of bone marrow. During 1969, the Institute developed several sources for the production or large quantities of antilymphocyte serum (ALS). This serum, produced in horses and rabbits, is of some use in preventing organ rejection. A facility for the evaluation by laboratory tests and by studies in monkeys and chimpanzees has been established. During 1970, studies will continue in the evaluation of ALS in animals. Products found to have some activity will be chemically fractionated and studies will be pursued in sub-human primates to determine toxicity and efficacy of these fractions. Upon the completion of these tests, consideration will be given to the use of this material in a controlled clinical trial using transplantation patients.

During the past year preliminary work has been completed in the fractionation of antigen material from human tissues. This material is of potential use in inducing tolerance. In 1970 studies will be continued in the purification of this antigenic material and in the sub-human primate evaluation of its efficacy.

The kidney transplantation registry has increased in its size and in the depth of information on human transplants it has collected. A registry has also been established to collect information on donors and recipients of other organ transplants including the heart and bone marrow. These two registries will function during 1970 to collect and disseminate scientifc information needed by the Program and outside investigators in planning future transplantation research and in evaluating the efficacy of current procedures. Studies will continue to further evaluate possible latent consequences in transplantation. These include serological screening for the presence of abnormal antibodies, the use of immunofluorescent and other techniques to examine transplant tissues for evidence of local antigen antibody reaction and the study of transplant recipients for evidences of the appearance of graft vs host disease, a form of reverse rejection, which is seen particularly in bone marrow transplant recipients.

An increase of $225,000 and 3 positions is requested for these studies.

Viral, Mycoplasma, Bacterial and Rickettsial Diseases:

In 1969, the Vaccine Development Program is continuing its efforts in two major areas, (1) the development and testing of experimental rubella (German measles) vaccines; and, (2) the further development of vaccines against a mycoplasma and several viruses which are known to cause severe respiratory illness, and it is initiating studies in another promising area: the development and testing of streptococcal vaccines.

The rubella virus is recognized as an important cause of congenital defects such as heart disease, blindness and mental retardation in children born to mothers contracting German measles during pregnancy. Every effort is being directed toward the development of a safe, effective vaccine to prevent the occurrence of these congenital defects.

In 1968 and 1969, a live attenuated strain of rubella virus, designated as HPV-77 and developed by scientists at the Division of Biologics Standards, has been extensively evaluated by clinical investigators in this country and abroad. Over 25,000 volunteers have been inoculated with various HPV-77 vaccines and 96 percent developed antibodies. Although vaccine virus was shed from the nose and throat, there was no evidence of transmission of the virus to uninoculated contacts. In the face of a rubella epidemic, the vaccine has proven to be more than 90 percent effective in preventing natural disease.

During 1968 and 1969, in addition to producing larger amounts of HPV-77 vaccine, the program has explored HPV-77 derivatives propagated in other tissue culture systems such as canine and rabbit kidney, duck and chick embryo, and WI-38 cells. During 1970, efforts are being directed to complete follow-up studies on rubella vaccines.

The need for a killed rubella vaccine, particularly for women in the childbearing age group, is evident; however, work on developing an inactivated rubella vaccine has been discouraging. A number of physical and chemical agents have been employed to inactivate the virus. Although most agents used did inactivate the virus, they unfortunately also inactivated the virus antigenicity. These studies will continue in 1970 to see if it is possible to completely inactivate the virus with the margin of safety that would be required and still maintain viral antigenicity.

During 1969, respiratory viruses vaccine development activities proceeded on a broad front. Extensive field trials of the adenovirus type 4 tableted vaccine have been conducted in the Armed Forces. About half a million military recruits received the oral vaccine during past years. The vaccine continues to be about 90 percent effective in protecting against the natural disease. No untoward reactions have occured. The yearly financial savings to the Armed Forces in preventing acute respiratory disease is estimated at more than $10,000,000.

A program for the development of streptococcal vaccines is just beginning. During 1969, the further clinical evaluation of these vaccine will continue. The need for a safe and effective vaccine that could hopefully prevent streptococcal throat infections and serious complications of rheumatic fever and kidney disease is obvious.

In 1969, clinical trials of live attenuated respiratory syncytial virus vaccines were extended to include younger children and in 1970 trial of live attenuated parainfluenza viruses and rhinoviruses will be initiated. Hopefully, live attenuated vaccines will offer significant protection in those cases where killed vaccines have generally been unsatisfactory.

The collaborative program on rhinovirus typing has succeeded now in delineating 100 separate rhinoviruses. The multiplicity of different rhinovirus types poses a serious obstacle to the development of a "common cold vaccine". However, it is expected that selected studies on a few rhinovirus vaccines will furnish significant scientific information applicable to other respiratory vaccines.

In 1969, a large scale nation wide surveillance of pneumococcal disease was activated in order to define those population groups which show high risk of morbidity and death from pneumonia. Approximately 400,000 persons are now being studied under contracts awarded in 1968. The participating investigators include the University of Pennsylvania School of Medicine in Philadelphia; Dorthea Dix Hospital, Raleigh, North Carolina; Coney Island Hospital, New York; Harvard University Health Center, Cambridge, Massachusetts; Permanente Medical Group, San Francisco, California; Washington County Hospital, Hagerstown, Maryland; Cushing Hospital, Framingham, Massachusetts; University of Washington School of Medicine, Seattle, Washington; and the University of North Carolina School of Medicine, Raleigh, North Carolina. Additional contracts for surveillance are currently being negotiated with the Navajo Indian Health Area in Arizona and New Mexico, and the George Washington University School of Medicine in Washington, D. C. These populations range from hospitalized chronically ill individuals to healthy normal individuals, and from old age groups to adults to pediatrics populations.

Eli Lilly Company of Indianapolis, Indiana is in process of producing 2 million doses of each of twelve types of pneumococcal capsular polysaccharide for the first lots of experimental vaccine against twelve specific types of pneumococci.

In 1970, the surveillance of pneumococcal disease will be expanded to include additional pediatrics populations by contracts with the University of Chicago and with Childrens Hospital of Washington, D. C. and adult populations with the U. S. Veterans Administration and possibly with the U. S. Air Force. Additional production of vaccine by at least one more manufacturer will be attempted. As new vaccine becomes available, laboratory testing will be done by the Massachusetts Department of Health, E. R. Squibb and Sons, and State University of New York at Buffalo. Negotiations are currently underway for clinical safety and efficacy testing procedures with Baylor University and Methodist Hospital of Houston, Texas. Finally, the testing of vaccines in limited populations should be underway by late 1969 or early 1970.

No increases are requested for these studies. Requirements for expansion will be met by reorientation of resources within the activity.

The Research Reference Reagents Program plans for and manages the production, certification and distribution of reference reagents (mostly purified seeds and standardized antiserum) essential in microbiological research. Currently, over 600 types of reagents are available to researchers and are distributed in quantities sufficient for reference purposes. These reagents are also available in working quantities for daily use of intramural researchers, collaborative contractors and other Federal laboratories.

In 1969 emphasis has been placed on (1) completion of reference reagent production for those accepted viral prototypes of the adeno, myxo, and enterovirus groups; (2) continued production, testing and certification of both type specific and grouping reagents for arboviruses; (3) continuation of the production, testing and certification of human and animal mycoplasma reagents in a cooperative effort with Division of Biologics Standards; (4) initiation of rhinovirus reagent production, testing and certification; (5) completion and issuance (October, 1968) of the Catalog of Research Reagents, and (6) surveillance of reagents which have been in storage three to five years.

In 1970 primary emphasis will be on (1) completing production of vitally needed rhinovirus, arbovirus and mycoplasma reference reagents. Rhinoviruses are responsible for a significant number of cases of human upper respiratory disease; (2) evaluating the benefits of the program thus far on biomedical research and instituting whatever means are needed to insure that reagents are available and are being fully utilized; (3) developing a program which will insure a stable, long term system for storage and distribution of reagents; (4) operation of the zonal centrifuge facility to be located near the NIH campus. This facility will be in full operation in 1970 and will provide intramural research and NIAID contractors with both expertise as well as physical facilities and equipment for the zonal centrifuge. The zonal ultracentrifuge is a sophisticated biophysical technique that has proven useful in the study of subunits of viruses, purification and concentration of vaccines for human use or antigens for the preparation of high titered antisera. The zonal centrifuge program also provides the opportunity for practical evaluation of rotors and zonal centrifuge systems developed by ORNL. The entire program represents application of bioengineering developments toward improved vaccines and biologic products which in the long run will benefit public health.

The Institute's Research Reference Reagents Program will continue to maintain close liaison with the National Communicable Disease Center, World Health Organization, American Type Culture Collection and other groups with specific reagents programs to assure maximum coordination of effort and effective utilization of program funds as well as specific cooperative efforts to yield new information on reference reagents.

The Geographic Medicine Program provides staff to support the scientific and administrative management of grants, contracts and conferences for the U.S.-Japan Medical Sciences Program, the International Centers for Medical Research and Training, and the International Research Career Development Program. This program is a part of the comparative transfer from "Research and Services, NIH."

An increase of $46,000 is requested to support this program in 1970.

Included in this net increase is $1,000 for annualization of 1969 pay costs and a decrease of $47,000 for centrally furnished services from the National Institutes of Health Management fund.

Training Activities

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	6	$90,000	6	$90,000	..	...
Other expenses	..	75,000	..	65,000	..	-$10,000
Total	6	165,000	6	155,000	..	-10,000

Introduction

The International Research Career Development Program (IRCDP) was started in 1963 by the National Institutes of Health to develop competence in the Public Health Service in medical research related to problems of an international nature which cannot ordinarily be undertaken in the United States and to provide opportunities for promising scientists to work abroad as members of the U. S. biomedical research groups. A variety of unusual or unique opportunities exist in foreign countries for pursuing studies of substantial importance to medical science in general and to the health of the people of the U. S. in particular. Investigations in the field of geographic pathology and epidemiology on an international basis are likely to provide important clues to the causes of certain diseases which cannot be studied adequately in more restricted environments.

Program Plans in 1969 and 1970

This Program responsibility was assumed in 1969 by this Institute following dissolution of the Office of International Research. In accordance with the OIR's previously stated plans, the six positions for this Program will be utilized for scientists to pursue research of specific relevance to selected international cooperative science agreements, e.g., the U. S.-Japan Cooperative Medical Sciences Program now managed by the NIAID and other programs of the Geographic Medicine Branch. Each assignment is tailored to the particular background and interest of the Associate as well as to the needs of the Public Health Service. The new Associates will take training in and work on those biomedical problems which international agreements have selected for joint effort, beginning with cholera, leprosy, malnutrition, tuberculosis, parasitic and virus diseases under the U. S.-Japan Cooperative Medical Sciences Program. The decrease of $10,000 reflects services furnished centrally by the National Institutes of Health Management fund.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	46	$534,000	47	$541,000	+1	+$7,000
Other expenses		904,000		990,000		+86,000
Total	46	1,438,000	47	1,531,000	+1	+93,000

This activity provides for the over-all coordination and administration of the Institute's grants programs. The activity is responsible for planning and developing scientific programs for research and training grants and fellowship awards. This involves the collection, processing, review and evaluation of applications; support of the National Advisory Allergy and Infectious Diseases Council; liaison with approriate organizations and scientists, continual vigilance by professional staff of program progress on scientific activities; and surveillance by supporting personnel on recording and reporting of varied information concerning grants management.

The requested program increase of $6,000 will provide one additional position for the grants management activity. The increase also includes $1,000 for annulization of 1969 pay costs, and $86,000 for centrally furnished services from the National Institutes of Health management fund.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	24	$282,000	24	$282,000	...	...
Other expenses		42,000		26,000		-$16,000
Total	24	324,000	24	308,000		-16,000

This activity supports the Institute Director and his immediate staff in the over-all administration, coordination and direction of all the Institute's activities.

The decrease of $16,000 is in centrally furnished services from the National Institutes of Health Management fund.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Laboratory and Clinical Research			
(3) Medical Officer	GS-13		$54,747
(4) Virologist	GS-11		40,812
Maintenance Engineer	GS-11		10,203
(2) Research Technician	GS-7		13,962
(5) Animal Caretaker	WB-4		26,830
		(15)	146,554
Collaborative Research and Development			
Medical Officer	GS-15		21,098
Medical Officer	GS-14		19,771
Clerk-Stenographer	GS-5		5,732
		(3)	46,601
Review and Approval of Grants			
Scientist Administrator	GS-13		14,409
		(1)	14,409
Total new positions, all activities		(19)	207,564

TUESDAY, APRIL 1, 1969.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

WITNESSES

DR. FREDERICK L. STONE, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GORDON J. KLOVDAHL, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
MRS. EMMA LOU AKERS, BUDGET OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 est.	1970 est.
Personnel compensation:			
Permanent positions	1,913	2,163	2,160
Positions other than permanent	58	67	67
Other personnel compensation	12	16	16
Total personnel compensation	1,983	2,246	2,243
Personnel benefits: Civilian employees	191	228	223
Travel and transportation of persons	122	170	164
Transportation of things	11	25	17
Rent, communications, and utilities	110	131	129
Printing and reproduction	112	147	139
Other services	4,990	4,871	4,907
Supplies and materials	58	82	77
Equipment	20	64	33
Grants, subsidies, and contributions	148,153	151,991	149,871
Total obligations	155,750	159,955	157,803

PERSONNEL SUMMARY

Total number of permanent positions	215	202	202
Full-time equivalent of other positions	6	6	6
Average number of all employees	196	202	202
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	83,217	83,717	84,263
(b) Fellowships	20,207	21,373	20,040
(c) Training	44,729	46,901	45,568
Total, grants	148,153	151,991	149,871
2. Direct operations:			
(a) Collaborative research and development	3,924	3,295	3,288
(b) Training activities	381	449	337
(c) Review and approval of grants	2,741	3,125	3,251
(d) Program direction	829	1,095	1,056
Total, direct operations	7,875	7,964	7,932
Total program costs, funded [1]	156,028	159,955	157,803
Change in selected resources [2]	−278		
Total obligations	155,750	159,955	157,803
Financing:			
Comparative transfers to other accounts	374	391	
Unobligated balance lapsing	4,126	3,168	
Budget authority	160,250	163,514	157,803
Budget authority:			
Appropriation	160,284	163,514	157,803
Transferred to other accounts	−34		
Appropriation (adjusted)	160,250	163,514	157,803
Relation of obligations to outlays:			
Obligations incurred, net	156,124	160,346	157,803
Obligated balance, start of year	110,847	108,580	132,378
Obligated balance, end of year	−108,580	−132,378	−133,383
Adjustments in expired accounts	−3,416		
Outlays	154,975	136,548	156,798

[1] Includes capital outlay as follows: 1968, $14,000; 1969, $33,000; 1970, $33,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $3,699,000; 1968, $3,421,000; 1969, $3,421,000; 1970, $3,421,000.

Mr. FLOOD. We now have the National Institutes of General Medical Sciences, Dr. Frederick L. Stone, the Director will be the principal witness.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

We will insert your biographical sketch in the record at this point. (The document follows:)

BIOGRAPHICAL SKETCH

Name: Frederick L. Stone, Ph. D.

Position: Director, National Institute of General Medical Sciences, National Institutes of Health.

Birthplace and date: Born, March 31, 1915, Biloxi, Miss.

Education: 1937 Middlebury College, Middlebury, Vt. (chemistry), B.S.; 1942 University of Rochester, Rochester, N.Y. (biology), M.S.; 1948 University of Rochester, Rochester, N.Y. (biology), Ph. D.; 1949–53 American University, Washington, D.C. (public administration).

Experience: August 1964– , Director, National Institute of General Medical Sciences, NIH; July 1962–August 1964, Chief, Division of Research Facilities and Resources, NIH; January–July 1962, Acting Chief, Division of General Medical Sciences, NIH; 1958–62, Assistant Chief, Division of General Medical Sciences, and Chief of the Division's Research Training Branch; 1957–58, Assistant Chief, Division of Research Grants, and Chief of the Division's Research Training Branch; 1956–57, Assistant to the Associate Director, NIH; 1955–56, director, Medical and Scientific Department, National Multiple Sclerosis Society, New

York: 1954–55, assistant for professional services to the vice chancellor, Schools of the Health Professions, University of Pittsburgh, Pittsburgh, Pa.; 1951–54, Chief, Extramural Programs, National Institute of Neurological Diseases and Blindness, NIH: 1948–51, Chief, Research Fellowships Branch, Division of Research Grants, NIH; 1947–48, instructor in biology, University of Rochester, Rochester, N.Y.

Association memberships: Association of American Medical Colleges, American Association for the Advancement of Science, American Academy of Neurology, American Society of Ichthyology and Herpetology, American Historical Society, Association for Research in Nervous and Mental Diseases, Association for Research in Ophthalomology, Cosmos Club, Washington, D.C., Sigma XI and the Royal Society of Medicine (affiliate).

Honors, awards: Superior Service Award, Department of Health, Education, and Welfare, April 10, 1964; the Secretary's Special Citation, Department of Health, Education, and Welfare, January 1966.

Mr. FLOOD. Please proceed, Dr. Stone.

GENERAL STATEMENT

Dr. STONE. Mr. Chairman and members of the committee, I welcome the opportunity to tell this committee about some accomplishments of the National Institute of General Medical Sciences during the past year.

It is a function of this Institute to identify and help solve broad, complex problems in health and medicine by marshalling manpower, the funds, and the sophisticated tools of modern science.

Traditionally, the Institute supports biomedical sciences that provide information about the nature and structure of man, especially those basic sciences that unite common concerns of all the research components of the National Institutes of Health. Some measure of the quality of research supported by this Institute is that 18 of its grantees have won the Nobel Prize.

To insure continuity of excellence in research, the Institute funds hundreds of research training programs and fellowships. Last year, these funds supported 7,000 young scientists who will not only conduct the biomedical searches of the future, but most of whom will teach the next generation of medical practitioners.

The strategy of the Institute's research program is to support a wide range of projects in fundamental sciences while organizing and developing a unified, concerted effort of research projects that relate to specific missions.

AUTOMATED CLINICAL LABORATORIES

The Institute's program for automating hospital and other diagnostic laboratories is a planned, balanced, integrated set of activities ranging from studies of chemical compounds in body fluids to the design and development of new instruments and specialized computers especially programed to handle laboratory data.

Through grants and contracts, the Institute guides the development of key components that, in combination or separately, will speed diagnostic tests, vastly increase their reliability, and cut unit costs.

Along with computer design goes the development of systems for automating processes that are now being carried out manually in most laboratories, using slow, often inexact techniques. After methods have been developed for automating these diagnostic tests, they will be put under the control of specially designed computers to insure speed, quality control, and precision not now possible with manual methods, and much faster reports to the physician.

Essential to the automation of clinical laboratories are standardized equipment, techniques, and chemicals so the test made in Seattle yesterday can be compared with the test made in Washington this morning. To automate laboratory tests, chemical reagents used as a basis of comparison must be standardized. As it is now, there are as many as five or more different versions of a chemical reagent. The Institute is taking a first step toward developing chemical standards as part of its automated clinical laboratory program.

It is anticipated that, in 5 to 7 years, the Institute's program could produce automated prototypes for the major segments of future clinical laboratories. Industrial production of these components would make possible the automation of 70 percent of hospital and other diagnostic testing laboratories in this country. Small hospitals would use those parts of the system that fitted in with their patient needs and laboratory manpower.

New types of tests are being devised that not only lend themselves to being automated, but which provide more precise information in some instances and, in others, test for anomalies recently identified by research.

At Oak Ridge National Laboratory, two new systems are being developed and tested that, using new ultrasensitive methods, can identify dozens of different chemical constituents in urine and blood serum. Continued support from the Institute will enable scientists to miniaturize components of these systems, thereby increasing their analytical potential and their output, as well as speeding their use in medical centers throughout the country.

PHARMACOLOGY AND TOXICOLOGY

The concept that two or more drugs interact is well known. What is not known is precisely how this interaction occurs, what effect one drug has on another, whether the interaction is toxic, or harmless, or whether one drug may neutralize another on which the patient's very life depends. These are the subtle questions for which answers are being sought day by day in animal and clinical studies.

One precise answer was discovered this past year by three scientists at the Emory University Pharmacology and Toxicology Center supported by the Institute. In treating a young epileptic, the clinical researchers gave the boy two drugs—diphenylhydantoin and primidone—that act on the central nervous system. In concurrently treating the boy for another problem, the physician-scientists also gave him a mild stimulant—methylphenidate—which normally brightens a patient's mood and improves his ability to concentrate, read, or work. Under the surveillance customary in such clinical studies, the investigators noticed that, after the mild stimulant had been administered, the drug diphenylhydantoin in the boy's blood stream rose to toxic levels and the level of the drug primidone also rose significantly. In studies of adult patients, the stimulant methylphenidate, when administered to patients who had received an anticoagulant drug, ethyl biscoumacetate, interfered with the metabolism of the anticoagulant. Further studies will determine the effect of this stimulant on drugs other than the three already identified.

A most important, largely neglected area of drug research is the effect that drugs taken by pregnant women have on their unborn children. At the new, Institute-supported pharmacology center at

Baylor University, studies already show that prenatal ingestion of tranquilizers has caused trembling and other coordination problems in infants. Investigations of this nature in the newborn have not been possible in the past because the very small blood samples which could be safely taken from infants and very young children were insufficient for analytical tests. New techniques such as mass spectroscopy and gas chromotography now make possible the analysis of minute samples.

Much of the evidence about the deleterious effects of drugs on the unborn is circumstantial. The scientists at Baylor pharmacology center expect to establish scientific evidence that can be used as a basis for prescription by physicians.

In the next fiscal year, scientists supported by the Institute will especially address themselves to studying factors that control the variability of drug response, to testing hypotheses about the action of drugs on immune response to organ transplants and allergies, and to the major problem of prolonged use of drugs for chronic illness with the resultant tolerance that nullifies the drug's effect or the gradual development of toxic levels.

TRAUMA

Every year 100,000 Americans die from injuries, half of these deaths are caused by car smashes; 50 million Americans are injured, 10 million are temporarily disabled, and 400,000 permanently disabled. In money alone, the cost is close to $20 billion. The enormity of this national disaster is exceeded only by the national indifference to it.

Trauma—the medical term for injury—is a two-faced disease: on one side, the obvious evidence of bleeding, broken bones, abrasions, bruises; on the other, the insidious, unpredictable results of serious injury—the disruption of the body's internal protective systems.

Violent injury, especially the multiple injuries from car crashes, affects the body like an internal earthquake. The mechanism that coagulates blood, that, in the instance of a minor cut, has time to do its work, is not geared for instant, massive action. Serious multiple injuries may trigger the blood coagulative mechanism all over the body. Clots form where there is no need for coagulation and may cause death. In many instances, despite skillful surgery and care, injured patients die for unknown reasons.

This year, the Institute funded four new, highly specialized trauma research units, bringing the total to seven. Studies at these centers concentrate on different aspects of injuries. All the centers are accumulating data that will have application to trauma treatment.

At the center at Parkland Memorial Hospital in Dallas, opened in April 1968, some 150 injured patients were admitted to the research unit in the first 7 months of operation. Eight of these patients who most likely would not have survived even with the best of emergency care, survived under the special care of the research unit.

A dread complication following many severe injuries is the stress ulcer. Inexplicably, the lining of the stomach disintegrates and the patient may bleed to death. In the course of gathering baseline data on the injured patients in the Parkland Hospital trauma unit, the scientists observed a difference in the nature of the gastric secretions of three patients. Those three patients later developed stress ulcers.

This is an important lead in solving one of the most baffling problems related to injury, the stress ulcer.

The Institute's modest trauma research program, besides the seven research centers, comprises 30 projects. Included are studies of changes in cells following injury, mechanisms of wound healing which, if understood, might be speeded artificially, and the special problems of chest injuries. Ten young surgeons, supported by the Institute, are being specially trained for research in the field of biological repair following injury. Here, the slightest bit of new information will save many lives, much suffering, and millions of dollars. The program also supports, with fellowships, 15 young scientists who are pursuing their own original trauma research ideas.

The Institute's trauma program, the new national program to investigate a broad spectrum of injury problems and to develop new methods of treatment, is the most recent example of how the Institute identifies a national, largely neglected health problem and marshals basic and clinical scientists to help solve it.

Mr. Chairman, the appropriation request for the National Institute of General Medical Sciences for 1970 totals $157,803,000, a decrease of $2,151,500 from the 1969 operating level of $159,954,500. Most of this decrease is in the fellowships and training grants program.

RESEARCH ON DRUGS AND IMMUNE RESPONSE

Mr. FLOOD. Apparently we can't keep these things under one roof. You say you are going to test hypotheses about the action of drugs upon immune response to organ transplants and allergies. Hasn't that been what we were talking about this morning and last Thursday and Tuesday, with an assortment of your colleagues? This question of the transplants and the immunization problem and the resistance of the body to these foreign substances. We are becoming expert, even on this side of the table, on this problem.

Now you want a piece of it. I thought somebody else was already doing this; testing the action of drugs on the autoimmune problem in connection with transplants. You have just changd the language a little bit. The only difference is you don't use the word autoimmune. You just say "drugs on immune response." That is semantics, isn't it; nothing else?

Dr. STONE. Let me digress for a moment. I believe I can understand some of the perplexity facing the committee.

Mr. FLOOD. That wouldn't be much of a trick. We are chronically in that condition.

Dr. STONE. One cannot predict precisely in advance where fundamental research may lead. In previous testimony heard by the committee——

Mr. FLOOD. You have been coming here since the Civil War. You never mentioned this before.

Dr. STONE. I think you will find, sir, that the point I will make was also brought out last year in our testimony on our pharmacology-toxicology program.

In our large, grant-supported, pharmacology-toxicology centers, there is a good deal of research conducted in which drugs are given to animals for the purpose of determining their effect on the immune response.

Mr. FLOOD. I don't think there is any doubt about this, Doctor, and there is no doubt the use of drugs to bring about the desired end in these transplants has been somewhat advanced by research, but why is your Department doing it, and also all these other fellows?

Dr. STONE. Drugs are part of the general armamentarium of researchers.

Mr. FLOOD. Armamentarium?

Dr. STONE. Yes.

Mr. FLOOD. Armament?

Dr. STONE. For research. Some of the modalities and techniques involve drugs in every Institute in the National Institutes of Health.

Mr. FLOOD. I am interested in your use of this term. Armamentarium to me means armament, weapons, a weapons system.

Dr. STONE. One might say that it is a collection of tools or weapons. Armamentarium might be considered somewhat less fashionable than weapons systems.

Mr. FLOOD. The fact that it is old-fashioned doesn't make it bad.

Dr. STONE. The reason you hear the term repeatedly is because we are all attempting to help each other. One focus of this Institute is on fundamental research under section 442 of the act. The research conducted is commonly of interest to two or more other Institutes and is important to their missions.

AUTOMATION OF CLINICAL LABORATORIES

Mr. FLOOD. We have talked for several years about the need for much more automation in the clinical laboratories. We have talked a great deal about it.

What progress are you making in that? We first started talking about this over in the Defense Subcommittee years ago; then it got over here.

In your shop, of course, it fits in. So what progress are we making?

Dr. STONE. In my written statement that was prepared last November I indicated that we could produce automated prototypes for the major segments of future clinical laboratories in 5 to 7 years. We now believe that a more correct estimate is something like 3 to 5 years. Within that period we will have developed prototype instruments, devices and systems that industry can take over for production, marketing and distribution.

In the past the personnel of the Institute have played an important role in the development of the LINC computer.

Mr. FLOOD. The same outfit that made the simulator for the Air Force, LINC?

Dr. STONE. No sir; not the same organization. I mention the role of the Institute in the development of this computer to indicate that we have had some modest experience and success in developing prototype instrumentation and making it available to industry for production and distribution.

Mr. FLOOD. What progress are you making? This is no new thing.

Dr. STONE. We have developed a second generation set of instruments that are now being tested. We hope these will provide more rapid and more accurate results at lower unit costs in the clinical laboratory.

Mr. FLOOD. Who is going to buy the obsolete first generation, the Department of Defense, as we have been doing for about 10 years? The salesmen come in and as the new baby is born they dump all these now obsolete things on the Defense Department.

Dr. STONE. The first generation of these laboratory instruments was not developed for use by the consumer, but rather as experimental models.

Mr. FLOOD. The same thing happened with the school boards over the country. They go back into the provinces and dump all the obsolete visual aids on the school boards and the next morning issue a declaration that an entire new generation has been born.

MINIATURIZATION

We have become very, very much interested in miniaturization. Again I come back to Defense. It is a bad habit of mine. I was present at the first showing in the Pentagon years and years ago of the first operational computer they had, and it was a Rube Goldberg thing the size of that wall. I have been back since and now it is about the size of a table. I expect to go back soon and see it half the size of the table.

The space people are doing a great job on this. Now, where are you in the area of miniaturization? Does miniaturization save money or merely space and size in hardware?

Dr. STONE. In miniaturization we are lagging behind in medical research generally. As far as miniaturization for the clinical laboratory, the technology is new and we are just beginning to exploit it.

Mr. FLOOD. Don't you tend to test things too long before you are willing to put them into operation?

Dr. STONE. The medical profession is dedicated to the welfare of an individual patient at a particular point in time. It is not surprising then that they are conservative. This attitude has contributed considerably to the success of American medicine to date.

Mr. FLOOD. Let me point this out. Is this an analogy or do you feel it is? During the war we had to have aircraft. That was "the" thing. Every time my committee met the fly boys were in with a design for a new plane. Then they would come in with another design for a new plane. Every time they came in they had a design for a new plane. Designs, designs, designs, designs.

We were getting ready to bomb Germany and all we had were designs. We finally had to say to them, "We need aircraft in England tomorrow, not designs. Build aircraft." We had to cut it out.

Dr. STONE. There is a degree of analogy here, but of course the war as disease has its own characteristics. At Oak Ridge, which is potentially one of the foremost centers for biomedical engineering we have a small group that operates as part of our automated clinical laboratory program. It is concerned with the reduction in size of instrumentation——

Mr. FLOOD. Why don't you ask the Japanese to do it for you? They are terrific in that.

Dr. STONE. It is difficult for us to go abroad for such work for reasons well known to you. There is the matter of the balance of trade and contract versus grant moneys.

The Johns-Hopkins Applied Physics Laboratory has strengths in this area and in the future it may prove purposeful to contract with them for certain types of electronic miniaturization.

Mr. FLOOD. You are as concerned about the problem as we are and you are on top of it, is that it?

Dr. STONE. It is a main mission of the Institute; we are certainly as concerned as you are.

Mr. FLOOD. As long as you are seriously concerned and are aware that you have a problem, I don't doubt that you will do it, but you have to get off your duff. You are behind everybody else in miniaturization.

Dr. STONE. We are indeed. You can be certain that it will get our continued attention.

Mr. FLOOD. Now, to what extent are your labs out there at Bethesda, to what extent are they automated?

Dr. STONE. I am glad to report that the general consensus across the country is that the NIH clinical laboratory under the direction of Dr. Williams and Dr. Cotlove, stands at the forefront of the automated laboratory effort. I would also like to note that Dr. Williams and Dr. Cotlove have been most helpful to NIGMS in the organization and conduct of its extramural automated clinical laboratory program.

Mr. FLOOD. You think that you are the best?

Dr. STONE. The Clinical Center's laboratory is one of the best, if not actually the best.

TRAUMA

Mr. FLOOD. On page 47 you say:

> Trauma, the nation's fourth leading cause of death and disability and the leading cause of death in young people between the ages of 1 and 35, is under attack.

How are you attacking trauma? How do you do that? And, by the way, what is trauma and, skipping the automobiles, give us a half dozen other types and kinds of routine trauma; not some exotic thing.

Dr. STONE. The term "trauma" is taken to include such problems as shock after major surgery, crushing injuries, burns, near drowning, massive overwhelming infection and the like.

Mr. FLOOD. Trauma is not just simply a punch in the mouth. It can be a lot of things.

Dr. STONE. It is an all-encompassing term and a poor one. We have been trying to find a better one. Quite frankly, every time someone mentions trauma somebody puts "psychic" in front of it.

Mr. FLOOD. I am very interested in words and derivations and this thing is awful. "Trauma."

Dr. STONE. We are moving ahead with the trauma program on a variety of fronts. Particular attention is being given to the establishment of trauma centers for research and research training where the team approach to the resolution of the problems presented by trauma in its various forms is accented. This is not to suggest that the individual project grant does not play an important part in the total program. It does. But we are greatly interested in these centers and the impact that engineering is having on the problems presented.

Mr. FLOOD. I still am not certain what you mean. How are you attacking trauma? Are you preventing it or are you talking about treating it after the fact?

Dr. STONE. We are treating trauma after the fact. We are not engaged in accident prevention. Typical of the avenues of investigation

are changes in body fluids in response to hemorrhage, measurement, identification and alteration of the blood and its constituents in severe burns, and effects on the lung due to injury to other parts of the body.

Mr. FLOOD. Severe burns are real honest-to-God traumas.

Dr. STONE. Among the worst. One of the most peculiar manifestations of the burned body is its tremendous need for energy. The need is far greater than for seemingly equally severe elective surgical procedures.

Mr. FLOOD. Have you worked with the Navy people in Bethesda on severe burns? They are probably the best in that.

Dr. STONE. At the moment we are working with the U.S. Army in their program.

Mr. FLOOD. Not this outfit in the Navy?

Dr. STONE. We have not to date because our program has been small. However, it certainly would be desirable as the program expands. At the moment findings generated by our program are made available to the Army and Navy through standard channels.

GENETICS

Mr. FLOOD. If there is one thing that your shop has been really excited about in the last few years, it is on research in genetics.

Suppose you tell us your accomplishments in this field. What practical values may come of them so far as Mr. and Mrs. Average American on Main Street are concerned? Research in genetics; they are not excited about it at all.

Dr. STONE. A problem to date has been that the implications of genetics in an everyday sense have not been well understood. However, the situation is improving. Young married couples whose families have a history of anomalies are increasingly going to their local medical school or university medical center for genetic counseling.

Mr. FLOOD. Do you use the word "anomaly" in connection with the retarded, underdeveloped, deformed?

Dr. STONE. I was thinking of physical anomalies and deformations. I was not thinking of mental retardation.

Mr. FLOOD. Or deformity?

Dr. STONE. The deformity might be of the nature of extra fingers for example.

Mr. FLOOD. Go ahead.

Dr. STONE. Much of the practical genetic counseling that is available today comes about as a result of the basic and applied research that the "G" program—now, this institute—supported for the last 20 years.

With respect to the current search for knowledge that will be used tomorrow, we are finding, for example, that the genetic constitution of one individual causes him to react—as in the metabolism of a drug—much faster or slower than another individual.

Mr. FLOOD. Do you take all your arsenal of weapons and go chasing down this path?

Dr. STONE. We do not. By virtue of the $8 million that we are providing for this program, many dedicated men are working on a variety of problems.

You have had extensive testimony, for instance, from Dr. MacNichol. Sixty percent of neurological disease is thought to be of ge-

netic origin so genetics is one of the sciences today available to medical practice.

Mr. FLOOD. Suppose you define genetics for the average man on the street. What do you mean by "genetics"?

Dr. STONE. It is the science of inheritance and development. It isn't only just inheritance; it is development as well.

Thirty years ago I trained as a geneticist and I have lost most of it in the intervening time. It has been one of the most exciting areas to watch in an administrative sense. I don't deal with the particulars of science; I deal with the generalities of it now. It has been one of the most exciting fields to watch in its development. I would like to note that in one of the subprograms of our genetics program, we are encouraging and bringing about a much closer and direct relationship between chemistry and physics in the study of the inheritance process than has been present to date. We call this genetic chemistry and, though it is a small program hidden in the overall genetics program, it is most exciting and I think it will provide us with a lot of important things to talk about in ensuing years.

Mr. FLOOD. Are you interested in determining the sex of a fetus when it is about 90 days old?

Dr. STONE. We are not supporting research in this area.

Mr. FLOOD. Determining if it is a male and at once attacking hemophilia if the family history indicated the likelihood of a hemophiliac.

Dr. STONE. I am not certain of the specific genetics of hemophilia.

Mr. FLOOD. Wouldn't you like to find out?

Dr. STONE. I certainly would.

Mr. FLOOD. Is there a very high incidence of hemophilia?

Dr. STONE. No. I can provide its exact incidence for the record if you like. It is sex linked; and its incidence is 1 in 10,000 of the population.

It is sex linked in that females carry the disease and only males have it.

Mr. FLOOD. At what point does Mendel get into this?

Dr. STONE. In the mid-1800's Mendel rediscovered, in Austria, the basic principles of genetics which had previously been discussed and written about by others.

Mr. FLOOD. The law of Mendel does not apply in the transmission of hemophilia?

Dr. STONE. It does with modifications.

BEHAVIORAL SCIENCES

Mr. FLOOD. I notice you are doing work in behavioral sciences. Well now, Doctor, if there is anything that upsets the metabolism of this committee, it is this kind of problem. We sat here and heard, for three and a half hours, Dr. Yolles—a fascinating presentation as far as I am concerned. But it seemed to me that he exhausted the subject; that he wrung it dry. It seemed to me that the Mental Institute is working on every conceivable aspect of the behavioral sciences.

Now, what in the world could you possibly be doing that the Mental Institute isn't involved in?

Dr. STONE. We support a very small program in the behavioral science field. It is less than 1 percent of our total research program.

However it is unthinkable to me, sir, that the National Institutes of Health should not be supporting some behavioral science in the interest of potentiating and making more readily available the results of its general program of applied research and development.

Just as biochemistry is supported in all of the National Institutes of Health and also in Dr. Yolles' distinguished institute, I believe that the behavioral sciences to a moderate degree, should be supported in three or four Institutes.

Mr. FLOOD. What are you doing that Yolles' institute isn't also involved in?

Dr. STONE. There are some fundamental areas that he doesn't support. The Neurology Institute supports a good deal in the behavioral science. The Child Health Institute has it written into their law with relation to learning. It is written into our law, which says something to the effect, "Support the basic and general medical sciences and the natural and behavioral sciences related to health." In effect, Congress, in its wisdom, has decided that no single science shall be the prisoner of any administrator.

Mr. FLOOD. You are very flattering. That takes care of that question.

RESEARCH ON ORAL CONTRACEPTIVES

Mr. MICHEL. How much are you spending on the side effects of the birth control pill, if any?

Dr. STONE. We have one contract at about $350,000. This is an important but not an extensive part of our program in pharmacology and toxicology. We share this interest with the Child Health Institute and their major interest in population control.

Mr. MICHEL. Broadening the inquiry in this area would more properly be in Child Health rather than in your shop?

Dr. STONE. We share the interest, but the center of gravity in this program is clearly in the Child Health Institute.

Mr. MICHEL. Has anything been disclosed which would indicate a correlation between taking the pill and circulatory ailments?

Dr. STONE. One of our grantees, Dr. Jick, a clinical pharmacologist at Tufts University in Boston, is working on this problem.

Over an intitial 2-year period of the study, 2,500 patients received an average of 10 different drugs during their hospital stay. I might say parenthetically most people do not realize how many drugs are injected by a patient during a hospital stay. Sometimes eight drugs precede an anesthesia.

Twenty-five percent of the 2,500 patients had moderate to severe reactions definitely or probably due to the drug in question that they were following.

Half of the women involved, over 60, receiving heparin, to minimize the formation of blood clots following heart attack or stroke, have bleeding complications as compared to 10 to 20 percent of women under 60, or men of any age. Particular care—this study indicates—must be exercised when giving heparin to women over 60. This is not a direct thing, but it indicates one of the studies we are doing.

A small percentage of these 2,500 patients received oral contraceptives and had thrombo-phlebitis or pulmonary embolism—that is to say, blood clots in the legs or the lungs.

Dr. Jick has shown that women with blood type O have only one-fourth as many cases of thrombo-phlebitis or pulmonary embolism

as might be expected, whereas women with blood type A have more frequent complications. Dr. Jick's findings suggest a direct relationship between blood type and the clotting phenomena. Incidentally, this study was computer-based and could never have been conducted without the computer's assistance due to the number of patients involved and the number of combinations and permutations that have to be considered statistically in the analysis of the results.

INDIANA UNIVERSITY RESEARCH TRAINING GRANT

Mr. MICHEL. Doctor, earlier in the hearing I made mention of my being party to a line of inquiry and investigation, personally in our family, by way of a National Institute of General Medical Sciences Training Grant No. 5(TI)-GM-1056, which was apparently awarded over the past number of years to Dr. A. Donald Merritt, Indianapolis Medical School. I found upon inquiry that this has been a program which has been funded since fiscal year 1963, and will continue through 1972, and the scientists consider it a very meritorious grant.

In fiscal year 1963 it was $37,368, again the same amount in 1964, $1 less for some reason or another in 1965 and 1966, and 1967, $32,706, 1968, $76,435, and in 1969, $71,516, or a total of about $330,127. What I would like to have for my own benefit is a synopsis following this question as to what we are really getting from this, and what in medical terminology we are pursuing.

Dr. STONE. We will respond for the record in this case.

Mr. MICHEL. I think it is very fundamental from our point of view here to get some idea. This morning I was pursuing a line of these grants that go on for extended periods of time. I know it takes a long time sometimes to get some real results, but every $37,000 item adds up and before long you have nearly a million dollars, and you put those all together and that makes the overall large figure that we get wracked up on the floor of the House every once in a while. If we can then in turn give them a little response of a very meaningful and personal nature, that will help the case.

Dr. STONE. We will be glad to provide the information.

(The information follows:)

I am happy to respond to your inquiry concerning the research training grant in genetics, 5 TO1 GM 1056, to the Indiana University Medical Center under the directorship of Dr. A. Donald Merritt, chairman of the department of medical genetics. Our records indicate that this active research training program has expended a total of $183,271 from its activation on January 1, 1963, through June 30, 1968. During this period $94,422 (51.6 percent) was used for direct support of trainees. Other costs included tuition ($5,297), salaries of technical staff ($14,104), equipment ($15,321), supplies ($22,227), and guest lecturers ($2.225), all of which are normal categories of expenditures from a grant of this kind.

Because this is a research training grant, the basic objective is not to accomplish research but rather to support and encourage the training of people for independent research and academic careers in the field of medical genetics. As is usually the case, this research training program functions in an environment of active research in medical genetics—a field in which there is a severe shortage of adequately trained people.

This program provides research training and experience for high-caliber, younger scientists at both predoctoral (Ph. D.) and postdoctoral (Ph. D. and M.D.) levels and emphasizes the training of young investigators who will have a double competence, obtaining skills in both clinical medicine and in research in medical genetics.

Since the beginning of this grant 31¼ man-years of training have been provided.

The staff of the program includes 16 scientists from a number of basic science and clinical departments who are doing research in a wide variety of problems related to human genetics, ranging from the inheritance of diabetes mellitus and cystic fibrosis, cleft palate and lip, clinical dental genetics, hereditary neurological disorders, hereditary studies on mental defects, and the inheritance of intelligence. The actual research of the staff is supported by a number of different Institutes, including NIAMD, NINDS, NCI, NICHD, as well as DRFR. Therefore the research training grant serves to bring together the talents of investigators whose research is supported by a number of Institutes for the training of young scientists for research teaching and clinical care in the area of human genetics.

Miss Marian Rivas, the young lady about whom you inquire, receives no support from training grant GM 1056. A graduate student at Indiana University, she receives partial support of her training in medical genetics from another source entirely. However, in order to answer your questions concerning Miss Rivas, and presumably others in a similar status, we have inquired of Dr. Merritt at the Indiana University Medical Center. Dr. Merritt, by the way expressed his appreciation of your gracious assistance and cooperation in helping Miss Rivas with this study. The trait of interest is a deficiency of thyroxin-binding globulin (TBG), a blood component which influences thyroid function. Through studies of families, it has been learned that there are at least five variants of the basic trait which may result in either a deficiency or excess of TBG. Understanding of this trait has clinical significance since affected persons may show a low level of protein-bound iodine suggesting a hypothyroid condition. As such persons are not hypothyroid, treatment with thyroid hormone, or thyroxin, would be harmful rather than beneficial. As these Indiana University studies suggests a 3 to 5 percent frequency of this trait in some populations, the number of people involved is not negligible. The fact that the trait is inherited assists in locating affected individuals. In order to determine the existence of the trait, it is necessary to conduct personal interviews and obtain samples. It is usually less expensive to do this by visit than it is to bring many individuals to the laboratory.

Grant funds supporting Miss Rivas' studies are quite modest. Dr. Merritt has told us that these funds provide her an annual stipend of about $2,600 plus University tuition. As for travel, on one trip she used a university-owned vehicle at a charge of 8 cents a mile. Anticipating that her continuing study would involve travel costs, Miss Rivas applied directly to the Indiana University Foundation and received a grant of $500 to support further necessary travel. From this grant she purchased a used car for $40 and had it put in operating condition by a high school class in automotive mechanics. Dr. Merritt tells us that over a 4-year period Miss Rivas has received support totaling $15,286, which includes research costs and tuition, as well as her modest stipend. During this time she has completed a master of science degree and is now a Ph. D. candidate.

Mr. FLOOD. Are there any further questions?

Mr. Casey?

ACTIVITIES IN CONNECTION WITH GENETICS

Mr. CASEY. On genetic counseling, do you get in all fields of it? How about cystic fibrosis?

Dr. STONE. That is a field that falls mostly within the province of the Allergy Institute. However, I am sure that many of our grantees do provide advice in this area.

Mr. CASEY. Every once in a while you will see some article about research in genetics, and they are on the verge of producing superbrain children, in other words, real ultrasmart kids. Are you involved in that?

Dr. STONE. No, sir.

Mr. CASEY. I am not opposed to it. I wish some of these kids would be a little smarter now.

Dr. STONE. On the matter of intelligence, the Mental Health Institute and several Institutes at the National Institutes of Health provide information and data through supported programs which bear on intelligence in one way or another. I believe once again I have to pass the bouquet on to Dr. La Veck because learning and the development of intelligence would be shared as a responsibility between his

Institute and the Mental Health Institute. I am not trying to dodge the question, I am really trying to answer it.

Mr. CASEY. I do not believe I have any more questions, Mr. Chairman.

Mr. FLOOD. Mrs. Reid?

SAVINGS THROUGH AUTOMATION OF LABORATORY PROCEDURES

Mrs. REID. You say that the achievement of a fully automated laboratory system would lower medical costs and a patient's time in a hospital. Have you conducted any studies as to how much these lab delays contribute to a patient's medical bill which automation might conceivably reduce—or are you talking in a hypothetical sense?

Dr. STONE. Although this Institute has conducted no formal studies to justify the fact that automation would lower medical costs and a patient's time in a hospital, our statements are based on several studies conducted by others which are:

Studies performed at the Clinical Laboratory of the Clinical Center, NIH, reveal that over the past 5 years the workload in the clinical laboratory has doubled while using fewer personnel to perform the tests, resulting in considerable savings in salaries.

Using the automated enzyme analyzer system, the Clinical Center performs these sophisticated tests five times as fast and with four times the accuracy as by manual methods.

The experience at the Kaiser Permanente Foundation, in Oakland, Calif., has shown that approximately four to five times the number of tests can be performed per patient dollar by partially automated methods as can be done by manual methods.

A group of 40 pathologists in Denver, Colo. sending their test specimens to a central laboratory are now charging $15 for a panel of 12 tests. The cost for these tests without automation is $60.

The United Medical Laboratories in Portland, using existing automation, perform a panel of 12 tests for $6 total charge—cost by manual methods is $60.

Thus through automation, costs per test have been reduced in the clinical laboratory from an average of $5 per test to approximately 50 cents per test.

In most hospitals a physician requests laboratory tests to back up or confirm a diagnosis. Usually no treatment is given to the patient until all laboratory tests are performed. In many laboratories this may require as much as 4 days delay in treatment while a test sample is sent to another laboratory for analysis and the results returned.

Through automation, the Clinical Center, NIH, has been able to reduce patients stay in the hospital by as much as one-third in instances where general medical problems are involved.

In many of the smaller hospitals not having automated procedures, some tests are performed only once a week due to small staff and large workloads. If, for example, a glucose tolerance test for the diagnosis of diabetes is performed only on Tuesdays and a patient is admitted on Wednesday, he may be forced to wait a full week before this diagnostic test is run. Automation of the procedures make it possible to perform these tests as they are requested—thus reducing the patient's stay in the hospital.

Mrs. REID. Thank you.

Mr. FLOOD. Thank you, Dr. Stone.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation

	1969	1970
Appropriation	$163,513,500	$157,803,000
Comparative transfer to "Salaries and Expenses, Office of Director"	-391,000	---
Cutback required by P.L. 90-364	-3,168,000	---
Total obligations	159,954,500	157,803,000

Disposition of cutback:

To be returned to the Treasury	3,168,000

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
47	Research		$83,717,000		$84,263,000		+$546,000
	General research support grants		(8,127,000)		(8,120,000)		(-7,000)
	Scientific evaluation grants		(1,437,000)		(1,437,000)		(---)
	Pharmacology-Toxicology research		(3,500,000)		(3,500,000)		(---)
	Anesthesiology and Diagnostic Radiology centers		(1,000,000)		(1,000,000)		(---)
55	Fellowships		21,373,000		20,040,000		-1,333,000
58	Training		46,901,000		45,568,000		-1,333,000
	Direct operations:						
63	Collaborative research and development	---	3,295,000	---	3,288,000	---	-7,000
65	Training activities	22	449,000	22	337,000	---	-112,000
66	Review and approval of grants	124	3,125,000	124	3,251,000	---	+126,000
67	Program direction	56	1,094,500	56	1,056,000	---	-38,500
	Total obligations	202	159,954,500	202	157,803,000	---	-2,151,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions.....	202	202	0
Full-time equivalent of all other positions.....	6	6	0
Average number of all employees.....	202	202	0
Personnel compensation:			
Permanent positions.....	$2,163,000	$2,160,000	-$3,000
Positions other than permanent.....	67,000	67,000	0
Other personnel compensation.....	16,000	16,000	0
Total personnel compensation.....	2,246,000	2,243,000	-3,000
Personnel benefits.....	228,000	223,000	-5,000
Travel and transportation of persons..	170,000	164,000	-6,000
Transportation of things.....	25,000	17,000	-8,000
Rent, communications, and utilities...	131,000	129,000	-2,000
Printing and reproduction.....	147,000	139,000	-8,000
Other services.....	4,871,000	4,907,000	+36,000
Supplies and materials.....	82,000	77,000	-5,000
Equipment.....	63,500	33,000	-30,500
Grants, subsidies, and contributions.	151,991,000	149,871,000	-2,120,000
Total obligations by object....	159,954,500	157,803,000	-2,151,500

Summary of Changes

1969 estimated obligations	$159,954,500
1970 estimated obligations	157,803,000
Net change	-2,151,500

Increases	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
A. Built-in				
1. Annualization of pay increases effective in 1969	---	---	---	+$4,000
B. Program				
1. Research grants	---	$83,717,000	---	+546,000
2. Review and approval of grants	124	1,721,000	---	+18,000
3. Program direction	56	1,006,500	---	+500
Total program increases	---	---	---	+564,500
C. Payment to the "NIH Management Fund" for centrally furnished services	---	1,461,000	---	+38,000
Total increases	---	---	---	+606,500
Decreases				
A. Program				
1. Fellowships	---	21,373,000	---	-1,333,000
2. Training grants	---	46,901,000	---	-1,333,000
3. Training activities	22	404,000	---	-92,000
Total program decreases	---	---	---	-2,758,000
Total decreases	---	---	---	-2,758,000
Total net changes requested	---	---	---	-2,151,500

Explanation of Changes

Research grants--The $546,000 program increase includes $553,000 for noncompeting continuations in regular projects offset by a decrease of $7,000 in general research support grants.

Fellowships--The program decrease of 258 awards and $1,333,000 to a 1970 level of 1,991 awards reflects a reduction of 307 new awards amounting to $1,808,000 and 33 competing awards for $506,000 offset by increases of 82 awards in noncompeting projects for $965,000 and $16,000 in supplemental awards. This represents a reduction of 205 predoctoral awards, 27 postdoctoral, 21 special and 5 career development awards.

Training grants--The program decrease of 478 trainees, 63 awards and $1,333,000, to a 1970 level of 525 awards reflects a decrease of 476 trainees in graduate training and 2 trainees in clinical training.

Training activities--The program decrease in 1970 of $92,000 represents a reduction in personnel compensation and benefits and other costs for research associates.

Review and approval--The increase in 1970 of $18,000 is for program increases.

Program direction--The program increase of $500 in 1970 is for equipment.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1969 House Report	
None	
1969 Senate Report	
None	

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301--Grants programs.....	Indefinite
Title IV, Part E, Institutes of Child Health and Human Development and of General Medical Sciences.....	Indefinite

PUBLIC HEALTH SERVICE ACT

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in section 301 of the Public Health Service Act.

"Sec. 442. The Surgeon General is authorized, with the approval of the Secretary, to establish in the Public Health Service an Institute for the conduct and support of research and research training in the general or basic medical sciences and related natural or behavioral sciences which have significance for two or more other institutes, or are outside the general area of responsibility of any other institute, established under or by this Act."

"Sec. 444. The Surgeon General shall, through an institute established under this part, carry out the purposes of sections 301 with respect to the conduct and support of research which is a function of such institute ...."

"Sec. 433. (a) .... In addition, the Surgeon General is authorized to provide training and instruction and establish and maintain traineeships and fellowships, in such institute and elsewhere, in matters relating to the diagnosis, prevention, and treatment of such disease or diseases with such stipends and allowances (including travel and subsistence expenses) for trainees and fellows as he may deem necessary, and in addition, provide for such training, instruction, and traineeships and for such fellowships through grants to public and other nonprofit institutions. The provisions of this subsection shall also be applicable to any institute established by any other provision of this Act to the extent that such institute does not already have the authority conferred by this subsection."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and Expenses, Office of Director"	$391,000	---	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH Management Fund.

National Institute of General Medical Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1966	$124,538,000	$124,538,000	$129,388,000	$127,188,000
1967	137,175,000	142,613,000	145,113,000	145,113,000
1968	160,284,000	160,284,000	164,284,000	160,284,000
1969	165,777,000	161,250,000	166,250,000	163,513,500
1970	157,803,000			

Note: Included in "General Research and Services, National Institutes of Health," appropriation prior to 1966.

National Institute of General Medical Sciences

Year	Estimate to Bureau of Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1966	$137,753,000	$124,538,000	$124,538,000	$129,388,000	$127,188,000
1967	146,854,000	137,175,000	142,613,000	145,113,000	145,113,000
1968	161,656,000	160,284,000	160,284,000	164,284,000	160,284,000
1969	175,277,000	165,777,000	161,250,000	166,250,000	163,513,500
1970	161,786,000	157,803,000			

Note: Included in "General Research and Services, National Institutes of Health," appropriation prior to 1966.

Justification

National Institute of General Medical Sciences

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	202	$2,474,000	202	$2,466,000	--	-$8,000
Other expenses.....	--	157,480,500	--	155,337,000	--	-2,143,500
Total.....	202	159,954,500	202	157,803,000	--	-2,151,500

General Statement

The National Institute of General Medical Sciences supports a broad base of fundamental and applied biomedical research activities aimed at the solution of certain major health problems. Specific programmed research objectives are to develop new knowledge for safer and more effective use of drugs, to understand the genetic basis of disease, to improve health services through the application of engineering knowledge to medical care; and to provide better diagnosis and therapy in medicine. The Institute also has prinicpal responsibility for training young medical scientists in some 20 pre-clinical and clinical disciplines, thus reinforcing strongly the total National Institutes of Health research effort. The research effort in the fundamental sciences is designed to provide a foundation for understanding disease processes and to furnish a unifying strand of basic information to the disease oriented program of NIGMS and the other Institutes of NIH.

The National Institute of General Medical Sciences is requesting a total of $157,803,000 for F.Y. 1970, a decrease of $2,151,500 from F.Y. 1969.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Regular Program.....	$69,653,000	$70,206,000	+$553,000
Special Program.....	14,064,000	14,057,000	-7,000
Total research grants....	83,717,000	84,263,000	+546,000

Introduction:

The NIGMS has been developing a sharply focused program of research in clinical and fundamental sciences which relates directly to human health and disease. A number of specific areas have emerged concerned closely with the welfare of sick or injured patients. These research areas are: Trauma, Anesthesiology, Diagnostic Radiology, Pharmacology Toxicology, Automation of Clinical Laboratories, and a small nucleus of a program for the application of Behavioral Sciences to biomedical problems. Engineering as applied to biology and medicine has also become a program supporting a number of projects specifically aimed at improving the care of the patient or speeding up the diagnosis of his illness or his therapy.

During the past year we have also organized the fundamental support program of our investigator-initiated research into three major areas which, although they are not sharply directed, have specific programmatic interest. These areas include Human Genetics and Genetic Chemistry, the study of Cellular Structure and Function, particularly at the subcellular and chemical level and the beginning of a program in adaptation of the organism to its environment.

Program Plans in 1969 and 1970

The only programs which will be expanded in fiscal year 1970 will be those which offer the greatest possibility of providing new information which can be immediately applied to the improvement of human health. These programs are: Automation of the Clinical Laboratories which will speed up and yet reduce the cost of laboratory diagnoses: the study of adverse drug reactions including possible mutagenic effects and clinical studies on trauma patients.

It should be noted that the Fundamental Science Program which will not be expanded has also made significant contributions toward the clinical programs during the past year through development of improved methods for the detection of extremely small amounts of materials in blood and in expired gases of patients. Improved diagnostic techniques have emerged from studies in Genetics and Cellular Structure and Function that will lead to the detection of genetic abnormalities and hopefully prevent these conditions or enable their early treatment.

Clinical Sciences

Trauma - Trauma, the nation's fourth leading cause of death and disability and the leading cause of death of young people between the ages of one and 35, is under attack in the NIGMS which has now started six centers for trauma research. The present center programs are concentrating on the detrimental metabolic changes in the injured patient, on biochemical changes at the cellular level in order to determine what happens to injured tissues and how they heal. Major advances have been made in these areas in the past year. Other investigators are studying infection as a result of burns or decreased resistance due to other major or multiple injuries. The use of on-line computers is being explored for the constant assessment of severely injured patients. Psychiatrists in one center are studying the behavioral responses to injury to try to determine why some people react poorly to a sudden physical disability.

The pathology and physiology of trauma also is being investigated. Certain symptoms may become predictable in relation to specific pathological injuries and this knowledge would aid the clinician with the minute-to-minute decisions that he must make--decisions which often are critical in life threatening conditions. The individual research projects in addition to supplementing the center studies are also concerned with different phases of shock, the repair of tissues and wound healing, treatment of burns, rehabilitation, prosthetic devices, and drowning. As forecast last year, two new trauma research centers were activated in 1968 at a total cost of $500,000--one in January at the University of Texas, Southwestern Medical School, and one in April at the University of Maryland School of Medicine. The present support of trauma research is approximately $2,500,000. It is planned that one additional center will be funded in 1970.

Anesthesiology and Diagnostic Radiology Research Centers - As a result of testimony before Congress relating to the Heart Disease, Cancer, and Stroke program, it became apparent that major advances in supporting specialties of anesthesiology and diagnostic radiology would be essential to the conquest of these diseases. NIGMS was directed to stimulate research in these areas. In F.Y. 1970, $1,000,000 will be used for the development and support of a limited number of centers of excellence for research in these fields. To date four important centers in anesthesiology have been established utilizing fully the funds made available. The center grant is important because it provides for a coordinated program of research on man and animals. A center substantially increases and improves an institution's and a region's research productivity because it can attract top-flight scientists in different disciplines to work on the activities of the center.

Anesthesiology - The modern specialty of anesthesiology is concerned with far more than rendering a patient unconscious so that otherwise painful procedures can be carried out. The anesthesiologist, because of his special combination of skills in clinical and related fundamental sciences, is concerned with all aspects of pain control, with the management of the unconscious patient from any cause, the treatment of respiratory emergencies, resuscitation, inhalation therapy, post-operative care, and many other problems. One of the significant achievements is in monitoring the conditions of the infant during labor. A technique of sampling scalp capillary blood of the human fetus has been established as a standard diagnostic technique in the obstetric service. In a population in which the major diseases are chronic and painful, a new center is working on the evaluation and control of chronic pain. Other work concerns the dangerous interrelationship of anesthetics and simultaneously administered drugs; and the effects of anesthesia on the heart during and after open-heart surgery. All of these areas are covered in the four new anesthesia research centers which have been established. The newest center was awarded in September 1968 to the University of Washington School of Medicine, Seattle. The present support of research in anesthesia, in addition to the four centers, includes 37 individual projects for a total of approximately $3,700,000. Little expansion is expected in 1970.

Diagnostic Radiology - The central and essential role of diagnostic radiology in clinical medicine is well known. The diagnostic radiologist functions primarily in the hospital setting where his service to every specialty creates a heavy work load which together with his need for very expensive, complex equipment makes research diffuclt. Nevertheless, new techniques and new approaches are essential if the radiologist is to meet the increasing demands for his services both in terms of the numbers of examinations required and the new types of procedures which should be developed. The NIGMS supports research to improve diagnosis through new instruments and computerized systems and to widen the range of techniques available to the clinician including such special procedures as autoradiography and thermographic analysis of body heat radiation patterns to establish the existence of tumors, blocked blood vessels, or other abnormal conditions. Diagnostic radiological research has demonstrated that minute temperature elevations exist at the surface of the skin which are sometimes associated with increased cellular or metabolic activity such as cancer. Another outstanding project is investigating the clinical applications of ultrasound in medical diagnosis to

obtain optimum differentiation of normal and abnormal anatomy. The present program includes nine regular grants and one program project for approximately $500,000.

Automated Clinical Laboratories - New horizons in medicine have created widespread expectations that a revolution in the treatment of human disease will occur. The analysis of samples for diagnostic treatment from human patients has not received the full benefit of basic research. The program in Automation in the Clinical Laboratory is an attempt to bridge the gap between this basic research and provision of adequate economical medical care.

The goal is the development of a completely automated laboratory. Completely automated systems do not exist at present although there are a number of partially automated systems in use. Therefore, during the coming year, the NIGMS program will concentrate on the development of new analytical tools and methods, and the development of automated systems for the rapid and accurate testing of biological fluids. These together with the development of appropriate computer hardware and appropriate controls for analytical methods will lead to the assemblying of a completely automated laboratory. It is anticipated, costs to the patients will be reduced through lower laboratory fees and shorter stays in the hospital.

Institute-sponsored research has produced a prototype of an instrument for the high resolution analysis of body fluids. This instrument is capable of identifying many of the metabolites and drugs which are excreted in the urine. Prototype instruments have been placed in large medical centers specializing in pediatric and internal medical problems.

The feasibility of a "minimum" computer installation for hospitals, housed entirely in an 8 X 10 room, has been demonstrated recently by an investigator on the West Coast. The instrument is providing a fully operational automatic printout of all chemistry, urinalysis and hematology reports. This is the first time that a small computer has been proved adequate for the 300-500 bed hospital at a cost of less than $100,000.

These programs together with investigations on counting white blood cells and identifying abnormal chromosomes by computer will be continued with modest expansion in the coming year.

Pharmacology Toxicology

The Pharmacology Toxciology program has as its ultimate objective the improvement of medical therapy through a better understanding of drug action and the factors which influence the response of the patient. As one of the major needs for medical care the Pharmacology/Toxicology Program is investigating how best to use existing drugs so as to produce maximum therapeutic benefit with the least risk of adverse effects.

Research in NIGMS demonstrated a significant correlation of age and sex with the occurrence of serious hemorrhage in the use of heparin, an anticoagulant agent and in relation of blood type to circulation disorders in women taking birth control agents.

A specialized, and badly neglected, area of drug study is that of the newborn and pediatric age group. The tendency has been to study drugs in adults and extrapolate the findings back to children without regard to the fact that many physiological and biochemical processes are not fully developed at birth. We are encouraged by the start made by the new pharmacology center at Baylor, studying the toxicity in newborn children of drugs given to the mother (alcohol and narcotics, for example), which indicates that severe reaction may be controlled through early knowledge of drug concentrations.

The importance of drug interactions is another major focus of this program.

A mild stimulant for example, may reduce the capability of the body to handle other drugs given concurrently and thereby result in the accumulation of toxic amounts of the other drugs.

Such discoveries as described above require collaboration between the laboratory and the clinical scientist to fully solve the therapeutic problem. Sometimes the original lead originates in the laboratory; sometimes in the clinic. These centers provide for an integrated continuity of effort from basic research to practical patient care. Many of them are in their infancy and will require careful nurturing to give a proper balance of disciplines and spectrum of activities.

During F.Y. 1970, particular emphasis will be placed on further developing of the clinical aspects of the program. The factors controlling variability of drug response will continue to receive special attention. Increased effort will be devoted to the effects of prolonged drug use in man and the action of drugs on the immune response to organ transplants and allergies.

Bioengineering Sciences

The program in biomedical engineering encompasses the applications of mathematical and physical sciences, including engineering sciences, to biomedical problems, and of engineering methodology to problems of processing medical information. It combines the mathematical skills, and the analytical ability of the engineer with the knowledge and understanding of biological systems by the life scientist, in order to focus upon the solution of engineering problems associated with living systems and with health care.

Significant progress is being made on research projects supported by NIGMS. Ultrasonics is being applied to refined and accurate diagnosis of brain lesions, obstetrical problems, and cardiovascular disease. A crystal-driven electronic implant has been developed and used to stimulate muscular movement in rehabilitation of amputees through electronics. Biomathematicians at the University of Southern California are developing mathematical models of biological systems. One such model has already been utilized in the control of dosage of digitalis administered to heart patients.

For F.Y. 70, particular accent will be placed on bioinstrumentation for the purpose of development of instruments, devices and systems pertinent to basic and applied biomedical research and the deliverance of health services, (patient monitoring, intensive care units, and the modular segments of hospital information systems).

Behavioral Sciences - The level of support in this area has been approximately $370,000. We have recently funded a single center, for an additional $125,000 at the Rockefeller University. This program combines the talents of several of the nation's best psychologists at the Rockefeller University. Drs. Miller, Pfaffman and Estes will be investigating the mechanisms of learning perception and cognition in an atmosphere leading to direct application of their findings. We are actively developing other large-scale research efforts in the relation of the brain and behavior and in the study of the learning process and its enhancement.

Studies on the role of behavior and social environment in illness, and the patient's behavioral response to his illness will provide a basis for application of this important science in medical care and medical training. Although most of the research on behavior is carried on outside the medical environment, a major thrust of the NIGMS program will be the application of behavioral science knowledge and skill in the hospital and the medical school.

Fundamental Sciences - The fundamental sciences program of NIGMS interrelates the biological, biochemical, and biophysical sciences. The unifying theme is one of gaining comprehensive understanding of life processes as they function in health and disease. A large part of these investigations are conducted at the

subcellular and molecular level where it is highly probable that the answers to most serious disease problems will be found. The information gained here is fed into the more applied areas of NIGMS research and in turn information from the clinic is fed back to speed basic discovery. Although NIGMS supports studies in chemistry and physics and other disciplines which are vital to an understanding of the activity of the cell, the Institute has three major areas of attack. We must learn how the cell reproduces and the defects which occur when such reproduction is faulty--this is the field of genetics. We must know how the cell is able to perform its myriad of activities in order to understand how changes occur in disease--this is the area of cell biology. Finally, one must know how the organism or the cell is able to respond to its environment as a unit or as a society--this is the study of adaptability.

Genetics - The Institute program in genetics seeks to improve health by understanding the role of human heredity in health and disease. It is known that genetic factors play a major role in the more common diseases which affect man which implies that a better understanding of genetics will help prevent some of the human suffering caused by genetic disorders.

Work in human genetics at several centers is providing new information on the rejection phenomena in transplantation of organs through fundamental research on human genetics and immunochemistry. The large number of transplants within recent months demands that the basic work be stepped up in order to provide practical information on mechanisms of cellular immunity and a better understanding of the genetic differences between individuals.

Cytogenetic and chromosomal studies also are basic to the NIGMS Genetics Program to determine which environmental or genetic factors predispose to chromosome abnormalities and how the chromosomes, normal and abnormal, behave and function during human differentiation and development.

The Institute is also concerned with the mutagenic properties of drugs and is investigating this complex problem through both grants and contracts. We are concentrating heavily on common drugs (caffeine) which have known mutagenic activity in lower organisms.

Even with improved methods, genetics research will not be soon completed. The realization that mammalian cells may each accommodate one million separate genetic messages in their approximately six feet of double-helical deoxyribonucleic acid (DNA) and the realization that thus far scientists have been able to recognize only about 1,000 gene markers has made the progress of geneticists to date seem small indeed.

The need for further research is enormous; to give one example the concept that the cancerous alteration of cells is associated with alteration of their genetic material and that such altered cells, in turn, pass on to their offspring the genetic defects and the resultant cancerous features must be investigated.

In 1970, we do not expect to appreciably increase the number of projects in this program; emphasis will be placed on selection of those projects which enhance and further the aims of this program, especially those areas of genetics research which can be applied directly to clinical problems.

Genetic Chemistry - The NIGMS program in Genetic Chemistry complements the Genetics Program, since it also seeks to improve health through an understanding of the role of heredity in health and disease. It differs from the Genetics Program, however, in seeking to enlist the aid of chemists in developing knowledge in a new phase of genetics - "manipulative genetics". Here, the important fact is that genetic material (DNA, and sometimes RNA) is a chemical, albeit a complex one. Hence, it can be manipulated or transformed, either inadvertently (for example, by pollutants in our environment) or on purpose (Genetic Engineering).

A formidable body of concepts and knowledge in this area has been built up over the last fifteen years. We now know, in principle, what genes are and how they work. We also know, in principle, how genes are altered by mutagenic chemicals in the environment, and how genes, (as, for example, for the production of insulin in diabetics) could be inserted by viruses into the chromosomes of man. However, the technology and increased knowledge for the effective medical use of these concepts is not as yet available.

Most of the conceptual work has been done with bacteria and bacterial viruses. It is now being applied to human tissues, and mammalian viruses. This is very difficult undertaking.

Chemical mutagens and radiation are an everyday fact of our own environment. Fungicides, insecticides, herbicides, anti-anxiety compounds, halucinogens, and many useful drugs, and even coffee are all suspected of being potential producers of harmful mutations. We do not, as yet, know how to adequately screen for the potential hazard of these substances to humans, but methods must be developed.

Cellular Structure and Function - An important part of the NIGMS Fundamental Science program is to gain understanding of how the cell functions in health and disease. All degenerative diseases of man, physiological processes such as aging, all drug actions, and toxic reactions, take place initially at the cellular or subcellular level. Therefore, the NIGMS sponsors a large group of investigator-initiated research projects which seek understanding of cell metabolism, enzyme action, cellular structure, and membrane function through cell biology, biophysical, and biochemical research programs.

Cell Biology - Large scale, highly automated and monitored, culture of specific cells which will be useful in the production of vaccines, in research on infectious diseases, and in the work of diagnostic laboratories is now under way with Institute support. The development and application of new techniques has also made possible the extensive culture and characterization of anaerobic organisms, with the immediate application of the knowledge thus gained to the diagnosis of human health problems.

During 1970 it is anticipated that further support will be directed to promising instrumentation studies, cell culture of various kinds, identification and characterization of anaerobic microorganisms and their relations to aerobes, and to fundamental studies at the molecular level.

Enzyme Structure and Function - Each chemical reaction in living organisms is, as far as we know, mediated by an enzyme or a group of enzymes, which control not only the occurrence of reaction but also its rate. In the absence of enzymes required for essential body processes metabolism will be altered, with resultant disease manifestations. Indeed, many diseases appear to have their origin in the absence of an essential enzyme or group of enzymes.

For 1970, NIGMS plans to continue its support of a program in enzymology. Several studies have been carried out in recent years on the administration of enzymes for the control of disease processes. For example, there have been reports on reversal of gout symptoms in adults following enzyme administration, and similar beneficial responses have been observed in enzyme administration to infants suffering from in-born errors of metabolism. Scientific insight into these uses of enzymes for the alleviation of disease comes from knowledge generated in the basic researches in enzymology.

Biophysics - Our program in biophysics is designed to delineate interactions of cells and cellular components. These are responsible for normal and abnormal body function including the use of energy for activity, the transport of material in the cell and the coordination of cellular activity. Since all the reactions deal with processes which occur at both the molecular and submolecular levels, we must be concerned with the development of sophisticated instrumentation which

permits us to investigate reactions at this level.

Dr. Lars Onsager, a grantee, was recently awarded the 1968 Nobel Prize in Chemistry for studies involving the measurement of those physical parameters which influence and are responsible for the production and utilization of energy in the living cell.

In addition, the investigation and evaluation of these systems provide us with direct evidence of how cellular and subcellular structures are altered by disease. The program in the biophysical sciences is providing the knowledge necessary for the exploration of these important mechanisms which in many cases is applied directly to patient care.

Human Adaptability - This represents a small group of investigator-initiated grants concerned with the adaptation of man and other species to adverse environments. They support research applicable to important health problems concerning the population explosion and human resourcefulness for living in the desert, the arctic, at high altitudes, and in the sea. They also relate to environmental health problems inasmuch as they may provide information on human tolerance to harmful changes in the environment.

These investigations also contribute to other programs within the Institute. For example, information on human physiological responses to cold may have a direct bearing on anesthesiology and kindred stituations where procedures involving hypothermia are used. Knowledge of physiological adaptability under various circumstances can be similarly important to the treatment of traumatic injury, to studies in genetics, and to activities in biomedical engineering.

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Clinical Sciences.....	$7,453,000	$7,658,000	+$205,000
Pharmacology Toxicology research centers....	3,343,000	3,435,000	+92,000
Bioengineering Sciences	8,428,000	8,659,000	+231,000
Behavioral Sciences...	906,000	931,000	+25,000
Fundamental Sciences..	49,523,000	49,523,000	--
Subtotal regular program.....	69,653,000	70,206,000	+553,000
General research support grants.....	8,127,000	8,120,000	-7,000
Scientific evaluation and planning.....	1,437,000	1,437,000	--
Pharmacology Toxicology research centers....	3,500,000	3,500,000	--
Anesthesiology and diagnostic radiology centers.....	1,000,000	1,000,000	--
Total research grants.	83,717,000	84,263,000	+546,000

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting continuations....	1,126	$51,771,000	1,171	$52,324,000	+45	+$553,000
2. Competing projects.....	204	17,882,000	204	17,882,000	--	--
3. Subtotal regular program.....	1,330	69,653,000	1,375	70,206,000	+45	+553,000
4. General research support grants...		8,127,000		8,120,000		-7,000
5. Scientific evaluation and planning.....		1,437,000		1,437,000		--
6. Pharmacology Toxicology research centers.....		3,500,000		3,500,000		--
7. Anesthesiology and diagnostic radiology centers.....		1,000,000		1,000,000		--
8. Subtotal special grants.....		14,064,000		14,057,000		-7,000
9. Total research grants.....	1,330	83,717,000	1,375	84,263,000	+45	+546,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Fellowships.....	$21,373,000	$20,040,000	-$1,333,000

Introduction:

The general objective of the Institute's fellowships programs is to encourage and support the training of promising young scientists for careers of research in the sciences related to health. To this end, funds are provided annually for predoctoral, postdoctoral, and special fellowships as well as for Research Career Program Awards. In keeping with the Institute's broad range of interests and responsibilities, this support embraces research training, not only in the fundamental biomedical sciences, but, with increasing emphasis, in interdisciplinary areas such as biomedical engineering, and in selected clinical sciences such as anesthesiology, diagnostic radiology and surgery. Evidence of the success of these programs is apparent from the fact that many former fellows and awardees are now acknowledged leaders in their respective fields of sciences, and many hold prestigious positions in medical schools and our Nation's universities.

Program Plans in 1969 and 1970:

The different fellowship programs vary widely in the stage of development attained by the individual at the time the award is made. By successive stages, the training proceeds from the rather broad, discipline-oriented training received at the predoctoral level, through a more sharply focused training experience at the postdoctoral and special fellowship level, to a well-defined long-term research plan in the Research Career Program. To assure the orderly development of manpower trained for biomedical research, the different fellowship programs must be carefully balanced against one another, allowing also for emphasis on those programs, particularly the special fellowship and the Development Award, which are most adaptable to the development of manpower for research in areas of particular interest to the Institute. Funds requested for 1970 will provide for 1,991 awards, compared to 2,249 in 1969, a decrease of 258. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Predoctoral Fellowships - These awards are made to highly selected graduate students who are pursuing a research doctorate degree in one of the health-related sciences. The objective in such studies is to enable the fellow to become highly knowledgeable in some particular discipline, such as biochemistry, biophysics or genetics, with a lesser exploration of one or more related disciplines, and also to learn the methods of research and to carry out an original piece of research. Although the majority of NIGMS predoctoral fellows are in the fundamental science areas, there are sizeable numbers receiving training in the program areas of pharmacology toxicology and biomedical engineering, and a few in the behavioral sciences. Within the fundamental sciences, a number of disciplines are represented, each preparing the fellow for later exploration of some aspect of basic or applied biomedical research.

Approximately 1,400 predoctoral fellows will be supported during the current year, representing over 120 institutions and nearly every state in the Union. The number of awards will be decreased by about 200 in fiscal year 1970.

Postdoctoral Fellowships - Fellows supported under this program fall into two main categories: Those holding a research doctorate, primarily the Ph. D. degree;

and those holding a professional doctoral degree related to the medical sciences, chiefly the M.D., and occasionally the D.V.M., degree. The holders of the research doctorate comprise by far the larger group. After the somewhat formalized training leading to the Ph. D. degree, these individuals are prepared to explore in depth significant aspects of a health-related research problem, and simultaneously receive training in sophisticated instrumentation or methodology.

It is estimated that the number of postdoctoral fellows supported by the Institute during the current year will slightly exceed 300, and this number will be reduced to 282 in 1970. In a recent study, the duration of postdoctoral fellowship awards was found to average 21 months, with the majority ranging between one and three years. In view of budgetary constraints, awards of more than two years' duration are now being discouraged except under unusual circumstances, such as those involving physicians who are seeking the Ph. D. degree.

Special Fellowships - The special fellowships provides a highly flexible and effective mechanism for the support of training in the Institute's important targeted program areas. Its flexibility has proved particularly useful for the training of experienced engineers for research in biomedical engineering, a group which now comprises approximately 20 percent of the total special fellowship program. Also included among the special fellows are many mature investigators who receive updating in one of the fundamental sciences or in a targeted program area and are thereby enabled to pursue their research more effectively.

This program, although still relatively small, has grown fairly rapidly over recent years. It is estimated that with the $2,410,000 available during the current year, a peak level of some 178 special fellows will be supported. A slight decline in program size is forecast in 1970.

Research Career Development Awards - Development Awards are made to young scientists with outstanding potential for independent research in the health-related sciences. Among the clinical sciences, anesthesiology is now relatively well represented in the Development Award program.

The present year has been marked by a significant increase in the number of new applications for Development Awards as compared with 1968, and an increment of about five percent in the number of awards funded. In actual numbers, the increase has been from 305 awards in fiscal year 1968 to approximately 320 in 1969. Five fewer awards will be made in 1970 with the $7,214,000 requested.

Research Career Awards - Although no new Career Awards are being granted, provisions must be made for the support of 37 ongoing awards, requiring an estimated $1,256,000 for fiscal year 1970.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations						
a. Noncompeting	1,282	$13,493,000	1,364	$14,458,000	+82	+$965,000
b. Competing...	112	1,450,000	79	944,000	-33	-506,000
2. Supplementals...	(20)	147,000	(30)	163,000	+(10)	+16,000
3. New Awards.....	855	6,283,000	548	4,475,000	-307	-1,808,000
4. Total fellowships.....	2,249	21,373,000	1,991	20,040,000	-258	-1,333,000

Fellowships (By type of award)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Predoctoral.....	1,405	$7,947,000	1,200	$6,947,000	-205	-$1,000,000
2. Postdoctoral....	309	2,546,000	282	2,346,000	-27	-200,000
3. Special.....	178	2,410,000	157	2,277,000	-21	-133,000
4. Development Awards.....	320	7,214,000	315	7,214,000	-5	--
5. Career Awards...	37	1,256,000	37	1,256,000	--	--
6. Total fellowships.....	2,249	21,373,000	1,991	20,040,000	-258	-1,333,000

Fellowships Program Analysis

Program Area	1969 Estimate	1970 Estimate	Increase or Decrease
1. Clinical Sciences	$1,299,000	$1,551,000	+$252,000
2. Pharmacology/ Toxicology.....	1,081,000	1,271,000	+190,000
3. Bioengineering Sciences.....	1,254,000	1,536,000	+282,000
4. Behavioral Sciences.....	330,000	404,000	+74,000
5. Fundamental Sciences.....	17,409,000	15,278,000	-2,131,000
6. Total fellowships.....	21,373,000	20,040,000	-1,333,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total training grants.....	$46,901,000	$45,568,000	-$1,333,000

Introduction:

The major goals of the NIGMS graduate research training program are to provide people who will translate biomedical research accomplishments into useful clinical applications, and to train scientists whose efforts will be directed to developing new medical knowledge. Additional goals are to improve the environments for such training, and to encourage and expand opportunities for research training in new and rapidily developing biomedical science areas. It is in the latter areas that the research training grant program differs significantly from the direct fellowship program and the programs of the Bureau of Health Manpower.

The Institute correlates its training programs with its research programs and is attempting to estimate the realistic needs for manpower in these various programs. The Institute also serves as the single unifying element for manpower needed in support of the program objectives of the other National Institutes of Health. Although research manpower needs are based primarily on research goals, estimates of need must also be based on the provision of trained scientists and faculty for the expanding staff requirements for existing and projected new medical schools, graduate schools, regional medical programs, research centers, and for the delivery of health services. Although much biomedical research is conducted within medical schools by their faculties and staff, it is noted that nearly one-half of the PHS research grant support is awarded to university schools other than medicine and to research institutes and industrial laboratories. Therefore, projected needs for research manpower cannot be based solely on future staff requests for schools of medicine. However, judging by the estimated needs for medical school faculty alone, (Journal of Medical Education, 42, p. 500, 1967) we are now training less than one-half of the estimated number of personnel needed for the health sciences over the next decade.

Nationwide, training grants awarded by the NIGMS support an estimated 40% of the total national enrollment of graduate students in the fundamental health sciences, and as high as 70% of the research trainees in certain disciplines. These programs therefore have a significant impact on the development of highly capable investigators who will have a vital part in the growth and direction of the national health research effort. This is particularly true in certain areas of critical research manpower shortages now receiving special program emphasis.

Experience has shown that persons trained in the Institute's research training programs to a major extent accept academic positions in institutions concerned directly or indirectly with the teaching of clinicians and with medically related research.

The Institute plans to continue a contract with the National Academy of Sciences for evaluation of the overall program for the purpose of determining the extent to which persons trained in programs supported by this Institute enter academic and research positions in fundamental biomedical and clinical research areas. This and other aspects of this study will aid significantly in planning future emphasis of the Institute's programs. Data obtained in 1968 from a direct survey of former trainees show that of persons supported during 1958-60 who received the Ph. D. degree, 80% are currently pursuing careers in research and teaching, 6% provide professional services and 11% are in administration primarily in universities, hospitals, government and industry or business. Similar patterns are seen in reported career intention from persons more recently

trained. It is also evident that training grants have had the effect of shortening by almost a year the time required beyond the baccalaureate degree for award of the Ph. D.

Program Plans in 1969 and 1970

The Institute's policy is to give clear preference for the award of new and supplemental research training grants to institutionally-based programs of high scientific merit and demonstrable productivity. Thus, support is being discontinued for a significant number of previously funded programs to insure initiation of grants to new programs of high promise plus full support to programs of demonstrated productivity and quality. This philosophy of operation will continue to prevail throughout F.Y. 1969. Funds requested for 1970 will provide for 525 awards, compared to 588 in 1969, a decrease of 63. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

The Institute's training programs are now organized into five areas of emphasis: 1. Clinical Sciences; 2. Pharmacology-Toxicology; 3. Bioengineering Sciences, including Automated Clinical Laboratories and Biomathematics; 4. Behavioral Sciences; and 5. Fundamental Sciences. Special attention has been directed to increasing support via new and supplemental grants, within the limitations of available funds, to quality programs in areas one through four while maintaining essentially level support, but with markedly increased quality and special focus in area 5 - the Fundamental Sciences.

Clinical Sciences

Ten new grants funded in 1968 are supporting in 1969 training in the Clinical Sciences for programs in Anesthesiology (1), Radiology (2), Surgery (2) Pathology (1), Epidemiology (1), and in Special Medical Scientists training for the combined M.D.-Ph. D. degrees (3). The three new Special Medical Scientist grants were awarded to the University of Chicago, Stanford University, and the University of Wisconsin where the purpose is to train carefully selected medical students to better bridge the gap between fundamental research and new clinical procedures, and is typically characterized by the award of both the M.D. and the Ph. D. degree to the trainee. These special awards have had significant effects on modernization of the medical curricula of the respective schools. At least ten additional medical schools are now planning programs to train medical scientists.

In 1966, the NIGMS further expanded and broadened its research training programs in anesthesiology, clinical anesthesiology, surgery, and diagnostic radiology, in response to specific Congressional appropriations to provide support in these areas where new knowledge and technology are urgently needed. Anesthesiology and radiology present special problems as there is such a critical shortage of physicians for patient care that few persons well-trained in these areas remain in medical schools to train additional teachers and other practicing clinicians in these areas. In 1967, a special appropriation of one million dollars was made available for support of clinical residency programs to increase the number of practicing physicians in anesthesiology. From 1968 funds (currently active grants) these programs were modestly expanded. However, in all clinical science fields, the Institute expects to be able to initiate in 1969 only one or two awards to new programs plus meeting sizable committed increases to already active programs for additional trainee support in anesthesiology, radiology, and surgery. Within the proposed budget for 1970, 148 grants are planned for the clinical sciences program as compared to 174 in 1969 and 204 in 1968. Because of rising costs, it is anticipated that there will be a net decrease in the number of trainees supported in 1970 compared to 1969.

Pharmacology Toxicology

At the present time, about 45% of all Ph. D. degree recipients in pharmacologic sciences are supported by NIGMS training grants. However, those individuals supported on training grants require an average of 1.5 years less time to achieve the Ph. D. degree than students not supported by training grants, and the percentage of degree recipients supported by NIGMS is increasing. The greatest need for increased training is clearly in clinical pharmacology and toxicology. It has been estimated that at least 90% of currently-prescribed medicinals were unknown 10 years earlier, and the search for effective and safer drugs continues increasing as technology advances. All new compounds must be evaluated by the pharmacologist, and the metabolism and interactions further studied by the toxicologist, and studies on promising compounds must be continued in humans by clinical pharmacologists.

F.Y. 1969 funds may permit the award of only one or two new grants in the total Pharmacology Toxicology Program in addition to meeting committed increases to outstanding ongoing programs.

Bioengineering Sciences

Six years ago, before the NIGMS program was started, there were no Ph. D.'s in Biomedical Engineering as such, and special training in Automated Clinical Laboratory Medicine was non-existent. Also, the number of people trained in Clinical Chemistry was decreasing rapidly and the general professional image of this specialty field was at a low ebb. At the present time, with an annual investment of about $1,600,000 in these segments of this broad area (exclusive of biomathematics), our output is of the order of 30 to 40 Ph. D.'s per year.

Behavioral Sciences

These programs are to encourage and enhance the development of the basic behavioral sciences as disciplines of extreme importance in solving health care problems. Furthermore, an urgent need exists to bring the behavioral sciences into clear focus within medical research and physician education programs of medical schools per se. Major new forces -- increased knowledge in health sciences generally, demonstrated capability for improved medical services and patient care, the changing structure of society with attendant problems resulting from urbanization, as well as the continuing search for solutions to the health problems of all citizens -- demand changes in current approaches to medical education, research, and service which recognize the fundamental behavioral dimensions of many medical problems. It is also apparent to most physicians, recognizing the practice of medicine to be 50 or 60 percent psychological or sociological, that basic medical and clinical science alone cannot totally explain the phenomena of the sick patient and especially the nature of his responses in living with his illness.

The ultimate goal of NIGMS programs in the behavioral sciences must be to enhance and elaborate the understanding by physicians of the doctor-patient relationship, the subtle role of psychological factors in health and disease, and of the interaction of the patient with his social environment. At the same time, behavioral scientists, especially graduate students, should be introduced to behavioral and social problems unique to the field of medicine. The clinical setting, in particular, provides a special opportunity for fruitful collaboration of physicians and behavioral scientists in extremely important research programs and innovative new approaches to significantly improve patient care.

Because of its great significance to the contemporary medical scene, development of the behavioral sciences in the medical setting should receive a high priority in funding. The F.Y. 1970 request does not provide funds to initiate additional new programs but funds will be reallocated where possible to give further emphasis to research training in this area within schools of

medicine.

The Fundamental Sciences

The Fundamental Sciences area, the fifth major program area of the Institute, is composed of seven basic medical science training disciplines: Anatomical Sciences, Biochemistry, Biophysical Sciences, Genetics, Microbiology, Physiology, and Multidisciplinary Biological Sciences. The research efforts of personnel trained in these principal areas of biomedical science provide the main body of basic knowledge upon which all fundamental advances of the clinical sciences must be based. This program area comprised nearly one-half of the Institute's training grants active in the current year - 324, funded at $20,434,649.

Increased quality of training necessitates academic environments with adequate numbers of well-trained research faculty and modern equipment. Rising salary scales, cost of equipment, and tuition increases necessitate significant dollar increases to maintain the status quo. The additional economic stress being imposed by increases in the sizes of medical school classes in existing institutions coupled with the demand for staff for new medical schools immediately impinges upon the medical school basic science departments which are responsible for the first two years of medical instruction. At present, recruitment for new schools and expansion of existing institutions is being accomplished largely on a "rob Peter to pay Paul" basis. Protraction or extension of this very intense manpower shortage will result in dilution and ultimate lowering of the quality of medical training as well as medical research at a time in our nation's history of burgeoning need for more and better trained biomedical scientists. The demand so far outstrips the available manpower supply at this time that "over-production" of basically trained, medically oriented scientists is clearly not a problem in the foreseeable future.

Summary

Although the F.Y. 1970 funding will permit the Institute to maintain its training grant commitments and to pay a small portion of the competing continuations, there will be an overall decrease of more than 10 percent in the number of students supported. Funds within the fewer continuing grants will be applied predominately to the direct support of trainees; however, it remains essential to also provide for faculty and staff salaries, equipment and other supportive costs to maintain the excellence of these carefully selected centers for biomedical research training. To protect the careers of trainees already enrolled in discontinued training programs, it is the intent of the Institute to provide direct fellowships through its research fellowships program until these individuals have completed their training. Nevertheless, individual student fellowships especially at the predoctoral level, cannot ensure or build quality training programs. Also, the fellowship program is financially less efficient than the training grants program at the predoctoral level.

Distribution of Training Grants

		1969 Estimate		1970 Estimate		Increase or Decrease	
		No.	Amount	No.	Amount	No.	Amount
1.	Continuations:						
	a. Noncompeting....	500	$38,611,000	434	$37,238,000	-66	-$1,373,000
	b. Competing.....	85	7,790,000	91	7,980,000	+6	+190,000
2.	Supplemental.....	--	--	--	--	--	--
3.	New Programs.....	3	150,000	--	--	-3	-150,000
4.	Scientific Evaluation and Planning..	(2)	350,000	(2)	350,000	--	--
5.	Total Training Grants.....	588	46,901,000	525	45,568,000	-63	-1,333,000

Training Grants (By type of program)

		1969 Estimate		1970 Estimate		Increase or Decrease	
		No.	Amount	No.	Amount	No.	Amount
1.	Graduate.....	558	$45,551,000	495	$44,218,000	-63	-$1,333,000
2.	Clinical Training Anesthesiology.....	30	1,000,000	30	1,000,000	--	--
3.	Scientific Evaluation and Planning..	(2)	350,000	(2)	350,000	--	--
4.	Total Training Grants.....	588	46,901,000	525	45,568,000	-63	-1,333,000

Training Grants Program Analysis

	Program Area	1969 Estimate	1970 Estimate	Increase or Decrease
1.	Clinical Sciences....	$16,100,000	$16,377,000	+$277,000
2.	Pharmacology Toxicology.....	4,365,000	3,920,000	-445,000
3.	Bioengineering Sciences.....	4,020,000	3,720,000	-300,000
4.	Behavioral Sciences.....	2,720,000	2,500,000	-220,000
5.	Fundamental Sciences.....	19,346,000	18,701,000	-645,000
6.	Scientific Evaluation and Planning..	350,000	350,000	--
	Total training grants.....	46,901,000	45,568,000	-1,333,000

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	--	--	--	--	--	--
Other expenses.....	--	$3,295,000	--	$3,288,000	--	$-7,000
Total.....	--	3,295,000	--	3,288,000	--	-7,000

Introduction:

The NIGMS uses a combination of program projects, centers and individually initiated research grants in order to develop sharply targeted programs to obtain specific objectives directly related to health. In general, the individual research grants serve to provide a foundation of basic research while the centers and program projects are used to channel the research towards more specific objectives. Inevitably gaps must arise in this process which occurs partly by chance. The function of the contract program is to close gaps--identified by the staff--and provide funds to achieve highly specific objectives, such as the development of instrumentation or the collection of data needed to advance a specific direction of research. For all practical purposes, contracts are used only in the targeted programs. Task orders issued to the National Academy of Sciences have been allocated largely for the purpose of evaluation of program and in the establishment of criteria for excellence, particularly for the research training programs. Contracts have also been awarded in the area of genetic chemistry where a specific product could be obtained readily and economically. It is our intention to maintain this basic philosophy of contract operations during the coming year.

Program Plans in 1969 and 1970:

Automated Clinical Laboratories

It is becoming increasingly evident that the only solution to the number, variety, and complexity of the clinical tests now required in the modern hospital is through the process of automation. Full scale automation should result in a clinical sample--from the patient--being placed in a machine which conducts the test and prints out final results on the patient's chart quickly, accurately and economically. Advances in this direction have been achieved during the past year. The large-scale program at the Oak Ridge National Laboratory is producing three instruments which show great promise in this direction: In one instrument, high pressure chromatography is being used to separate many of the constituents of urine with the object of determining how these vary with disease states. A device has been developed and placed on test in hospitals which will automatically separate the sugars which are present in the body and which may indicate the presence of such diseases as diabetes by changes in their concentration. A new machine to simultaneously run as many as 100 clinical tests of various sorts at a time is under development. The program will continue in 1970 at its current annual level of $500,000.

Pharmacology Toxicology Developments

Major advances have been made in the pharmacology program during the last year and further advances are anticipated. The large-scale program for the analysis of steriods and other drug metabolites at the Research Triangle Institute has succeeded in identifying contaminants in a widely used drug for treating cardiac conditions which affect its efficacy and toxicity. The group at Tufts University has succeeded in tying adverse drug responses to genetic makeup of the

individuals taking the drugs which raises new questions about the administration of drugs to individuals and to populations in general. During the coming year these programs will be continued at the level of about $1,600,000.

National Academy of Sciences

The National Academy of Sciences' study on the efficiency of the research training program of this Institute is producing results which demonstrate that students supported on such programs receive better training, receive degrees in a shorter time at less cost to the Government and apparently succeed better in their chosen profession than do other students in the same field. A definitive report will be published during the coming year. During the coming year the National Academy of Sciences task orders will total approximately $100,000.

Other Contracts

The Institute supports several other small contracts involving a variety of activities contributing to the development of programs in pathology and human genetics. We do support a large-scale chemical operation at the Oak Ridge Institute of Nuclear Studies for the production of large amounts of RNA for distribution to qualified investigators. Considerable amounts of the material in a high degree of purity have been made and delivered. It may be recalled that recent Nobel Prizes have been in the field of genetics and in fact our material has been used by some of these individuals. We plan to continue to produce highly purified material of various types. The annual cost of this contract is about $800,000. The Institute also supports a small program in instrumentation by contract where a specific instrument designed to produce a specific result can be obtained at optimum cost. One of the major instruments under study is a high voltage, high-resolution electron microscope which will lead to an entirely new dimension in the study of human cells. Considerable progress has been made in the development of power supply and other component parts of this instrument and a prototype may be completed during the coming year. The cost of these contracts approximate $288,000.

The 1970 level for the Collaborative Research and Development activity reflects a decrease of $7,000 in payment to the "National Institutes of Health management fund" for centrally furnished services.

Training Activities

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	22	$266,000	22	$233,000	--	-$33,000
Other expenses.....	--	183,000	--	104,000	--	-79,000
Total.....	22	449,000	22	337,000	--	-112,000

This intramural program was established in 1966 for the training of young scientists as well as more mature investigators for both basic and applied research in pharmacology and related areas of biomedical sciences.

The request reflects a net decrease of $112,000 of which $33,000 is in personnel compensation and benefits, $59,000 is in other expenses and $20,000 is a reduction in payment to the "National Institutes of Health Management Fund" for centrally furnished services.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	124	$1,487,000	124	$1,511,000	--	+$24,000
Other expenses.....	--	1,638,000	--	1,740,000	--	+102,000
Total.....	124	3,125,000	124	3,251,000	--	+126,000

This activity provides the staff support required for the planning, direction, review, analysis and overall management of the extramural grant programs of the Institute, including special organized research programs. This activity also supports the National Advisory General Medical Sciences Council.

This activity reflects a net increase of $126,000 which includes an $18,000 program increase, $3,000 for annualization of pay increases effective in 1969 and an increase of $105,000 for payment to the "National Institutes of Health Management Fund" for centrally furnished services.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	56	$721,000	56	$722,000	--	+$1,000
Other expenses.....	--	373,500	--	334,000	--	-39,500
Total.....	56	1,094,500	56	1,056,000	--	-38,500

This activity provides support for the overall administration, coordination and direction of the varied programs and activities of the Institute. The Director and his immediate staff provide the professional leadership and technical guidance of the current operating programs and for the planning, development and review of new and expanded areas.

The net decrease of $38,500 provides an increase of $1,000 for annualization of pay increases effective in 1969 and $500 for equipment offset by a decrease of $40,000 payment to the "National Institutes of Health Management Fund" for centrally furnished services.

TUESDAY, APRIL 1, 1969.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

WITNESSES

DR. PAUL KOTIN, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GEORGE M. KINGMAN, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
ROBERT H. BRAMLET, BUDGET OFFICER, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	1,058	1,659	2,191
Positions other than permanent	59	64	64
Other personnel compensation	3	7	7
Total personnel compensation	1,120	1,730	2,262
Personnel benefits: Civilian employees	134	173	225
Travel and transportation of persons	111	110	180
Transportation of things	25	25	50
Rent, communications, and utilities	207	259	350
Printing and reproduction	18	20	40
Other services	1,800	1,803	1,658
Supplies and materials	363	544	581
Equipment	477	520	757
Grants, subsidies, and contributions	12,301	12,498	12,901
Total obligations	16,556	17,682	19,004

PERSONNEL SUMMARY

Total number of permanent positions	171	194	229
Full-time equivalent of other positions	8	9	9
Average number of all employees	122	184	220
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	8,496	8,406	8,967
(b) Fellowships	42	200	194
(c) Training	3,763	3,892	3,740
Total grants	12,301	12,498	12,901
2. Direct operations:			
(a) Laboratory and clinical research	4,357	4,432	5,322
(b) Review and approval of grants	396	440	443
(c) Program direction	266	312	338
Total direct operations	5,019	5,184	6,103
Total program costs, funded [1]	17,320	17,682	19,004
Change in selected resources [2]	−764		
Total obligations	16,556	17,682	19,004
Financing:			
Comparative transfers to other accounts	153	232	
Unobligated balance lapsing	580	103	
Budget authority	17,289	18,017	19,004
Budget authority:			
Appropriation	17,289	17,820	19,004
Transferred from other accounts		197	
Appropriation (adjusted)	17,289	18,017	19,004
Relation of obligations to outlays:			
Obligations incurred, net	16,709	17,914	19,004
Obligated balance, start of year	18,278	13,907	15,893
Obligated balance, end of year	−13,907	−15,893	−16,986
Adjustments in expired accounts	−368		
Outlays	20,711	15,928	17,911

[1] Includes capital outlay as follows: 1968. $744,000; 1969, $520,000; 1970, $956,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $2,861,000 (1968 adjustments, $12,000); 1968, $2,109,000; 1969, $2,109,000; 1970, $2,109,000.

Mr. FLOOD. Now we have the National Institute of Environmental Health Sciences. Dr. Paul Kotin, the Director, will be the principal witness. We will place your biographical sketch in the record.

(The biographical sketch follows:)

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name.—Paul Kotin, M.D.

Position.—Director, National Institute of Environmental Health Sciences.

Birthplace and date.—Chicago, Ill., August 13, 1916.

Education.—B.S., University of Illinois, 1937; M.D.; University of Illinois Medical School, 1940; Diplomate, American Board of Pathology, 1953.

Experience.—November 1966, present, Director, National Institute of Environmental Health Sciences, Research Triangle Park, N.C. 27709; 1966, Scientific Director for Etiology, National Cancer Institute, Bethesda, Md. 20014; 1963–65, Associate Director Director for Field Studies, National Cancer Institute, Bethesda, Md. 20014; 1962–63 (June), Chief, Carcinogenesis Studies Branch, National Cancer Institute, Bethesda, Md. 20014; 1960–62, Paul Peirce, professor of pathology, University of Southern California School of Medicine, Los Angeles; 1949–59, University of Southern California School of Medicine; 1946–48, private practice in pathology and internal medicine, San Luis Obispo, Calif.

Associate memberships.—American Association for the Advancement of Science; American Association for Cancer Research; American Association of Pathologists and Bacteriologists; American Institute of Biological Sciences; American Medical Association; American Society for Cell Biology; American Society for Experimental Pathology; International Academy of Pathology; fellow, New York Academy of Sciences; Sigma Xi.

Special awards, citations, or publications.—Chairman, Gordon Research Conference on Cancer, 1965; Department of Health, Education, and Welfare Superior Service Award, 1966; Dr. Kotin has authored and coauthored over 100 published papers relating to experimental carcinogenesis, experimental pathology, air pollution, environmental health, and the role and action of environmental agents in the pathogenesis of disease.

Mr. FLOOD. Doctor, I see you have a statement.

Dr. KOTIN. May I read it, sir?

Mr. FLOOD. Yes, go right ahead.

GENERAL STATEMENT

Dr. KOTIN. Mr. Chairman and members of the committee, since my last appearance before this committee, the Division of Environmental Health Sciences has been redesignated the National Institute of Environmental Health Sciences and is taking its place alongside the other nine NIH Institutes charged with the responsibility for investigating questions crucially important to the health of our Nation. The Institute is concerned with unprecedented hazards to health from environmental sources. Only by a concerted attack on the sources of the hazards can we hope to prevent the deterioration from our present state of potential threat to one of national disaster.

Man, in his drive for material goods, greater resources, and the other components of what he has chosen to call the better life, has largely ignored the inevitable disturbances both physiological and social wrought in the environment as a direct result of his activities. Although, from the beginning, man has built his civilizations on a foundation of waste and neglect, the penalties in the past have been light. The accelerated pace of technological development, population expansion, and aggregation in large cities has resulted in telescoping of hazards that have ominous implications.

The unanticipated dangers of industrial progress demand action at a time when prevention of catastrophe is feasible; because remedies applied in times of disaster are for the most part ineffectual and inordinately costly.

The price of progress though high can be met by greater understanding, improved vigilance, and responsible foresight. Of these, greater understanding or more knowledge is paramount. It is imperative that we know the envoironmental circumstances and agents that are harmful, how they act and interact, and their ultimate consequences. Limitations in time and resources demand prompt and effective action.

The National Institute of Environmental Health Sciences seeks increased knowledge that will permit the sensing of dangers, forestalling their effects, and countering their threats. Its mission is to identify the chemical, physical, and biological factors in the environment that can adversely affect man; to learn how these operate; and to provide the scientific basis for the development of adequate control measures by other agencies. It is particularly concerned with the effects of agents at low concentrations acting over long periods; the interaction of multiple agents resulting in enhanced effects; and the modifying effect of variable physical and biological states within man himself on susceptibility to and the course of disease induced by these agents.

We seek subtle hallmarks of impending ill health at a time when effects are reversible or controllable. Only by this means can we assure truly beneficial social and economic development with minimal risk.

My associates and I are keenly aware of our obligation to insure that our program and priorities are developed within the context of national need and concern. Therefore, on an ongoing basis, the knowledge developed by the Institute is immediately available to the categorical programs charged with environmental control, particularly those encompassed by the Consumer Protection and Environmental Health Service—for example, air pollution, radiological health, occupational health, environmental sanitation, solid waste management, and safety of foods and drugs. Close liaison is maintained with these agencies to insure the inclusion of their requirements for supportive research in the Institute's program planning. Man himself is, of course, the ultimate beneficiary of our efforts.

The Institute is located in the Research Triangle Park, N.C., in leased interim facilities. A firm of architects and engineers is completing a master site plan for the development of the adjacent 509-acre tract of land deeded to the U.S. Government in September 1967 on which the permanent facilities for the Institute will be located. The office of extramural research and an epidemiological unit are currently located in Bethesda, Md.

INTRAMURAL RESEARCH

The Institute's intramural research program, the National Environmental Health Sciences Center, is organized so that its efforts are directed to specific, defined environmental health problems. Research studies are in progress on the potential health hazards in the following areas: pesticides and pesticide synergists, natural products including fungal contaminants of food and consumer products, fibers and polymer dusts, alpha radiation, trace metals and their compounds, hydrocarbons and their reaction products, tobacco smoke, and certain occupational hazards.

In addition to those ongoing studies, programs relating to the unique hazards associated with exposure to asbestos and to beryllium are in various stages of development. Finally, pilot feasibility studies on the environmental presence of trace metals aimed at determining their implications for human health are in progress. Under investigation is human contact with these agents either from their natural or synthetic sources, through their use as consumer products, or from exposure as environmental pollutants. The information obtained will tell us whether these substances, in potentially hazardous forms, are increasing or decreasing in use and distribution; whether the substances are general or restricted population hazards; and whether the technological trends are such as to encourage expansion or deemphasis of research.

In the intramural research program we seek to duplicate circumstances of human exposure, both qualitatively and quantitatively, in appropriate experimental models. Our in-house program, therefore, is concerned with: the totality of response to a given agent; the effect of exposure, either singly or in combination to a variety of agents from

different sources; the effect of host status on response and, above all, the applicability to man.

The intramural research program is supplemented by collaborative research programs supported by contracts. At present, contract-supported research includes investigations on: the effects of heavy metals—lead, in particular—on the functions of the brain, liver, and kidney; the interaction of pesticides and other organic chemicals with cell membranes; the production of mycotoxins by fungi found on tobacco; and the health hazards to which uranium miners are exposed.

EPIDEMIOLOGY STUDIES COMPLEMENT NIEHS LABORATORY INVESTIGATIONS

There is a crucial need for new and imaginative epidemiological techniques capable of predicting environmentally induced disease patterns that may appear within the near future. Epidemiological studies, therefore, are in progress to complement laboratory investigations. Correlation of data from both is expected to yield new and essential information.

Among the studies currently being supported by the Institute are: the establishment and support of registries on specific occupationally induced diseases such as mesothelioma and berylliosis; updating and analysis of data on uranium miners; analysis of medical histories of persons in isolated communities; and assessment of data on industrial personnel such as those in the steel, zinc chromate paint, and cutting oil industries.

EXTRAMURAL RESEARCH

Through an extramural program the institute is providing funds for the support of research and research-training activities within educational institutions, research institutes, and other public and nonprofit organizations.

Grantees are working to develop new or improved methodology for analysis and characterization of the biological effects of known and potentially hazardous agents. Others are conducting epidemiological studies to test theories on the relationship of environmental factors to disease in man—particularly long-term sequential exposures to low-level concentrations of these factors. Additional projects include: studies of the correlation of heredity and smoking histories in producing respiratory and cardiovascular symptoms; patterns of home use of pesticides in relation to pesticide residues in human tissues; baseline values of metal content in human tissues; and the effect of lead on one of the defense mechanisms of the lung.

Mr. Flood. Do you get into the area of fluoridation?

Dr. Kotin. No, sir.

Currently six university-based centers for research and research training are being supported from funds specified for this purpose. These centers were developed as national resources to supplement the intramural research program of the Institute and to provide a comprehensive approach to the problems of environmental health.

Mr. Flood. Would you get into the area of lead poisoning from paint? This is a very serious problem.

Dr. Kotin. Our responsibility would be to provide the scientific base to determine whether indeed any lead at all is tolerable in paint.

We would give the control agencies the basic information upon which to develop standards.

Two examples illustrate the scope of the programs of these centers. The center established at Oregon State University is concerned with systems analysis of problems in environmental health management, particularly assessing the interactions of pesticides in their immediate and long-term effects on certain organisms.

Through its training and research activities, the center serves as a resource to agencies responsible for establishing and carrying out public policy in environmental management. The Institute also supports a center at the Harvard University School of Public Health. The basic objective of this center is to gain a better understanding of the relationships of man to his physical and chemical environment. Its program includes research in environmental toxicology, radiobiology, medical aspects of community air pollution, epidemiological studies in industries, and combined studies of solid- and liquid-waste management. The investigation of various environmenal factors is concerned with resource analysis, on the one hand, and the methods of eliminating or lessening hazards to human health, on the other.

ENVIRONMENTAL DISEASE REGISTRIES—ASBESTOS AND BERYLLIUM

During the past year, the Institute sponsored a working conference attended by leading scientists and authorities to define the general problems of asbestosis and the specific occurrence of mesothelioma, a cancer induced by asbestos, and to outline a course of action. Worldwide representation assured utmost breadth and depth as well as currency.

Mr. FLOOD. What is the problem with asbestos—the fiber itself or a gas when it is heated?

Dr. KOTIN. No, it is the actual physical fiber that is the indispensable component for the initiation of the changes.

The outcome of this conference has provided the foundation for the establishment of an asbestos-disease registry in the National Environmental Health Sciences Center. This registry will have worldwide responsibility for participating in and providing leadership for accurately assessing the extent of the asbestos hazard.

Similarly, the Institute has assumed responsibility for a somewhat different form of registry in the field of beryllium hazards. Again, the Institute is actively participating through both national leadership and its own research efforts in an effort to gain a higher level of understanding of an environmental health problem.

Mr. FLOOD. Where is the danger in handling beryllium?

Dr. KOTIN. There is a danger in product fabrication and in the milling process.

Mr. FLOOD. Most, of course, in the milling.

Dr. KOTIN. Again milling and fabrication usually are a tandem effort. The millers are the ones that produce most of the beryllium ores themselves.

Mr. FLOOD. But the fabricator could be someplace else.

Dr. KOTIN. Could be, surely and usually is.

Mr. FLOOD. Is there a danger in the fabrication?

Dr. KOTIN. Yes, there is, particularly when inadvertent exposure results as a result of accidents in the actual processing. So a closed

system can become an open system, or the material is volatilized under conditions when it really was not meant to be.

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LIAISON AND COLLABORATION ACTIVITIES—URANIUM MINING

In my remarks today, I have emphasized the need for information so that adequate and responsible control measures can be initiated. In the field of environmental health, the Consumer Protection and Environmental Health Service is charged with control responsibility.

The institute collaborates with the Consumer Protection and Environmental Health Service on a wide variety of programs, an example of which is our joint effort in the study of hazards in uranium mines. As part of our close and effective relationship, we are engaged in a program of fundamental research on: the biological effect of alpha-emitting radon and its decay products; the anatomic and metabolic fate of these radioactive elements after host entry; the determination of host response; the detection of a threshold for effect if indeed such exists; and the characterization of the interaction of alpha emitters with diesel exhaust, uranium hard-rock dusts, and cigarette smoke in the production of cancer.

Mr. Flood. What did you say about the machinery in itself?

Dr. Kotin. In the mine the engines that provide the power are mostly diesel engines with the exhaust being emitted into the mining area.

These fundamental laboratory studies are complemented by epidemiological studies ocnducted by institute scientists thereby assuring that the laboratory data are constantly being assessed for compatibility wiht observations in man. The latter includes monitoring of uranium miners for radioactivity in tissues and excretion products. Our joint effort in this total undertaking eloquently supports, we believe, the wisdom of identifying specific areas of responsibility in specific organizations with special talents and resources. Finally, my associates and I work in close collaboration with Consumer Protection and Environmental Health Service scientists responsible for other phases of environmental health problems. We have achieved an effective synthesis in the areas of berylliosis, abestosis, and other environmental problems as well as that of uranium mining.

SUMMARY

If man is to avoid the hazards of the future, there must be vigorous and integrated study of all facets of environmental effects upon human health, longevity, and productivity. There is a great need to establish the basic information upon which realistic control measures can be

devised and adjusted to continual changes in both the environment and the population.

It is neither economical nor feasible to attempt individual bioassay of every potentially toxic agent. It is important, therefore, that we determine the principles on which the probable toxicity of new, as well as existing, contaminants can be predicted. These principles of the mechanism of adverse-response production will be the foundation for predictive guides to be used by control agencies for protective and preventive measures.

In 1932, a French philosopher, Henri Bergson, said, "Humanity is groaning, half crushed, under the weight of its own progress. Men do not sufficiently realize that their future depends upon themselves." Today, 37 years later, Bergson's comments have an all too ominous currency.

At the National Institute of Environmental Health Sciences, the future is our concern. We believe deeply in the concept that fundamental research is the key to the understanding and control of environmental health hazards—epidemics of the future. We agree with Bergson that the future depends on ourselves.

In conclusion, to develop the programs of the Institute, which, in turn, will help our nation prepare to cope with the future, Mr. Chairman, we propose a budget of $19,004,000. This is an increase of $1,322,000 over the 1969 operating level of $17,682,000. The $19,004,000 includes $8,967,000 for research grants, $3,394,000 for fellowship and training grants, and $6,103,000 for direct operations.

I shall be happy to answer any questions.

Mr. FLOOD. What is the significance, Doctor, of adding "National Institute of" to the name of this organization unit? You have been around for some years, without being a National Institute. What is the significance of "National Institute." Does it deify you or dignify you?

Dr. KOTIN. No, it recognizes a reality.

From the very organization of the environmental health program within NIH the Division had the characteristics of an institute. It has an intramural program, and an extramural program, with project grants, centers, fellowships and training grants, but it was felt that to organize the activity as an institute from the very beginning might, because of certain legal requirements, have a delaying effect.

At least this was a feeling I had.

For instance, an institute has certain formal obligations, periods of meeting of advisory panels and the like.

Starting from the ground up, and as you are well aware as you indicated last year, on January 31, 1967, the Division was essentially myself, a secretary, one or two others, a pencil and a pad. We felt we could get the program underway more rapidly within the framework of a division. Ample precedent for this exists at NIH.

Mr. FLOOD. Is there any change in your authorities or functions at all?

Dr. KOTIN. Not at all, sir.

BUDGET INCREASE FOR LABORATORY AND CLINICAL RESEARCH

Mr. FLOOD. You do not have a very large change in your budget except for the increase of $890,000 and 35 jobs for laboratory and clini-

cal research. In dollars that is just a little over 20 percent. I am sure you know very well that this is going to be a very, very tough year to get anything through Congress like that. So you had better come up with some mighty good reasons why Congress should make an exception for you and your item.

Dr. KOTIN. There are several reasons. First the center in North Carolina has until very recently occupied all but one of the buildings on our temporary site. The building No. 7 was occupied by the National Center for Health Statistics for some of their data-reduction activities. They have since had their own facility built in the research triangle area, and the space Building 7, is now becoming available to us for much needed laboratory space for which efforts have already been programed. The space was scheduled to have been available shortly after our last hearing before this committee, but it just took this long. So we are really not asking for anything that was not envisioned virtually at the date of the organization and establishment of the Institute and the first projections of the program.

It doesn't represent a striking out in a new dimension, although heaven knows, the national need in this area would support striking out in many, many areas that are going by default now. It looks new and indeed it is new money we are arking for, but it is to implement something that was built into the original design, as it were.

RESEARCH ON PESTICIDES

Mr. FLOOD. Take a look at page 154 of your justifications, you speak of the hazards of exposure to "the pesticidal synergist piperonyl butoxide." What is that chemical? What is this used for, and what have you found with regard to its hazard? First, what is a synergist?

Dr. KOTIN. A synergist is a compound which when interacting with another compound yields a product greater that the arithmetic summation of the two. So you get more response from the elements that go into the reaction.

Mr. FLOOD. What about the butoxide?

Dr. KOTIN. There was some concern over the amount of pesticides present in both the household bug bomb as well as those used in large-scale agriculture exposures. The industry sought methods to reduce the amount of pesticide being distributed in the environment while still retaining its effectiveness. So they hit upon the idea, and it is a time-honored one, that if they could interfere with the breakdown of the pesticide, either in the environment or in the host, be it an insect or man, the effect would be a depot effect. You would get a much longer response from the same amount because the disappearance of the effectiveness of a chemical is correlated with its degradation.

Mr. FLOOD. What do you use it for?

Dr. KOTIN. It sticks around a greater period of time and has a greater effect. However, apparently what had not been thought of was the fact that the cell cannot discriminate between a pesticide and other chemical agents. So the same synergist which prevents the breakdown of pesticides also prevents the breakdown of many other chemical agents and interferes with the defense capabilities of the body.

Mr. FLOOD. It that the hazard?

Dr. KOTIN. Yes. The unwarranted prolonged pathological persistence of the agent in the body.

DIESEL EXHAUSTS

Mr. FLOOD. I am a hard coal miner. On page 155 you talk about studies of uranium mining. Anything having to do with miners, I become intensely interested in. I was curious about your comments about the fumes from the diesel motor in the mines as a cancerous potential, seperate and distinct from the mineral itself.

Dr. KOTIN. The components to warrant suspicion of cancer are certainly there.

Diesel exhaust contains inordinately large amounts of cancer-producing chemicals.

Mr. FLOOD. So regardless of what mining it may be, whether it be hard or soft coal or producing black lung or miners' asthma, the use of the diesel itself in the mine results in a potential hazard.

Dr. KOTIN. The variable is ventilation. In an adequately ventilated mine the hazard is not much different than driving down the highway behind a semitrailer spewing out black smoke.

STUDIES OF URANIUM MINERS

Mr. FLOOD. What about your studies on uranium miners?

Dr. KOTIN. First, we are attempting to identify the extent of the risk with lung cancer, that the risk exists, is known.

Mr. FLOOD. Is there any doubt about that?

Dr. KOTIN. No, except as I say, the extent of the risk is unknown.

Mr. FLOOD. Suppose it does not show up for 25 years?

Dr. KOTIN. You can correct for this timelag by following miners who have been mining the ore for some period of time, for 15 to 20 years. We have to use retrospective studies to follow up the miners who develop lung cancers and try to get histories.

Mr. FLOOD. You are doing that?

Dr. KOTIN. Yes, sir, we have been doing that for many years. Again I would emphasize that these studies were going on long before the activation of the Environmental Health Institute but we have on the basis of the talents we have and our interests and responsibilities continued these studies.

We have assumed the responsibility for them. In concert with our epidemiological studies during the past year we have launched some fundamental studies.

Mr. FLOOD. Why have you not been up in the hard coal fields in the last 25 years?

Why have you not been worrying about miners asthma and black lung? What is the matter with us?

Dr. KOTIN. There is nothing the matter with you. Perhaps the matter is with me as an individual.

Mr. FLOOD. That is a good way of stating it.

Dr. KOTIN. As an individual, before the environmental health assignment, my field was cancer and happily I know of no provable cancer risk associated with the mining of coal, either hard or soft.

RELATIONSHIP TO ENVIRONMENTAL CONTROL PROGRAM

Mr. FLOOD. Where is the dividing line between what you do in the occupational health field and what is done under the appropriation for environmental control? What is the difference?

Dr. KOTIN. The difference is essentially the fundamental information that we can provide them that lets them give other than seat-of-the-pants judgments in establishing standards. So that we participate with the National Air Pollution Control Administration in establishing standards for SO^2 and particulates in the air. They are going to establish some for lead. The fundamental laboratory data, the criteria—and criteria are the facts of a biological response, the standards they set are numbers—the more precise and accurate your criteria are, the more meaningful and more valid your numbers are, the less prone and susceptible they are to questions by persons who suffer great dislocation by the establishment of standards.

Mr. FLOOD. When one of our brothers upstairs reads this environmental health sciences and then turns over a couple of pages and sees environmental control, he is going to ask Mr. Michel what is the difference.

Dr. KOTIN. I would hope Mr. Michel would give him the answer I just gave. Essentially there is a scientific base that the control organizations require. First, this scientific base can operate most effectively within an organization dedicated to and identified with the accumulation of fundamental information, the National Institutes of Health. Secondly, the scientific base housed in an organization which has neither police powers nor monitoring responsibilities approaches research as a fundamental problem in human biology, with really no identifiable threat to the sources of information that you must rely on to get some valid data.

We have to go to the miners, let us say, in your neck of the woods to study the hazards to see whether what we are seeing in our experimental models has any compatability.

I can imagine that going—I do not imagine, I know—going to large industries, such as the petroleum and automotive industries, as an organization interested in elaborating scientific facts, people being what they are, our welcome is infinitely more cordial than it might be if in the back of their heads they reacted as humans and felt, here is a "cop," let us be a little wary. It just worked out. Maybe success is too strong a word but really nothing succeeds like success. We have access to industries in a most cooperative way. These are both private organizations as well as nationwide industrial organizations. The American Iron-Steel Institute, the Coal Tar Producers Association, the Asbestos Manufacturers Association, the tobacco industry, all essentially serve as laboratories of ours in the study of diseases in man.

ENVIRONMENTAL HEALTH SCIENCES CENTERS

Mr. FLOOD. You want an increase of $500,000 for environmental health sciences centers. We would like to know how many you have now and where are they?

Dr. KOTIN. We have six now. We have one at the Harvard School of Public Health, one at New York University in the School of Industrial Hygiene and Medicine, one at Washington University in

St. Louis, one at the University of Cincinnati in the Kettering Institute, one at the University of Oregon State, and one just very recently established at Vanderbilt University in Nashville.

Mr. FLOOD. How many more would you have with this money if you get it?

Dr. KOTIN. We would like to establish two more. In establishing these centers what we try to do is identify research programs—multidisciplinary research programs—ongoing that would benefit from a coalescence into a center. So we are now exploring various institutions. The University of Washington at Seattle is an institution that we are now profiling to see if they have the critical mass which would provide the nucleus for a center.

The advantages of a center are first the cohesive identity that goes with being part of a program so that interchange takes place. Secondly, the support provides a small amount of core money which permits the director of the center and his advisory group to engage in pilot research in areas of particular promise.

Mr. FLOOD. You do not know where the next one will be as of now.

Dr. KOTIN. If I had to guess, the next one would probably be at Washington.

FUNDS FOR RESEARCH GRANTS

Mr. FLOOD. Look at page 150: you indicate you will fund 27 new research projects in 1970 and you have only 15 in 1969. Yet you estimate no increase in the total funds required. How do you do that? I never heard of a bureaucrat doing that before.

Dr. KOTIN. There is an explanation. To begin with, when the Institute, or the then Division was established, a portfolio of research support was taken from our then existing predecessor in the Bureau of State Services. These were ongoing programs in areas that were relevant to the mission of the Division and some were in their second year, third year, or fourth year of investigation. The advancing years of a program, as was noted earlier, are the more expensive ones. These large grants in their final years are being phased out. We are now beginning a series of programs in support of research that again fall under the rubric of mission relevance.

We are getting started in a rather modest way. So there is really no ouija board or mumbo jumbo. We are phasing out some very expensive activities.

Mr. FLOOD. There is a close analogy with the Pentagon weapon system. Your first batch costs a million and a half. But when you buy them the 45th time, it costs $700,000.

That makes sense.

PREDICTING TOXICITY OF NEW CHEMICALS

Take a look at page 149 where you say:

> Developing a capability to predict the toxicity of a new chemical before its introduction into man's environment is urgent.

How do you go about developing such a capability? How close are you to doing it?

Dr. KOTIN. For certain areas we have it already. Let me give you an example, and this was done in the United Kingdom and not here.

The most effective and potent pesticide that probably has been synthesized is a compound with a fancy name which we call AAF. This compound was synthesized by British Industries and tested in their labs and was found to be a very potent cancer producer, and the item never got on the market. That is one way using bioassay systems, testing them and developing animal models which in a reasonably short time will give evidence of toxicity, which on the basis of the best available knowledge, have some degree of relevance to man.

Secondly, particularly in relation to cancer-producing chemicals, while it is by no means universal and probably does not apply for most of the compounds, there is a certain molecular configuration of compounds that suggest that they are likely to produce cancer.

Mr. FLOOD. Must the public depend on the conscience of the manufacture? If it is a drug, we have some way of controlling it.

Dr. KOTIN. I do not like to pass judgments. I do not know whether we have to depend on the conscience of the manufacturers. They all have consciences.

MONITORING DANGEROUS CHEMICAL MANUFACTURING

Mr. FLOOD. How do you find they have a dangerous cancer-producing chemical? Here is a company making a pesticide. Who found out it is a very, very dangerous thing?

Dr. KOTIN. We are far enough along so that for those compounds with high indices of suspicion we are monitoring them; monitoring them in the sense that we don't know every compound. It would be foolish to say we know every new compound that DuPont, Monsanto, or Dow turns out. Essentially we know that they know that there are certain properties of compounds which would indicate the likelihood of a great hazard.

Mr. FLOOD. Do they have to report to you, or what is the relationship?

Dr. KOTIN. The matter is not one of reporting in the sense of reacting to an ad hoc situation. There is a permanent dialog going on and we do not know everything. There is a permanent dialog going on. The Institute has an information program or information component headed by an associate director. It is as important to us as the animal research in the laboratory or the grant with which we support a scientist in a university.

Mr. FLOOD. You have confidence in the relationship and the progress.

Dr. KOTIN. Confidence to the point where some of the industries try to be too good to use in the sense of providing us with more information than we can digest in terms of our size.

Mr. FLOOD. You have no quarrel with the relationship up to this point.

Dr. KOTIN. Speaking personally?

Mr. FLOOD. Yes.

Dr. KOTIN. No quarrel would be understating it. We have a close and effective relationship with industry.

Mr. FLOOD. Mr. Michel.

FILLING NEW POSITIONS

Mr. MICHEL. Doctor, you are asking for 35 additional positions.

Dr. KOTIN. Yes, sir.

Mr. MICHEL. How many authorized in 1969 are unfilled at this point?

Mr. KINGMAN. There are approximately 16 unfilled as of this date and about half of those have commitments in terms of names against them.

We are actively recruiting for the others.

They are the kind of people that we will ordinarily have no difficulty in hiring. We only recently got authority to proceed with recruiting for them.

Mr. MICHEL. Where in the main are they being recruited?

Dr. KOTIN. At the professional level, I could answer. At the supporting level perhaps. Mr. Kingman can answer better than I can.

Mr. KINGMAN. At the supporting level typically we recruit just as you do in Washington—locally. This goes as high as we can find qualified people in the local community. Obviously it is cheaper for us and it is of advantage to the community for us to hire them locally. We hire a scientist in the same way that any research organization hires a scientist—we look for the best person available wherever he is and we try to convince him to come to North Carolina.

He may be in North Carolina when we find him.

EFFECTS OF PESTICIDES

Mr. MICHEL. What, if anything, have you found are the injurious effects of pesticides on human health?

Dr. KOTIN. You have to answer that as a two-part question. At concentrations under usual conditions, low level, which produce no discernible symptoms, this really is an essential part of our mission. It is reasonable to suppose that because of the acute response following a high-level exposure that the exposure to low levels may have a more subtle effect. At the low-level long-range toxicity this varies with the type of pesticide and we are in the middle of studying this at present. Pesticide is a generic term. Some affect the liver, some the central nervous system, still others the kidney. So what we are trying to do is to see whether these long-range exposures to non-immediate-symptom-producing concentrations are hazardous. For this I would say that the evidence we have is still too premature, just on the basis of long term low level which means virtually a lifetime exposure study. Without predicting, hopefully, we will have some specific answer to your question.

Acute toxicity can be anything from a lethal effect to acute liver atrophy for example. It can include degeneration and destruction of the liver from the high concentrations of chlorinated hydrocarbon, to the suppression of the marrow from some which concentrate at that site.

Mr. MICHEL. Is it your obligation to also make a distinction between adverse effects on humans as against animals and wildlife?

Dr. KOTIN. No, but we almost cannot ignore the effect of nonhuman exposure, because many of the nonhuman environmental sites are a

one-order-of-magnitude-removed hazard. A shellfish can concentrate pesticides many hundreds of times. So while a person may not be exposed to a pesticide sprayed from an airplane he can be exposed by eating enough lobster with enough pesticide in it, for example, to receive a toxic exposure. Similarly, many pesticides undergo metabolic change in the intermediate host, the insect target or the cow that inadvertently gets abnormal amounts of pesticide in the fodder and so on. The latter can result in abnormal concentrations in dairy products, milk, butter, and so on. We cannot study man alone. We have to study the terrain and the environment. Here we try to utilize judgment as to balance between the two.

Mr. MICHEL. As you go down the road and you get an experience table over a period of years, are we to assume that you would set certain tolerances on various pesticides?

Dr. KOTIN. We would not, but the control agency which has the responsibility would have, we would hope, as the result of our research efforts and collaborative efforts with them, a meaningful level, a threshold level, below which for the average person, the great middle of the standard deviation curve, it is essentially an innocuous exposure. As I say, frequently legislative demands far outdistance scientific knowledge. But one can understand the necessity for these. What we are trying to do is catch up, and give as much as possible in the way of a scientific base for these control judgments. But the control judgments are not ours. We are part of the National Institutes of Health with no standard setting, monitoring or all the other things that go with environmental regulation.

Mr. MICHEL. That is all, Mr. Chairman.

ESTABLISHMENT OF THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Mr. NATCHER. Dr. Kotin, you now are No. 10 as far as National Institutes are concerned.

Dr. KOTIN. Yes, sir.

Mr. NATCHER. I believe that the first eight were established by legislation, is that correct?

Mr. KOTIN. I would defer to Mr. Kingman on that.

Mr. KINGMAN. If there is an expert around here, I will defer to him, but in the absence of one, most of the institutes were actually established by administrative action.

Mr. FLOOD. You are away from home, so you are an expert.

Mr. KINGMAN. Yes, but I am where the experts live. Most of the institutes were established by administrative action following some positive action on the part of the Congress to authorize the establishment of an institute. I think there are only actually two that were established by the Congress, and I think one of them is the Eye Institute where no administrative action was required on the part of the executive branch.

Mr. NATCHER. Mr. Kingman, are you acquainted with the environmental health letter of January 1, 1969?

Mr. KINGMAN. Yes, sir.

Dr. KOTIN. This is a private newsletter like the Kiplinger Letter or the Blue Sheet that is edited by Mr. Gershon Fishbein who provides

presumably authoritative inside advance information in matters dealing with environmental health.

Mr. NATCHER. Dr. Kotin, you say advance information. In other words, they attempt to read your mind individually, is that correct?

Dr. KOTIN. Or look for leaks, or whatever.

Mr. NATCHER. Let me read you a little statement and see if you and Mr. Kingman will agree with this statement.

"The Institute is the 10th within NIH, the only one headquartered outside the Washington area and only the second to be created by administrative action rather than by legislative authorization. The other was the National Institute of Arthritis and Metabolic Diseases more than a decade ago."

Do you disagree with this, or is this correct?

Dr. BERLINER. That is correct. It certainly is correct with regard to a majority of the institutes. There may be one other that was created without legislative action but I am not certain about that.

Mr. NATCHER. But you do agree that for this time this mind-reading organization is correct as to that statement?

Dr. KOTIN. It has been correct many more times.

Mr. NATCHER. Then I believe you are now No. 10. You are the only one outside of the metropolitan area.

Dr. KOTIN. More than 50 miles from Washington.

Mr. NATCHER. Is that an advantage or a disadvantage, Dr. Kotin?

Dr. KOTIN. In balance because of where the triangle is, and it may cost me my job, an advantage.

Mr. NATCHER. You are a good man, Dr. Kotin. What is your answer to that easy question, Doctor?

Dr. KOTIN. It is an advantage.

Mr. NATCHER. It is an advantage?

Dr. KOTIN. Only because of the unique location of the Institute in the triangle.

Mr. NATCHER. Just because it is in North Carolina?

If it was in Louisiana would you still answer the question the same?

Dr. KOTIN. If it were as close to LSU and Tulane as it is to North Carolina, North Carolina State, and Duke, my answer would be the same.

Mr. NATCHER. Now, Doctor, you started out in 1967 as you described it with a pencil and pad and maybe one or two to help you pick up the pencil and the pad. Is that about it in 1967?

Dr. KOTIN. I said it too dramatically, but it is about right.

Mr. NATCHER. You got on the good side of my friend, Mr. Cardwell, here, and you got money transferred. How much did you have transferred in the year 1967? What did you start with?

Mr. KINGMAN. The action that was taken was that we fell heir to the environmental health appropriation, which was in excess of some $24 million, and then an amount in excess of approximately $11 million was transferred to what is now the Consumer Protection and Environmental Health Service. So we started at a level of about $13 million in 1967.

Mr. NATCHER. About $13 million. And now you are up to $19 million, which is now pending before the committee.

Mr. KINGMAN. Yes.

NEED FOR INCREASED FUNDS

Mr. NATCHER. Dr. Kotin, as our chairman pointed out to you, this is the year 1969 when we must save money. We have heard about that a long time, and my chairman is sincere with you about it.

Why do you have to have any part of the $1,322,000 increase? Why can you not operate on the same amount that you have in 1969?

Dr. KOTIN. I think it would be a disservice, and I speak very personally of course, to the national health needs. I think it is a disservice, and I may as well be candid, to even operate at the level we are requesting. We are given a rare opportunity in the field of environmental health, to deal with a problem affecting 200 million people at all ages from the first breath of polluted air in the city to the last breath. This opportunity comes at a time when, rather than dealing with the results of exposure, we can hopefully institute control measures whose rate of positive return in terms of national well-being, and productivity, would be much more than our investment.

This I happen to believe. It is a creed with me supported I think by some substantive information and records.

Now the limiting factor in this budget, sir, is not the magnitude of the problem because I would put three zeros after it in terms of magnitude of the problem, but the limiting factor is the resources other than dollars, the space to do it, the scientific capability to do it, just the resources other than dollars.

We are moving into a different world of health. Infectious diseases are pretty much controlled. I think that the era of medicine we are now in is not so much curative as it is a maintenance one. We do well, and I speak now as a physician, to keep a patient with degenerative heart disease or renal disease as well as he was when he came to see the physician.

Essentially these diseases are ones accompanied by organic change in large measure the result of environmental experience.

If we can, on the basis of identifying these adverse environmental experiences, reduce the toll, much the same as was done spectacularly with infectious disease, although this is infinitely more complex, the disease patterns are different, I really cannot conceive of any increment of the gross national product it would not be worth.

DUPLICATION OF EFFORTS OF OTHER AGENCIES

Mr. NATCHER. Dr. Kotin, are not services being performed at the present time in your new Institute duplicating other services that are presently being performed in other National Institutes and throughout the Department of Health, Education, and Welfare?

Dr. KOTIN. If so, it is a reflection of our ignorance, not our intent. We are complementing these other programs, and essentially this really represents our role, our wedge of the pie in the totality of not only the NIH, the HEW, but in fact the total health commitment of the Nation.

I think the Institute is perhaps different than virtually any other component of the establishment dedicated to health because it is a bridge organization, it is concerned with people and the laboratory, but also concerned with the economics, I do not mean in terms of dollars, but the industrial aspects.

LONG-RANGE FUNDING PLANS

Mr. NATCHER. The National Institute of Environmental Health Sciences is No. 10 and you are now requesting $19 million plus to operate on for the fiscal year 1970.

Dr. KOTIN. Yes, sir.

Mr. NATCHER. What could we expect in the fiscal year 1991, Dr. Kotin, from the standpoint of amount?

Are you going to be competing with heart and cancer and these others? Will you be in here asking for 4, 5, 600 million? Where are you going, Doctor?

Dr. KOTIN. I would say the amount we would ask—and this really is not the right answer—would almost be a reflection of our success. I would say the more successful we are after peaking, and I would have——

Mr. NATCHER. When are you going to peak?

Dr. KOTIN. Scientific data would determine when we peak, sir. When we have a rubric which will unequivocally identify a hazardous compound so it is not introduced into the environment, or develop a metabolism modifying procedure which will protect an individual if we cannot clean up the environment. Actually we are trying both the host and the environment as two approaches.

I just would not know how to predict either when we will peak, sir, or the amounts of money we would ask for. I would say we would have the right to be legitimately questioned and cross-examined each year to see if what we are asking for is a reflection of what we have accomplished.

Mr. NATCHER. Down through the years the legislative branch of the Government, Doctor, in passing upon the requests of the Department of Health, Education, and Welfare, and prior to the time it was established, has always believed that where possible you should confine the number of institutes, the number of operations.

Is that not generally true, Dr. Kotin? Have you heard this?

Dr. KOTIN. In all candor, I have not. I can appreciate the genesis of such an opinion. I would again say that this opinion through the years would have validity at any given point in time, because a radiobiology institute prior to nuclear fission would have been unthinkable, really. So would the need for a program in radiobiology.

Similarly, a pesticides synergist's study 10 years ago would have been unthinkable. So I think the realities of the ambient situation *are* probably the major determinant of what direction you chose to strike out in.

COST OF LABORATORY FACILITIES

Mr. NATCHER. Doctor, you point out to the committee in your statement that the Institute is located in the Research Triangle Park in North Carolina in leased facilities at this time.

You further state that a firm of architects and engineers is completing a master site plan for the development of the adjacent 509-acre tract of land deeded to the Government in September of 1967.

Can you give the committee some idea as to what this facility or facilities will cost? Can you give us any idea at all as to what we are running into from the standpoint of dollars?

Dr. KOTIN. I think this can be answered in two ways:

In terms of our development of the facility, it is obviously going to have to be a phased activity, and the first phase which we project will be three dimensional in 1974, will probably be $10 million.

Mr. KINGMAN. The master site planners are planning the utilization of this 500-acre site as you said, sir, and they are planning the use of that site by both our Institute and the National Air Pollution Control Administration. The early planning figure they have come up with——

Mr. FLOOD. Who are "they"?

Mr. KINGMAN. The architectural firm, sir. I will include the name for the record. It is a——

Mr. FLOOD. I do not care about the name.

Mr. KINGMAN. It is an architectural-engineering firm.

Mr. NATCHER. If you will pardon me for interrupting you, the cost is here in print.

Mr. KINGMAN. I think the planning figure in the budget is some $24 million.

Mr. NATCHER. No. We are going to have to tell you, too.

The figure we have set out here is $41,392,000.

Dr. KOTIN. I was speaking of it in phases.

Mr. NATCHER. Is this figure right—$41,392,000?

Mr. KINGMAN. It is the best figure we have as of this date, sir.

Mr. NATCHER. You mean within the next few years or sometime between now and the year 2000?

Mr. KINGMAN. The cost estimates which I think are reflected in that budget are cost estimates developed by very conscientious and competent people in a field I am not competent in. But the fact is that when you talk about what is the cost of construction of any facility at this point in time, for a time span longer than the day after tomorrow, any estimate you have, sir, is purely an estimate.

Mr. NATCHER. I think you are right, Mr. Kingman. I think you are exactly right.

Dr. Kotin, you are not competing with any of the other Institutes as far as the amount of your request; are you? You are not in any competition with them?

Dr. KOTIN. My silence is predicated on essentially being dumbfounded. I have thought many things about the Institutes, but competition has not been one of them. We are different than the others.

PROJECTED FUTURE BUDGET

Mr. NATCHER. We had this up last year and the year before, and the question was asked as to how fast you expected to expand and where you expected to go moneywise from the standpoint of just having a division, not an Institute. So it is of concern to the committee, Doctor.

Dr. KOTIN. I can appreciate that, and probably the feebleness of my answers is a direct reflection that my concern—and this is not meant to pass judgment—stems from the national need and the magnitude of the problem that the Institute is addressing itself to.

Mr. NATCHER. Dr. Kotin, do you anticipate that your Institute now will finally go into a two and three and 400 million dollar category, with achievements that you point out to the committee?

Dr. KOTIN. I would be less than honest to answer anything other than yes.

Mr. NATCHER. And you still maintain to the committee, Doctor, that you need the amount of the increase that you show here of $1,322,000?

Dr. KOTIN. If by saying emphatically I can make my position that much more indelible, I would answer emphatically yes.

EFFECT OF EXPENDITURE CONTROL ACT

Mr. NATCHER. How much reduction did you have to take under the $6 billion reduction of the Revenue and Expenditure Control Act? What did you end up with as far as money is concerned?

Mr. KINGMAN. We took a reduction of approximately $240,000 as a result of that, some of which we are proposing for restoration to pay for the additional costs of the pay raise in 1969. That amount is contained in a supplemental also pending before this committee.

Mr. NATCHER. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Shriver?

Mr. SHRIVER. As I understand the recent testimony, the increase is for the two additional envoironmental health science centers and 35 additional people.

Dr. KOTIN. Not intramural increases. The 35 extra people are for the intramural program for the staff of the center.

FACILITIES COST

Mr. SHRIVER. Do you lease the buildings or facilities down there?

Dr. KOTIN. Yes, sir.

Mr. SHRIVER. From?

Dr. KOTIN. Research Triangle Park Corp., a nonprofit corporation chaired by Governor Hodges, which has the operating responsibility for the Research Triangle Park.

Mr. SHRIVER. How much do you pay?

Mr. KINGMAN. We are currently paying $14,928 a month, about $179,000 a year.

Mr. SHRIVER. How many people are occupying it?

Mr. KINGMAN. Just under 200.

CREATION OF INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Mr. SHRIVER. I think most of my questions were asked by Mr. Natcher, but I am wondering how the date of January 12, 1969, for the change in name, or creation of the designation happened. Why that date? Why not the 21st of January?

Dr. KOTIN. This is the decision of the Secretary of Health, Education, and Welfare.

Mr. SHRIVER. Do you know?

Dr. KOTIN. I cannot say, sir. Maybe Dr. Marston knows.

Mr. SHRIVER. Had this been before him a long time?

Dr. MARSTON. The last discussion we had I guess was in September on it, Dr. Kotin, when you informed me of it. Actually I suggested

that you give me a written recommendation, which I forwarded on to the Secretary's Office after discussion with various people.

Mr. SHRIVER. In September?

Dr. MARSTON. The actual formal paper would have gone up later in the fall than September, possibly October.

Mr. SHRIVER. This was just about 8 days prior to the change in administration.

Mr. KINGMAN. Mr. Shriver, in the establishment of the Division of Environmental Health Sciences, which was done in November of 1967, with his proposal for the establishment of the center to Mr. Gardner, who was then Secretary——

Mr. SHRIVER. His?

Mr. KINGMAN. The Surgeon General's proposal. The Surgeon General stated in his memorandum at that time that it was his view that the organization would evolve into an institute. So that the lag between the concept and the formal act was something on the order of 18 months rather than a matter of days or just a few weeks.

Mr. SHRIVER. That is all, Mr. Chairman.

Mr. FLOOD. Mr. Hull?

SMOKING AND HEALTH

Mr. HULL. Thank you, Mr. Chairman. Dr. Kotin, questions have come up before in this committee and elsewhere about the degree of cooperation between the tobacco industry and the Government research agencies in resolving the smoking and health question. The industry seems to be putting out between $4 and $5 million a year through independent grants, and the reports these people issue indicate that very basic research is involved.

Are you doing much the same thing, Doctor?

Dr. KOTIN. Yes, sir, and in addition I am on one of the advisory committees of the AMA Committee on Smoking and Health, which has the responsibility for awarding these funds for research that were made available to the American Medical Association through a consortium of companies, I suspect.

Mr. HULL. Doctor, what efforts have been made to see that the money that is being spent in this field is being spent most efficiently?

Dr. KOTIN. There are several.

First, there is ongoing publication in the scientific journals. Certainly in the professional organizations concerned with diseases that are related to smoking, those of the American Heart Association, the American Association for Cancer Research, segments of the programs are devoted to the area of both tobacco chemistry, tobacco biology, and the like.

Secondly, the American Medical Association and the Advisory Committee to the Council for Tobacco Research and the Lung Cancer Task Force work together very closely. Of the three committees, I would say that approximately 60 percent of the members are members of at least two of the three. So there is ongoing information exchange both on the basis of the persons involved and a formal mechanism.

The Council for Tobacco Research, through its executive secretary Dr. Hockett, makes known to the AMA and NIH and, conversely, the other two sides of the triangle make known a listing of the grants, the

funding of the grants; and the principal investigators' progress reports are circulated.

So there is an ongoing planned rather than catch-as-catch-can exchange of information. I would say that is about as far as anybody can go. Real coordination in the sense of staking this out as your area, my area, this person's area, this really is not being done. It happened almost by natural selection. The AMA committee is emphasizing the cardiovascular and cardiorespiratory research, the scientific advisory board to the Council for Tobacco Research is heavily deployed in research related to carcinogenesis and the NIH programs, on the basis of its Institutes; categorical responsibilities, are investigating many aspects of the problem.

SCIENTIFIC INFORMATION PROGRAM

Mr. HULL. Doctor, what is the new scientific information program mentioned in your justification?

Dr. KOTIN. That is a program which is concerned with the transfer of information prior to publication in scientific journals. There is a lag period of from 6 months to a year to a year and a half before a paper gets published.

If you look at a journal, "accepted for publication July 1," and the following February it is published. So we have established within the Federal establishment and other organizations, including industry, concerned with environmental health, a mechanism for the exchange of progress reports, staff papers, and other materials that either have a long lapse time before they get into accredited or usual literature or would never be printed because they might include a lot of negative data which editors of journals are reluctant to print, but very, very important.

In attacking a problem, you can attack in two ways, either by creating new information or preventing the dissemination of misinformation or erroneous information.

One of the problems we have been concerned with in this area has been the sporadic reporting that some fungi which naturally infect tobacco and have potent toxins have these delivered over in the smoke. Two reports from very reputable universities reported they demonstrated this.

Our scientists feel this is not so. We have met with the university scientists and, we have compared our spectra, our chromatographic charts and the like and they agreed that the infinitesimal differences between the true compound and a related compound are such that confusion is possible. In any event this would never get into the scientific literature, the fact that we were party to prevention of the publication of what appears to be erroneous information. This is what the scientific information program that we have is concerned with, this type of nonpublished information, as well as the more traditional forms of scientific communication.

Mr. HULL. Will this system avoid duplication or overlap in any research that may be under way or planned by any other agencies?

Dr. KOTIN. It certainly would. This is its primary goal. This accounts for really the hit and miss nature of what our program would look like to somebody, say a visitor from Mars, who would ask, "how

did you happen to pick out these six areas, they appear to be unrelated."

Actually, the picking out of the areas reflects the areas we feel are important and for the most part are either going by default or not getting the investigation in depth we think national needs would dictate.

AMOUNTS BUDGETED FOR SMOKING AND HEALTH RESEARCH

Mr. HULL. You told us last year that your division planned to spend $307,000 on tobacco and health research. That figure included $175,000 in grants. Your justification material last year listed only $92,000 to be spent for smoking and health. Your justification this year gives the 1969 estimate of $100,000. And this year you are asking for more than twice as much, $250,000.

Can you straighten me out on this, Doctor?

Dr. KOTIN. Yes, sir.

With the establishment of the lung cancer task force, it became obvious that this concerted action, concerted action of scientists from NIH, industry and universities and so on, was ultimately going to evolve just what you are inquiring about, a coordinated program, so that there will be a minimum of overlap and major emphasis on the more important aspects of the problem.

What we decided, Dr. Endicott, Dr. Cooper and myself, the three categorical interests in NIH, the representatives of the universities and so on who are members of the working groups on the lung cancer task force, let's just see what comes out of the deliberations in the way of a highly structured program and then go ahead full force.

The lung cancer task force, is represented by members of the Institute of Environmental Health Sciences, Dr. Falk, and until recently by myself as well. The lung cancer task force met yesterday and today with what I hope is the final structuring of the program. With this structure we feel we can deploy the increased amounts, and alternatively it accounts for our spending less than we anticipated this year while we awaited the final evolution of a structured collaborative coordinated program.

Mr. HULL. How much are you planning to spend in all in your Institute on smoking and health?

Dr. KOTIN. $473,000, sir.

EFFECTS OF TAR AND NICOTINE ON HEALTH

Mr. HULL. Dr. Kotin, has it been scientifically established that nicotine as found in cigarette smoke causes any human disease?

Dr. KOTIN. I would say there is no question that nicotine can adversely affect the optimal operation of certain parts of the cardiovascular system. It is a long-winded answer, because the specific role of nicotine is really not yet determined beyond the fact that there is an apparent association between the action of nicotine and interference with the normal physiological activity of certain parts of the body.

Mr. HULL. You have not found out yet, in other words?

Dr. KOTIN. We have not found the mechanisms, but we have epidemiologic evidence that suggests it plays a role. We certainly cannot

say we have identified the mechanism of the role or even the magnitude of the role. At least I cannot.

This is really not a field I am expert in. However the average working scientist's awareness of the problem is something I do have and I think it is a fair statement.

Mr. HULL. Now we are told the tar content of the cigarettes may be important. In your opinion, is there any solid scientific support for predicting the effect of tar on human beings, any effect that reduction of this tar content would have?

Dr. KOTIN. Yes, sir, I think tar reduction would be associated with the reduction in the hazards associated with cigarettes.

Mr. HULL. Do you think the present evidence provides any solid evidence of the reduction of any disease rates, assuming there would be any?

Dr. KOTIN. I do not think we have this evidence. I know the Institute is devoting a considerable portion of its statistical resources to developing just these types of mathematical models so that we can benefit from the actual reduction in tar and nicotine contents of cigarettes that have just taken place over the years.

Also, there is an apparently growing desire or attachment of consumers for lower tar and nicotine. While I cannot predict what the extent of the benefit would be, cigarette smoking is an environmental experience really no different than virtually all the others. There is a spectrum of response, and since there are no magic chemicals in cigarette smoking, a dose response is a reasonable anticipation. We just do not know what it is.

SIGNIFICANT RESEARCH FINDINGS ON SMOKING AND HEALTH

Mr. HULL. What research would you include in a list of the most signicafint work done in smoking and health since the 1964 Surgeon General's report?

Dr. KOTIN. First, I think from the point of view of the total problem, the reduction in risk associated with the cessation of smoking, I think, is a very important observation, with great implications for the mechanism of action of the individual components of cigarette smoke that may be associated with the hazards. That one is the epidemiologic demonstration.

Second, I think the demonstration that the effect of cigarette smoke on the mucous secreting and ciliary activity of the epithelium does respond in something resembling the dose response manner. We do not have all the points established well enough so that we can draw a curve.

Third, I would say the implied evidence that a threshold does exist. I think the data shows that for a given amount, and you pick it—some data would suggest that the risk associated with five to seven cigarettes smoked per day, independent of length of smoking, really is no different than the nonsmoker, and then other data would carry this as far as the 10 per day smoker. Again these little bits of contributions of dose response are crucial if we are ever going to be able to predict whether there is a threshold for such a thing as reducing the hazards created by smoking.

LUNG CANCER TASK FORCE

Mr. HULL. I see no mention of the lung cancer task force this year in your budget justification. Does your Institute still have managerial responsibility, as you termed it last year, for the collaborative efforts of the task force?

Dr. KOTIN. Actually, both Dr. Endicott and I used the term "managerial responsibility", and this morning in meeting with him we discussed this. What the task force is going to recommend will be decisive in determining where managerial responsibility should reside. Theoretically we felt it would be better for the Institute, NIEHS, to have managerial responsibility. This was just an educated guess.

Depending upon what the task force comes up with, we will then decide. Our intention last year, both Dr. Endicott and myself, was to have managerial responsibility reside in the Institute.

Mr. HULL. What is your personal role with the task force?

Dr. KOTIN. My personal role now is being a member of the task force. Dr. Falk, the Director of the Laboratory Research in the National Institute of Environmental Health Sciences is chairman of one of the subcommittees of the task force, and a contributing scientist of considerable knowledge in this area.

And then again, the relative participation of the Heart Institute, the Cancer Institute, and the Environmental Health Sciences Institute is something Drs. Cooper, Endicott, and myself, and our representatives have discussed. Since last appearing before this committee, we have had at least three meetings.

Again, the task force recommendations would probably be the most intelligent base on which to decide who is going to do what.

Mr. HULL. What did you do in that capacity last year?

Dr. KOTIN. As a member, my capacity then was as a scientist rather than a director of an institute. I worked in the field of pulmonary disease, as a bench scientist for the better part of two decades. And then wearing my other hat as a director of an institute, in conjunction with Dr. Endicott and Dr. Cooper, attempted to establish priorities in terms of what we felt the pressing aspects of the problem were.

Mr. HULL. What did your institute do?

Dr. KOTIN. We did several things.

First of all, through the use of emission spectroscopy we have been doing some studies on trace metal components in cigarettes. We are supporting through a contract at North Carolina State University work aimed at the factors which govern the survival or the intensity of contamination of tobacco by fungicidal agents.

We are studying the affects of individual components of cigarette smoke on model systems to again dissect the components and then reunite them to see what the effect of the individual agents are and what their joint effect is. Studying things like the effect on the integrity of the linings of the lung, the cells lining the lung and so on.

Mr. HULL. Will any part of the $1.3 million asked for the task force in the NCI budget be spent in your Institute?

Dr. KOTIN. I do not know, but I can tell you the same question is one that Dr. Endicott asked me this morning, and I asked him as well.

I take refuge again in saying we just sort of moratoriumed everything until we see what the Task Force recommends.

COOPERATION WITH INDUSTRY

Mr. HULL. We expressed the hope last year the task force would have the support of other scientific and industrial organizations. What part has anyone outside government had in task force research or planning?

Dr. KOTIN. By company, the task force has representatives of Wakeham from Philip Morris, Dr. Sincus from Reynolds, Dr. Kensler from A. D. Little, whose work is supported by Liggett and Myers. Every major company except one, and this deficiency is now in the process of being corrected. The British American Tobacco Co., the Brown and Williamson people are in the process of being invited to participate at the scientific level. At each task force meeting that either I have attended, or have gotten the minutes of, the attendance by industry scientists has been 100 percent, as has been attendance by NIH scientists and specialists from the universities in the research world.

IMPROVED DIAGNOSIS AND TREATMENT OF LUNG CANCER

Mr. HULL. You told us last year that the task force would be supporting research aimed at facilitating early diagnosis and improved treatment of lung cancer. Have any advances been made in these two areas in the past 12 months?

Dr. KOTIN. I think Dr. Endicott might have been responsible for that testimony. If I did say it——

Mr. HULL. Can you get it for the record?

Dr. KOTIN. First, again I do not recall having said that last year, but I can talk to Dr. Endicott and get a reply to that.

Mr. HULL. I wish you would.

Dr. KOTIN. I have had no personal participation in the efforts to improve diagnosis or treatment of lung cancer.

(The information follows:)

ADVANCES IN DIAGNOSIS AND TREATMENT OF LUNG CANCER

In considering the research approaches to the problems of lung cancer, the lung cancer task force agreed in 1967 that major emphasis should be devoted to prevention through development of a less hazardous cigarette. The group also agreed that significant efforts should be placed on improved diagnosis and treatment and laid-out estimates for the funding that would be required to launch these programs. Inasmuch as funds for the support of task force activities have been limited, task force-sponsored efforts have been confined to one needed area of research; namely, development of a less hazardous cigarette.

The National Cancer Institute continues to provide research grant support for a number of programs and projects directly related to the extraordinarily complex fields of lung cancer detection, diagnosis, and treatment. Included are 2 cooperative clinical groups which are exploring the effects of radiation and chemotherapy in large numbers of patients with advanced lung cancer. Furthermore, NCI and Veterans Administration investigators are collaborating in a NCI chemotherapy-oriented program located at the Washington, D. C. VA Hospital. It is anticipated that on-going fundamental research concerning the characteristics of solid tumor growth and drug effects will continue to provide the scientific basis for developing further improvements in the chemical attacks on lung cancer. Due to the complexity of the disease, the time required for its initiation, growth and clinical expression, and the lengthy period required for the development, application, and evaluation of new research findings, the program against lung cancer and achievements through improved diagnosis and treatment reflected in decreased mortality, will most certainly become evident, not dramatically, but gradually over the years.

COST OF REVIEW AND APPROVAL

Mr. HULL. I notice that your Institute appears to be spending twice as much of your research grant moneys as other institutes on review. Why is it necessary to spend 5 percent of your total research grant money on review and approval, when NIAID, for instance, spends only 2½ percent?

Mr. KINGMAN. I think the answer to that is a matter of the critical mass we are so often talking about.

You may remember last year essentially the same question was asked us by the committee, and our response was that in developing the program management structure of the organization we had to garner all the requisite skills in order to carry out our responsibility in the award and management of our grants program.

It is our view that staff is adequate to handle a program larger than the dollar amount of the program currently being handled and that this staff will be adequate to manage our program for some time to come.

Allergy has a significantly larger grant program than we.

RESEARCH ON SPICES

Mr. HULL. Dr. Kotin, I have not congratulated you upon the upgrading of your division to Institute status, recognition by HEW of the importance of studying the health hazards in our environment.

I wonder, however, how parsley, celery, and numeg fit into the environmental health picture. We have been reading recently about dangers to humans.

Will you tell me why you have included in chemical studies for this year research on the intermediate metabolism of the main constituents of essence oils, parsley, celery, nutmeg, and other dietary components.

Dr. KOTIN. First, they are widespread, ubiquitous, an integral part of our daily diet, and the chemical structure of many of these compounds is similar to the pesticide synergist that the chairman of the committee asked about earlier.

The volatile components of the spices in and of themselves are nonhazardous, but their ability to modify the metabolic handling of other agents is very, very important. So that a person taking some drugs or exposed to some environmental chemicals that depend on a certain class of enzymes for their degradation, for their detoxification, these enzymes are interfered with significantly by abnormal concentrations of volatile substances of these spices.

Under normal conditions, under usual conditions, you can take these spices in the ambient amounts without hazard, but if you happen to be taking a tranquilizer or are exposed to an environmental chemical which depends on these enzymes for detoxification, for a transient period you neutralize the enzymes and rob the body of the host defense mechanism that it has.

So we are concerned about these, we are concerned about them, because they are in the diet of the little infant, to the aged man, at the time when the reserves that are inherent and available to all of us around this table are not available to a 2-week-old child who may have some of these seasonings in his food, or a person far along in years and his reserve has been pretty much diluted.

So essentially, it is the long-range low-level exposure that we are concerned with. Indeed, if we were to study this and this alone, it would almost border on the ludicrous, but it is part of the constellation of dietary exposures. They are very, very important in the sense that I would say if you are taking a drug or a class of monoamine oxidase inhibitor, do not eat excessive amounts of Roquefort cheese as the effect could be fatal, as several people have, due to combination of effects.

And what we are trying to do is establish some principles where we can elucidate the mechanism for this and prevent it if possible, or alternatively make the hazard known.

Mr. HULL. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Casey?

UNIVERSITY ENVIRONMENTAL HEALTH SCIENCE CENTERS

Mr. CASEY. Thank you, Mr. Chairman.

You have six operational centers now, do you?

Dr. KOTIN. Yes, sir.

Mr. CASEY Where are they?

Dr. KOTIN. Harvard University School of Public Health, New York University Medical Center, Kettering Laboratory at the University of Cincinnati, and the State University at Corvallis, Oreg., Washington University in St. Louis, and Vanderbilt University in Nashville, Tenn.

Mr. CASEY. You contemplate establishing two more this coming year?

Dr. KOTIN. We would like to.

Mr. CASEY. Where would they be, or do you know?

Dr. KOTIN. We do not know, but we are exploring one at the University of Washington at Seattle.

The programs at Tulane and LSU in New Orleans we feel merit investigation. I cannot name the two, but this is some forward thinking we are doing.

RELATIONSHIP TO PROGRAMS OF THE CONSUMER PROTECTION AND ENVIRONMENTAL HEALTH SERVICE

Mr. CASEY. Doctor, in this request for appropriations this year, the Food and Drug Control has asked for $72.6 million, an increase of $5.4 million over last year; Air Pollution Control asks for $95.8 million, an increase of $7.1 million over last year; and the Environmental Control asks for $57.6 million, an increase of $14.7 million.

Do you believe that what you do is radically different from what these three operations requesting all of these appropriations do? They are asking a total of $27.2 million more than they got last year.

Dr. KOTIN. Yes, I believe they are different for different reasons.

FDA is concerned with drugs. Consumer Protection is concerned in large measure with the research towards the development of more effective control measures. The Air Pollution people are concerned with research towards a better vehicle exhaust control unit, a better method for trapping stack gases, a better technique for the dispersion of pesticides, et cetera.

These are examples of the technological research that are wholly foreign to our needs.

Mr. CASEY. Let me just read you a few tidbits from their justifications submitted here.

Under Food and Drug, they have medical evaluation, "Research grants are awarded to universities and other eligible institutions to support studies of accidental poisoning, burns, and other product-related injuries."

They state that they are charged, and their administration is designed to protect the public against dangerous misbranded and adulterated foods, drugs, therapeutic devices, cosmetics, and other products. They also state that medical policy pertaining to the efficacy and safety of drugs are developed and promulgated.

Adverse reaction program. Under scientific research, this activity awards research grants to State agencies and other qualified investigators to promote the study of pesticide-caused hazards.

Mr. CARDWELL. Mr. Casey, it might pay to stop there because you are going to build quite an accumulation for him to trace back. If you take food and drug and move on to air pollution, it might give you a better dialog.

Dr. KOTIN. Is that all right?

Mr. CASEY. Yes. You have $1 million requested.

Dr. KOTIN. There is a general answer that would apply to all.

Essentially the organizations that you have named have an immediate problem, they have got today's problems with today's answers. I guess I did not quite adequately emphasize our concern with the need for long-range projections. They really cannot afford the scientific time requirement, the scientific luxury, if you will, of long-range studies because they need answers today.

We are concerned with answers that are going to be necessary in 1990 when there will be tens of thousands more chemicals in the environment, synthetically produced chemicals being turned out even now at the rate of 5,000 a year.

Our problem is to see, since we are not going to stop the production of these chemicals and we should not, they serve a useful purpose or they would not be manufactured—our problem as distinguished from theirs is not to concern ourselves exclusively with the effect of production 1969, but to see whether we cannot establish a biological basis which will, as the years roll by, give us a rubric against which to measure potential hazard as distinguished from innocuous, provide them with guidelines for their own research and development on the basis of avoiding hazards.

So while we are looking at the same thing, our orientations are more than slightly different, they are complementary.

Mr. CARDWELL. Could I interject at this point, that we have looked at this from the Secretary's perch any number of times. One way I think to make the distinction is to go back to Mr. Michel's question of Dr. Kotin—will you at some point in time establish standards and issue regulations which would determine the levels of a given toxin on a food product, and his answer was—no, we are not in the regulation-making business, we are not a regulatory agency.

The Food and Drug Administration is a regulatory agency—it has a charge under law to regulate the quality and efficacy of foods and drugs. In a way they draw on whatever knowledge happens to be available at the time they have to establish the regulations.

To give an example in establishing a pesticide tolerance level for a new pesticide coming on the market, FDA draws from the scientific community whatever knowledge is available and applies that knowledge to the practical problem of that moment, Dr. Kotin's point.

Dr. Kotin's mission is to add to man's knowledge, and the Food and Drug Administration, the Air Pollution Control Administration, and mankind in general will draw from whatever knowledge Dr. Kotin adds up for us. His efforts may pay off today, they may pay off tomorrow, they may never pay off.

This to me is the distinction between the two agencies. In the field of research, if anybody is duplicating within HEW the search for basic knowledge, I would say the other agencies are duplicating Dr. Kotin and not Dr. Kotin duplicating them, because basic research is his basic mission.

In Food and Drug Administration, their research should be directed to finding better methods of detecting toxins in food and drugs, not to add to the accumulative knowledge of mankind about the effects of drugs on the environment. Their research mission is related to short term application—to help them regulate. Dr. Kotin's research is much deeper, much broader, much longer term.

Mr. MICHEL. How does the proposed research to be carried on in this big laboratory to be built in Cincinnati tie in?

Mr. CARDWELL. With regards to the Cincinnati lab we are talking about two major components—milk, food and water; and air. Again the research mission relates to short-term developmental work relating to methods of identification of toxins when they appear in elements of the environment.

AIR POLLUTION

Dr. KOTIN. Let me give a specific example, lead.

The National Air Pollution Control Administration is going to have to establish lead standards. There are certain fundamental aspects of the lead toxicology which can only be elucidated by long term exposures. You feed animals for virtually their entire life or they inhale for their entire life. You look at everything from the most minute components of cells to the total animal. It is this fundamental information that is going to determine first whether there is a safe level, is there any level of lead we can be exposed to at all. This requires the type of research we are concerned with.

On the basis of this information then, they can establish meaningful numbers. They are going to have to issue some numbers that are going to be predicated on less than ideal information, as indeed they have had to do for SO_2 and for particulates in other things. It is a body of information that does not exist.

What I think our Institute is dedicated to is the development of the information so that if indeed it becomes necessary to control our environment, because technological genius is pushing it faster than we can control it, that the restraint will be as solid as can be. This is accomplishable only through long term studies at low levels, and this is the point.

As pointed out, we are not falling over dead from lead poisoning when we stand on the corner of Fifth and Main, but heaven knows we are inhaling a lot of lead. Is the amount we are inhaling going to

affect us 15 years later with relation to another experience or just by the accumulation in our bodies for 15 years?

Mr. CASEY. Let's take air pollution next.

They have asked for 95.8 million, 7.1 more than they had last year, and they have as part of their justification that they have grants to public agencies to assess their air pollution and so forth, but also, grants are awarded universities and other nonprofit institutions to conduct research into air pollution problems, contracts relating to fuels and vehicles—which I mentioned—accelerated research and development of new and improved methods having industry-wide application for advancing control of air pollution resulting from combustion fuels.

I think this would tie-in with your example of the engine down in the mine. They also say that their responsibility is for the investigation of causes of air pollution, the determination of its effects upon life and property, and the development of an effective means of prevention, control, and development of air quality criteria.

Would you like to answer that? Of course they have more in here, too. They have in here "Activity includes research on the nature and extent of air pollution, its transport, and atmospheric behavior, the effects on humans, and other biological systems."

Dr. KOTIN. They indeed do all of that at levels consistent with providing them with enough information, or information sufficient for them to meet their legal responsibility as control agencies. They do not and would not—in fact, on the basis of our collaborative efforts I can say I know not—be concerned with long-range studies because they just do not have the time for long-range studies to determine whether any one of the agents present in polluted air represents a hazard.

The Donora episode, or London fog, required no intensive studies on man to demonstrate.

Mr. CASEY. Of course if they wipe out air pollution, they would not need you, would they?

Dr. KOTIN. In our testimony I said we were discussing technological trends. We do not want to get hung up on a 5-year program that engineers are going to tell us is going to be technologically obsolescent, because 3 years from now this procedure is not going to be used any more, this product is going to be superseded by something else.

We do monitor the environment for that reason to attempt to profile the action of an agent in the environment. There would have been no point in starting to study the effect of a solid rubber tire, let's say, if we had been in existence 35 years ago when pneumatic tires were going to supersede them.

It is a bum analogy, but the only one that comes to my mind.

So we do not want to research on things that are going to disappear by force because of technological advance, rather than by any great advancements in the health research field.

Mr. CASEY. They also had in their more detailed justification that grants are in the following areas: Air pollution and respiratory infection to determine the true pathogenesis of human air pollution disease and, "to see what actual respiratory changes occur from chronic and prolonged exposure to air pollutants at realistic concentration."

Dr. KOTIN. This is a collaborative effort between ourselves and them. The activity is going to be pursued under contract in chambers built at the University of North Carolina with air pollution funds. The record will show that they are footing the bill and we are contributing knowledge. It is a joint activity. This was part of the discussions in which I participated early—it had no effect on the ultimate decision of the wisdom of putting air pollution next to us on the adjacent hill, on the 509 acres in North Carolina.

ENVIRONMENTAL CONTROL

Mr. CASEY. Let's look at environmental control. They ask for $57.6 million; $14.7 million more than they got last year. They state that they "support national program for prevention and control of environmental hazards and health problems in order that man may more efficiently deal with his environment," which is, like you were saying, going to be swallowed up if we don't take care of it. And they mention solid wastes, occupational safety and health, radiological health, water hygiene, community and environmental management, which includes housing hygiene, sanitary marketing of milk, food, et cetera, including mosquitoes. They also say, "This program has responsibility for conducting a national program for control and prevention of radiological hazards to public health."

They also have training grants—research, training, demonstration, planning grants in support of this activity. That is under solid waste and I think you stated that you work with them on that. This is an intermural sort of a program.

Dr. KOTIN. Our relationship to solid waste is, again, concerned with fundamental information. As an example, polyvinyl chloride, one of the plastics that records are made of, are disposed by throwing them in dumps. If the dumps are incinerated, this polyvinyl chloride emits poisonous gases. The solid waste program is concerned with the technology of the storage of waste, distribution, and the like. They are concerned with the chemistry as we are, but essentially the long-range toxicity of this, as with all their programs, is a responsibility that, per force, is our responsibility as a complementary one to theirs.

Let me give you a brief example—and this may be where the confusion may exist—they have to use the term and do basic research and fundamental research, as we do, but their basic research is concerned with research responsible and immediately relevant to their control efforts. Our basic research is broader in the sense that it is providing a body of information which will not only give them a background to complement their own research, but essentially will have a long-range implication in terms of environmental protection and control.

We are not going to do the controlling, but intelligent control requires a body of scientific information accumulated under circum-

stances which their regulatory responsibility just does not permit under the present situation. And it should not, because it is alien to their immediate—as Mr. Cardwell points out—it is alien to their immediate legislative and governmental responsibilities.

DIVISION OF RESPONSIBILITY FOR RESEARCH ON ENVIRONMENTAL HEALTH

Mr. CASEY. The point I want to make is this: This was created as an institute. It was stated you would have to pay at least a half million dollars just for administration of a separate institute. Here we have these other three organizations. I don't think they are prohibited from doing what you are doing—that may be what they are limiting themselves to, but they have broad directives in all three of these fields that they can do anything and everything they want to do.

Mr. CARDWELL. Yes, sir, I think that is true. If left unattended and given the resources, they might strike out to do what Dr. Kotin is attempting to do. Time, however, I think, would work against them. The demands of the moment would always keep them from spending very much energy and effort on long-range basic research. It is very much like running my house or my own immediate office. The Federal Budget process is run today much the same way it was 10 years ago and some of the new people coming in, for example, ask me, "Gee whiz, why haven't you automated it?" And the answer is, "We are too busy doing what has to be done today. There are too few of us to spend any significant share of our time in developing ways to do the job better—adding to our own knowledge about that rather simple process."

Now, there is a tendency—I worked in the Food and Drug Administration for quite a while and I discovered a tendency among some of the scientists to talk as if they were going to do studies to identify the biological implications of aflatoxin, its mechanisms and why it possibly produces cancer. I never thought that was their mission. It is true they talked as if they were going to do it. The truth of the matter is, if you look back at those same scientists, you will find they haven't done it. Even though they would talk about pursuing this course if given their own head, and they might have set out to do it, too—but because those very same scientists have to work on regulations, on standard-setting and the like, they could never find the time.

But more importantly, it is the role of the Assistant Secretary for Health and Scientific Affairs, though, to sort these things out and to keep the various agencies on the right track.

It was the need for long-range basic research on the environment that led to the creation of the original division and for which the Institute now exists. As time goes on, and as they prove themselves, I think the opportunities for duplication will actually narrow. There will always be some there. But as long as the Institute pursues its goals with energy and imagination the opportunity for others to jump into the breech will be narrowed. Every now and then a scientist in one of

these other agencies may strike out in a new direction and he might even discover something, but it will not be the basic mission. He will not have been assigned that task.

Dr. MARSTON. Mr. Chairman, this leads me to comment on some of the broader NIH concerns the committee has been exploring this afternoon.

Last summer, particularly during the month of August, Dr. Shannon and I had several 7:30 in the morning meetings to talk about the major areas of concern where I should place my attention as I became Director of NIH. In one of those very first meetings, the Division of Environmental Health Sciences was one of the factors he brought up, in terms of his special concern and the potential of the division and the need for a priority as the division was getting underway.

We discussed three reasons for needing to look at this area as a special area of opportunity. First was that it is in a critical phase of development. It doesn't have a critical mass at present.

Secondly, the importance of the work along the lines Mr. Cardwell was just outlining. The need to establish a program that could look to the future needs for basic research concerning environmental hazards.

Third, the effectiveness of Dr. Kotin and his staff in a very brief period to launch a very complex and difficult program of great national importance.

So, one of the first things that I did very early was to make sure that I made a trip to North Carolina and did see what was going on.

They have gone back twice to meet with the scientists, to examine the programs and this operation has been really a shining example of the cooperation across the Institutes and I think across agencies as a complementary and as a liaison-type of activity.

Part of this, I think, has been Dr. Kotin's own very strong personal feelings that he has the responsibility to work in a cooperative fashion rather than in a competitive fashion on it. I would like to put in this hearing the very deliberate and strong feelings of high priority that the NIH has for this institute at a critical phase of its devlopment.

Mr. FLOOD. Mrs. Reid?

COORDINATION WITH OTHER INSTITUTES

Mrs. REID. The Institute was only recently elevated from Division Status—in January, I believe. Have you encountered any problems in this transition as far as coordinating your activities with those of the other Institutes is concerned?

Dr. KOTIN. No. Our mission is so complementary to those of the other Institutes that a clearly visible and easily definable interface for cooperation and collaboration exists. We have areas of common interest with the Cancer Institute. For example, the scientific staff of

both Institutes is represented on the lung cancer task force, thus assuring coordination between our Institute and the Cancer Institute. Similar excellent cooperative efforts are taking place with the National Heart Institute and the National Institute of Allergy and Infectious Diseases.

FUTURE PROGRAM PLANS

Mrs. REID. Your center was established to measure the long-term, low-level exposure to environmental hazard in terms of its effect on human health. I am curious to know your program for the next 5 years—do you have a master plan, so to speak, or is it possible to be so definitive in your particular field? Can you program your particular research in this way?

Dr. KOTIN. In response to the President's requests for planning information under the planning, programing, and budgeting system, we have had 5-year program plans which are updated each year. However, we are only at present in the final stage of developing a comprehensive plan for research in the environmental health field.

There will be a meeting in June of the task force on research planning in environmental health sciences. The objective of this task force is to provide the NIEHS with a series of documented recommendations to aid in the development of our intramural and extramural programs. The membership will include the best and the most knowledgeable people now working in the field of environmental health, and we hope their recommendations can be used to establish a detailed and very comprehensive plan for all our research and training activities. There will be subtask forces on air pollution, community and industrial exposures, food and water toxicology, and physical factors in the environment.

The meetings will be attended by representatives from the Consumer Protection and Environmental Health Service so that whatever plan is finally developed will be fully coordinated with the people who will be called upon to enforce future regulations of environmental hazards.

Background papers for discussion at the meeting are now being prepared and submitted and we are looking forward to what we hope will be called upon to enforce future regulations for control of environmental hazards.

If I may, I would like to insert the program of the task force at this point in the record.

PROGRAM OF THE TASK FORCE ON RESEARCH PLANNING IN ENVIRONMENTAL HEALTH SCIENCES

Meetings of Subtask Forces

JUNE 22 THROUGH JUNE 28

Air pollution

Effects of pollutants in the community.
Effects of pollutants in laboratory animals.
Estimation of dose to human receptors in the community.
Technics for estimation of effects on humans.
Cancer epidemiology and environmental agents including air pollutants.

Community and industrial exposures

Health and safety hazards of consumer products.
Concept of threshold limit values: Present applications and future needs.
Prevalence, hazard, and mode of action of trace metals.
Respiratory disease: Etiologic role of industrial agents.
Health consequences of industrial environments on perception, decisionmaking and fatigue.

Food and water toxicology

Potable water, microbial and viral aspects.
Potable water, chemical contaminants.
Health aspects of nonfood use of water.
Microbiology and virology of foods.
Natural toxicants and contaminants in foods.
Intentional food additives and chemical residues in foods.
Environmental chemodynamics.
Laboratory assessment of mutagenicity and carcinogenicity.

Physical factors in the environment

Acoustice and vibratory environment.
Lasers and microwaves.
Heat and infrared radiation.
Health implications of living space.
Ionizing radiation.

Exploration of broad research influences

Epidemiology.
Toxicology.
Technological trends.
Behavioral sciences.

Meetings of subcommittees on policy and derivative areas

JUNE 29 THROUGH JULY 5

Research priorities and goals.
Training needs.
Organization of research.

RESEARCH CAREER DEVELOPMENT AWARDS

Mrs. REID. In discussing your fellowship program, I note that this year you inaugurated a new program called research career development awards. You plan to grant 18 such awards in 1970. How are these research fellows selected—who makes the selections? Is there an attempt at geographical distribution?

Dr. KOTIN. They are selected through the regular NIH review process whereby any person who meets certain requirements in educational background, achievements, and so forth can submit an application for such an award. The application is referred to NIEHS by the Division of Research Grants, and it must be approved by the training committee and the NIEHS Advisory Committee.

Mrs. REID. On page 139 of the justifications you list $12.9 million for "Grants, subsidies, and contributions." What is the difference here—and how will this be divided?

Dr. KOTIN. The terminology "Grants, subsidies, and contributions" is not ours, but is a category of expenditures established by the Bureau of the Budget. In this case, the $12.9 million is all grants, including research grants, center grants, fellowships, and training grants.

Mrs. REID. Thank you. That is all, Mr. Chairman.

Mr. FLOOD. Thank you, Dr. Kotin. You are an excellent witness.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Environmental Health Sciences

Amounts Available for Obligation

	1969	1970
Appropriation	$17,820,000	$19,004,000
Transfer from "National Cancer Institute"	+197,000	---
Comparative transfer to "Salaries and Expenses, Office of the Director, NIH."	-232,000	---
Cutback required by P.L. 90-364	-240,000	---
Total currently authorized for obligation	17,545,000	19,004,000
Plus: Proposed release of reserves for increased pay costs	+137,000	---
Total available for obligation	17,682,000	19,004,000

Disposition of cutback:	
To be used for pay costs in this account	137,000
To be returned to the Treasury	103,000
Total cutback	240,000

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
148	Research		$8,406,000		$8,967,000		+$561,000
	General research support grants		(551,000)		(567,000)		(+16,000)
	Environmental Health Sciences Centers		(3,000,000)		(3,500,000)		(+500,000)
151	Fellowships		200,000		194,000		-6,000
152	Training		3,892,000		3,740,000		-152,000
	Direct operations:						
153	Laboratory and clinical research	151	4,432,000	186	5,322,000	+35	+890,000
157	Review and approval of grants	23	440,000	23	443,000	---	+3,000
158	Program direction	20	312,000	20	338,000	---	+26,000
	Total obligations	194	17,682,000	229	19,004,000	+35	+1,322,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions..	194	229	+35
Full time equivalent of all other positions.....	9	9	...
Average number of all employees.....	184	220	+36
Personnel compensation:			
Permanent positions.....	$1,659,000	$2,191,000	+$532,000
Positions other than permanent.....	64,000	64,000	...
Other personnel compensation.....	7,000	7,000	...
Total personnel compensation.....	1,730,000	2,262,000	+532,000
Personnel benefits.....	173,000	225,000	+52,000
Travel and transportation of persons.	110,000	180,000	+70,000
Transportation of things.....	25,000	50,000	+25,000
Rent, communications, and utilities..	259,000	350,000	+91,000
Printing and reproduction.....	20,000	40,000	+20,000
Other services.....	1,803,000	1,658,000	-145,000
Supplies and materials.....	544,000	581,000	+37,000
Equipment.....	520,000	757,000	+237,000
Grants, subsidies, and contributions.	12,498,000	12,901,000	+403,000
Total obligations by object.....	17,682,000	19,004,000	+1,322,000

Summary of Changes

1969 estimated obligations	$17,682,000
1970 estimated obligations	19,004,000
Total change	+1,322,000

Increases	Base Positions	Base Amount	Changes from Base Positions	Changes from Base Amount
A. Built-in				
1. Annualization of positions authorized in 1969	---	---	---	$121,000
2. Annualization of 1969 pay raise	---	---	---	4,000
B. Program				
1. Research grants	---	$8,406,000	---	561,000
2. Laboratory and clinical research	151	3,560,000	35	1,470,000
3. Review and approval of grants	23	338,000	---	11,000
4. Program direction.	20	312,000	---	9,000
Total program increases	---	---	35	2,051,000
Total increases	---	---	35	2,176,000
Decreases				
A. Program				
1. Fellowships	---	200,000	---	-6,000
2. Training grants	---	3,892,000	---	-152,000
B. Payment to "National Institutes of Health management fund" for centrally furnished services	---	974,000	---	-696,000
Total decreases	---	---	---	-854,000
Total net changes requested	---	---	35	1,322,000

Explanation of Changes

Research grants--The requested increase of $561,000 includes $45,000 to fund noncompeting renewals of regular research grants, a $16,000 increase in general research support grants, and $500,000 to initiate 2 additional environmental health sciences centers. These university-based centers provide a framework within which a broad spectrum of research can be integrated and brought to bear on problems of environmental health. These centers also furnish a locus for graduate training and provide advanced training in a depth that is available in few other places.

Laboratory and clinical research--The program increase of $1,470,000 and 35 positions would provide continued development of the National Environmental Health Sciences Center at the Research Triangle Park, North Carolina. The amount of space available at the present site will double during 1969 from 25,370 to 54,582 square feet. Late in 1970 an additional 30,000 square feet of space will be ready for occupancy. The additional space will make it possible for the Institute to purchase large equipment items which could not be accomodated in its present facilities as well as provide work space for the 35 additional laboratory personnel. The 35 positions will provide additional staff for ongoing programs in synthetic organics, natural products, pesticides, metals, and biometry and the initiation of programs in aerotoxicology.

Review and approval of grants--The increase of $11,000 will make it possible to finance the travel required for additional committee meetings, consultants, and site visits, as well as additional data processing and printing costs for analysis of grant data and information to be made available to committee members, etc.

Program direction--The requested $9,000 increase will make it possible to finance the travel required for the Director and his staff to attend working meetings and conferences at the National Institutes of Health in Bethesda, and at other institutions throughout the country.

Significant Items in House and Senate Appropriations Committee Reports

Item 1969 Senate Report	Action taken or to be taken
1. Careful investigation of the environmental factors in disease -- and, especially, of the man-made dangers to health -- has already been too long neglected. It is therefore particularly important that the work of this Division not be impeded by the lack of adequate facilities. The committee will expect to be informed at next year's hearings that the long-delayed facilities are not only available but in use. (Page 54 of Senate Report).	1. Additional interim facilities will be completed by mid 1970 which will approximately double the space available for research activities. Architect/Engineering design work should be initiated by mid 1970 for the permanent facilities.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301--Research and Investigation, In General	Indefinite
Title III, Part A--Division of Environmental Health Sciences	Indefinite

PUBLIC HEALTH SERVICE ACT

Title III, General Powers and Duties of Public Health Service, Part A, Research and Investigation. --

"Sec. 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man, including water purification, sewage treatment, and pollution of lakes and streams."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Transfer from:			
"National Cancer Institute"..	$197,000	---	To transfer funds covering expenses of research contracts pertraining to carcinogenesis of occupational environments.
Comparative transfer to:			
"Salaries and Expenses, Office of the Director, NIH".....	232,000	---	To provide funds covering expenses for the Office of the Director, NIH, which were previously funded through the NIH Management Fund.

Environmental Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$10,920,000	$9,380,000	$9,730,000	$9,380,000
1966	15,933,000	15,933,000	15,983,000	15,983,000
1967	24,312,000	24,298,000	24,298,000	24,298,000
1968	20,615,000	17,289,000	20,615,000	17,289,000
1969	18,099,000	17,541,000	18,099,000	17,820,000
1970	19,004,000			

Environmental Health Sciences

Year	Estimate to Bureau of the Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$10,993,000	$10,920,000	$9,380,000	$9,730,000	$9,380,000
1966	18,049,000	15,933,000	15,933,000	15,983,000	15,983,000
1967	26,516,000	24,312,000	24,298,000	24,298,000	24,298,000
1968	21,994,000	20,615,000	17,289,000	20,615,000	17,289,000
1969	24,165,000	18,099,000	17,541,000	18,099,000	17,820,000
1970	19,539,000	19,004,000			

Justification

ENVIRONMENTAL HEALTH SCIENCES

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	194	$1,903,000	229	$2,487,000	+35	+$584,000
Other expenses.....	---	15,779,000	---	16,517,000	---	+738,000
Total.....	194	17,682,000	229	19,004,000	+35	+1,322,000

General Statement

Introduction

In the two years since its establishment as a component of the National Institutes of Health, the National Institute of Environmental Health Sciences has established its intramural program in the Research Triangle Park, N. C. and has strengthened and broadened its support of research and training project grants of particular relevance to the mission of the Institute. The development of the Institute's programs was recognized by the Secretary of Health, Education, and Welfare on January 12, 1969 when he elevated the previously existing Division of Environmental Health Sciences to Institute status.

Purpose

The National Institute of Environmental Health Sciences was created to provide the essential basic knowledge of environmental health problems. Its mission is to discover what chemical, physical, or biological factors in the environment are likely to disturb man's well-being, to learn how these factors operate, and to provide the scientific basis for the development of adequate control measures. It is particularly concerned with the effects of agents acting in low concentrations over long periods, with the interaction of agents with another in synergistic fashion, and with the effect of variable states in man himself on the course of diseases induced by those agents.

The direct beneficiaries of the basic knowledge so developed by the Institute are the categorical programs in environmental control, particularly those encompassed by the Consumer Protection and Environmental Health Service -- such as those concerned with air pollution, radiological health, occupational health, environmental sanitation, solid waste management, and food and drugs. Close liaison is maintained with these activities, to ensure the inclusion of their requirements for supporting research in the Institute's program-planning. Man himself is the long-range beneficiary of the Institute's efforts.

Extramural Research and Training

The research and training sponsored extramurally by the Institute are directed toward quantification of hazards, elucidation of mechanisms of biological effects, and ultimate indication of possible methods for protection against hazards either through (a) establishing a need and basis for requiring removal of an agent from the environment, (b) identifying and verifying non-toxic concentrations of the agent in the environment, or (c) developing host-buffering techniques or other biologically feasible procedures for protection of the host.

Grant-supported research and training are an essential means through which the Institute helps to achieve a national focus on the mission of assessing actual and potential risks. These risks may be associated with exposure to environmental agents of all forms (chemical, physical, and biological) entering the host through all portals (skin, respiratory tract, and gastrointestinal system).

Intramural Research

The National Environmental Health Sciences Center, the intramural program of the National Institute of Environmental Health Sciences, was created for the purpose of investigating at the fundamental level the long-term and subtle effects of environmental agents potentially hazardous to man. These studies are directed to the development of a base for establishing standards and devising remedial measures. The increasing complexity of our environment makes it imperative to view the problems of environmental hazards from the vantage point of total health effects. It is this information that is necessary before an effective foundation can be constructed so as to assure protection of exposed populations. Complementing the experimental laboratory studies, the Center will engage in long-term epidemiological studies of populations with unusual environmental experiences or unique morbidity and mortality experiences.

In summary, the Center is to provide a central facility for research on the total health effects of physical, chemical, and other environmental factors to which the American people are exposed.

The function of the Center is to identify harmful agents in the environment, discover the mechanisms by which they affect an individual's health, and develop data on the effects of chronic exposure, thereby providing a scientific base upon which control measures can be developed. The seven classes of environmental agents on which research is now being carried out are natural products, metal compounds, hydrocarbon reaction products, tobacco smoke constituents, polymer dusts, pesticides, and pesticide synergists.

The narrative material which follows gives greater detail regarding both current and planned investigations for support and conduct either through grants or contracts, or in the Institute's own laboratories. The programs of the Institute are discussed here in terms of the mechanism employed for their support. However, these programs are viewed and planned in terms of a total national program with each component being complimentary to the others, and all aimed at the understanding of the hazards to health resulting from man's interaction with his environment.

The National Institute of Environmental Health Sciences is requesting a total of $19,004,000 for 1970, an increase of $1,322,000 over 1969. The increase will allow the initiation of two additional Environmental Health Sciences Centers supported by Special Research Grants. Regular Research Grants and Fellowships will be supported at about the same level. The National Environmental Health Sciences Center will be strengthened by the addition of 35 positions, allowing planned expansion of existing elements as well as initiation of further elements of the planned intramural research program of the Institute.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research projects	$4,855,000	$4,900,000	+$45,000
Special programs	3,551,000	4,067,000	+516,000
Total research grants	8,406,000	8,967,000	+561,000

Introduction

Research grant funds support activities in the environmental health field within universities, hospitals, laboratories, and other public or private nonprofit institutions. These grants will stimulate new studies in fields where further exploration seems likely to be productive. Most of the projects supported by these funds represent a continuation of ongoing research concerned with the source, mode of entry, and biological effects of noxious agents in man's environment. The projects vary in scope from cellular and subcellular studies of the mechanisms of toxicity to field investigations to identify environmental determinants of disease in man. They range in complexity from the small circumscribed activity of the individual researcher to broad-based programs that involve the integrated efforts of investigators from a variety of scientific disciplines. Knowledge derived from these projects will ultimately provide a basis for the setting of standards and the development of control activities.

Program Plans in 1969 and 1970

Grant-supported research will continue to emphasize studies aimed at determining the effects of actual and potential environmental hazards acting singly and in combination on basic biological mechanisms and vital processes; correlating the distribution and exposure levels of specific environmental factors with the occurrence of abnormalities and disorders in man; and, developing promising new concepts, instruments, and methods for improving the rapid detection, measurement, and tracing-to-source of specific deterimental environmental factors.

Support will continue for research directed toward the determination of subtle, long-range effects of environmental agents on the health of man. To achieve this goal, the Institute will continue to encourage studies of the molecular changes brought about by the interaction of toxic chemicals with biological systems and the development of unique biochemical assays which would be diagnostic of specific cellular intoxication long before any irreversible damage can be observed.

Emphasis will be placed on the initiation of projects in areas where little research is presently being conducted. The Institute will attempt to exploit opportunities in some of these areas. For example, the hazards of chemical mutagens in the environment are poorly explored. It is doubtful that current investigations could detect a genetic emergency if one resulted from exposing human populations to chemical mutagens. Epidemiological methods should be developed for the extremely difficult job of assessing mutation rate changes in humans. Hereditary traits must be identified that can serve as genetic markers to study mutagenesis in man. Assessing the genetic effects of such potential mutagens as chemosterilants and other pesticides, air and water pollutants, industrial chemicals, drugs, food additives, vaccines and contraceptives is essential. Such assessments require the development of both epidemiological and bioassay procedures.

New starts will be encouraged in comparative pharmacology and toxicology. Developing a capability to predict the toxicity of a new chemical before its introduction into man's environment is urgent. Identifying species that metabolize given chemicals similarly to man is necessary for extrapolating from experimental results to humans. Information is needed about interspecies variations in reactions to chemicals and about the physiology of such variations. Research should elucidate the metabolism of toxicants and should correlate structural with functional effects on whole animals, organs, cells, and subcellular components in various animal species.

The requested increase of $45,000 is needed to meet noncompeting requirements in FY 1970. Although there is to be no increase over the amount available in FY 1969 for competing applications, the anticipated $800,000 will fund 12 more awards in FY 1970 than in the preceding year. This change reflects a preponderance of new grants among the competing awards, as well as the fact that the average new grant will be substantially below the average for competing renewal applications.

Special Programs

The program of university-based centers helps to meet the special needs of this Institute for a concentration of effort and research skills on the more complex and challenging problems in environmental health. Because of their unusual combinations of disciplines and breadth of research specialties these centers are capable of correlating laboratory work with epidemiological studies, clinical observations with animal tests, and models with actual conditions. The exceptional opportunities for research training in university centers also receive support from these grants for trainee stipends and instructional costs. The duration of support and administrative features of these programs are helpful in attracting career scientists, permitting the development of unique integrated team capabilities that could not otherwise exist.

Each of the six operational centers for environmental health sciences is engaged in an area of specialization. Because of the interrelationship of the center programs, the ability to identify and anticipate important problems in environmental health is substantially enhanced. In coordination with the National Environmental Health Sciences Center in North Carolina, the centers constitute a resource for objective investigation of national environmental health emergencies as they arise.

Among the special areas of interest pursued by the centers are the following: environmental toxicology, biology of natural systems, respiratory diseases and aerosol physiology, environmental management, and pesticide biology.

The $500,000 increase requested for FY 1970 will encourage further development of these centers for research and training and will provide funds for establishing two new programs in such areas as food toxicology, chemical mutagenesis, and synergistic pharmacology.

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting continuations.....	73	$4,055,000	73	$4,100,000	0	+$45,000
2. Competing projects..	15	800,000	27	800,000	+12	0
3. Supplementals.....	0	0	0	0	0	0
4. Subtotal.....	88	4,855,000	100	4,900,000	+12	+45,000
5. General research support.....		551,000		567,000		+16,000
6. Environmental Health Sciences Centers..		3,000,000		3,500,000		+500,000
7. Total research grants		8,406,000		8,967,000		+561,000

Research Grants Program Analysis

Fields	1969 Estimate	1970 Estimate	Increase or Decrease
Toxicology.....	$2,136,000	$2,056,000	-$80,000
Pesticides.....	1,748,000	1,515,000	-233,000
Natural products.....	388,000	541,000	+153,000
Synthetic organics.....	204,000	206,000	+2,000
Heavy metals.....	182,000	186,000	+4,000
Smoking and health.....	100,000	250,000	+150,000
Alpha emitter.....	97,000	146,000	+49,000
Subtotal regular program	4,855,000	4,900,000	+45,000
General research support grants.....	551,000	567,000	+16,000
Environmental Health Sciences Centers.....	3,000,000	3,500,000	+500,000
Total research grants..	8,406,000	8,967,000	+561,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Fellowships.....	$200,000	$194,000	-$6,000

Introduction

The fellowship program is a highly flexible means for supporting the research training of individuals whose career development extends from the predoctoral period through the more advanced stages of scientific attainment. The program is competitive at the national level and provides opportunities for full-time study and research training for the best qualified predoctoral, postdoctoral, and advanced applicants.

Program Plans for 1969 and 1970

During 1969 the Institute inaugurated a program of Research Career Development Awards. These provide salary support over a five- to eight-year period for selected young scientists who have completed their basic research training and who have displayed outstanding aptitude for research. The awards afford an opportunity for these highly selected individuals to become established as independent investigators.

Funds requested for 1970 will provide for 18 awards, compared to 20 in 1969, a decrease of 2. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting..	10	$60,000	11	$123,000	+1	+$63,000
b. Competing.....	3	25,000	2	18,000	-1	-7,000
2. Supplementals.....	(1)	5,000	(1)	5,000	0	0
3. New awards.....	7	110,000	5	48,000	-2	-62,000
4. Total fellowships...	20	200,000	18	194,000	-2	-6,000

Fellowships (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Predoctoral.....	6	$36,000	4	$24,000	-2	-$12,000
2. Postdoctoral.....	5	32,000	5	36,000	0	+4,000
3. Special.....	4	44,000	3	26,000	-1	-18,000
4. Development awards..	4	80,000	5	100,000	+1	+20,000
5. Foreign.....	1	8,000	1	8,000	0	0
6. Total fellowships...	20	200,000	18	194,000	-2	-6,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Training grants.....	$3,892,000	$3,740,000	-$152,000

Introduction

Graduate research training grants are made to institutions to improve and to enlarge the supply of qualified scientists who can engage in research on environmental health. These grants also open competitive opportunities for institutions to strengthen their capabilities for research training in subject areas related to the mission of this Institute.

Program Plans for 1969 and 1970

The anticipated reduction in requirements for competing renewal and non-competing grants in 1970 leaves $597,000 available for the activation of eight new programs. The new grants will permit modest starts in research training in two important but neglected areas of environmental health training -- epidemiology and pathobiology. These new grants will average less per grant than those being terminated, and the net result is an increase of 4 grants although funds are reduced by $152,000.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting...	41	$3,777,000	35	$2,823,000	-6	-$954,000
b. Competing.....	2	95,000	4	300,000	+2	+205,000
2. Supplementals.....	0	0	0	0	0	0
3. New programs.....	0	0	8	597,000	+8	+597,000
4. Scientific evaluation	(1)	20,000	(1)	20,000	0	0
5. Total training grants	43	3,892,000	47	3,740,000	+4	-152,000

Training Grants (by program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Graduate.....	43	$3,872,000	47	$3,720,000	+4	-$152,000
2. Scientific evaluation	(1)	20,000	(1)	20,000	0	0
3. Total training grants	43	3,892,000	47	3,740,000	+4	-152,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	151	$1,386,000	186	$1,968,000	+35	+$582,000
Other expenses.....	---	3,046,000	---	3,354,000	---	+308,000
Total.....	151	4,432,000	186	5,322,000	+35	+890,000

Introduction

All of the intramural research units of the National Institute of Environmental Health Sciences, with the exception of the Occupational Studies Group, are located at the National Environmental Health Sciences Center in Research Triangle Park, North Carolina. The Center will serve as the focal point of a nationwide collaborative effort for research in environmental health problems.

The interdependence of disciplines and the assured scientific exchange inherent in the problem-solving approach has been a recognized need in the biological sciences. The unprecedented accomplishment in the physical sciences has been achieved in large measure through the marriage of disciplines in problem-solving teams. The use of this approach facilitates the accumulation and utilization of data from the Center's own research efforts, university-based centers, and the scientific community in general -- all of which provide complimentary information.

It is the function of the Center to identify harmful agents in the environment, discover the mechanisms by which they affect an individual's health, and develop understanding of the effects of long-term, low-level exposure, thereby providing a scientific base upon which standards can be developed and control measures established. The classes of environmental agents for which research programs are now underway are natural products, metal compounds, hydrocarbon reaction products, tobacco smoke constituents, polymer dusts, alpha radiation, pesticides, and pesticide synergists. Within each of these areas a number of agents will be selected for study based, first, on laboratory observations of adverse effects in animals exposed to a given agent, and, second, based on epidemiological studies suggesting adverse effects on human population groups exposed to those same agents in the environment.

In addition to those ongoing studies, the Institute has programs in various stages of development relating to the unique hazards associated with exposure to asbestos and beryllium. Further, there are in progress pilot feasibility studies aimed at determining the extent of environmental presence of trace metals and their natural or synthetic sources through ultimate contact with man as either consumer products or environmental pollutants. This will help us to learn whether potentially hazardous substances are increasing or decreasing in use and distribution; whether they represent general or restricted population hazards; and whether the technological trends are such as to encourage expanded research or de-emphasis.

Program Plans in 1969

Preliminary biological studies of toxins produced by fungi on fruit, vegetable, and other crops are in progress. Strains of fungi, isolated from apple and from grain, have been found to be toxic to mice and in human tissue cultures. Basic studies of the fine structure of the dividing somatic nucleus in fungi also are being conducted in an effort to identify the effects of mitotic poisons on this aspect of nuclear division.

Five cell lines have been established in tissue cultures, thus providing a selection of cell types with different morphology and growth cycle characteristics. Adequate quantities of cells can be provided from these cultures for isolation and characterization of enzymes and organelles. Cell cultures are being used for studies of cytotoxic agents, the effects of which are measured in terms of growth inhibition and morphological alterations. These cells can be used also for determining effects of cytotoxic agents on RNA, DNA, and protein synthesis.

Investigations are underway in the areas of subacute toxicology, biochemical pharmacology, and physiological pharmacology in addition to current projects in growth and development. Three lines of research have been initiated: (1) research on malformations resulting from the administration to animals of teratogenic agents; (2) testing of environmental compounds for the production of malformations either because they have been suspect or to confirm initial reports from other sources; and (3) research on interacting factors in the pharmacology and toxicology of environmental agents. At the present time, components of natural products and selected pesticides are being tested.

Analytical and synthetic chemical studies augment the functional programs of the Center by developing new and improved analytical techniques for micro qualitative and quantitative determination of many chemicals. The metabolism of the pesticidal synergist piperonyl butoxide has been elaborated in the rat. This chemical compound is in almost universal use because of its ability to enhance the effectiveness of a variety of pesticides. The research has shown that significant amounts of piperonyl butoxide can adversely affect the normal functions of cells throughout the body. This finding as well as the earlier observations of the prolonged biliary and urinary excretion of the pesticide reemphasizes the potential hazard of exposure of man to this material.

Present pathologic and physiology studies are concerned with the effect of environmental toxicants on the structure and function of the body's tissue and organs. Studies are being initiated at the intact host, organ, cellular, and subcellular levels. One area of current research is a study of the possible role of contaminants in the atmosphere and food in the causation of pulmonary edema. Two of these under investigation are ozone, a major constituent of "smog", and piperonyl butoxide. Also in progress is an extensive evaluation of the response of the nucleolus to a variety of carcinogenic environmental agents, drugs, and specific toxins. The nucleolus is the structure within the cell nucleus implicated in the elaboration of ribosomal RNA which controls protein synthesis. One potential benefit from studying such nucleolar changes is their possible predictive value for early toxicologic evaluation of environmental chemicals. Histopathologic evaluation has been extended from classical light microscopic techniques to interpretation on the ultrastructural level through the use of electron microscopy.

The Center provides, maintains, and monitors all animals used in its research programs. Hematologic, serologic, and microbiological monitoring is provided on an ongoing basis. A developmental program has been undertaken to provide a "closed" colony source of small marsupials (Marmosa mitis). A thorough study is being made of their behaviour, reproduction, physiologic processes, and adaptability to environmental research.

The objectives of the Occupational Studies Unit (located in Bethesda, Maryland) are to characterize disease states resulting from exposure in the occupational environment and to evaluate interrelationships among host and environmental factors necessary for an understanding of disease causation. In contrast with many studies of the occupational environment, the emphasis in this program is placed on the identification of disease states that appear many years after exposure to causative agents. Due to the frequent lack of medical histories and records of illness occurring over long periods of time, studies initiated by the

Unit are frequently limited to an analysis of mortality data. In several of our studies, however, arrangements have been made to collect medical histories over shorter periods of time in the hope of identifying early disease and precursor states. The activities of the Unit can be catagorized into five broad areas: (1) identification of problem areas, (2) establishment of industry contacts, (3) selection of populations for study, (4) collection of occupational histories and tracing of the study populations, (5) analysis of data and development of mathematical models. Major activities, at present, center around the studies of uranium miners, steelworkers, and cutting-oil workers. The studies of uranium miners are carried out as part of a collaborative effort with the Consumer Protection and Environmental Health Service. Two reports on the mortality experience of uranium miners with special reference to smoking are being published and a special report on uranium-miner mortality was prepared for the Federal Radiation Council. The first of a series of papers on steelworker mortality is in press. Records on men exposed to cutting oils continue to be collected and the first phase of the mortality analysis will soon be completed.

Support on the statistical design and analysis of experiments for all division personnel engaged in laboratory and human population studies is provided. The purpose of this support is to insure more definitive results from multi-factor animal and human studies through the use of the effective collection and analysis of data. Based on the theory and techniques of mathematical and analytical statistics and experimental design, this is accomplished by independent and cooperative research studies on the biological effects of environmental agents and their interactions with each other. The biometry program has been initiated only recently. The program will be expanded throughout the Institute in the application of statistical techniques to the design and analysis of experimental studies in environmental health.

The intramural research program is supplemented by collaborative research contracts that assist the Institute in fulfilling its mission. At this time, contract-supported research includes investigations on the effects of heavy metals -- lead, in particular -- on the biochemical functions of the brain, liver, and kidney; the interaction of pesticides and other organic chemicals with cell membranes; the production of mycotoxins by fungi that grow naturally on tobacco; the extent of man's exposure to specific toxic metals; and the health hazards to which uranium miners are exposed.

The scientific information program provides scientific liaison with categorical environmental health programs to maintain mutual awareness of relevant scientific and technical activities. A system for quick retrieval of information on scientific topics relevant to the Institute's programs is being developed and a limited library facility in the Center now contains some 150 periodicals and 1,000 books and reference volumes. Recently initiated has been a personal user service to intramural scientists, by which incoming items are brought to the attention of research personnel, searches are facilitated, and external sources of scientific information tapped as required.

Program Plans in 1970

The cell biology programs will be expanded to include other toxicants of importance which are not being investigated. Studies on mutagenic effects will be emphasized. Attempts will be made to determine the reactivity of organic and organometallic compounds toward the nuclear genome of mammalian cells in tissue culture and toward isolated DNA from mammalian tissue. The agents selected will be among groups used as insecticides, herbicides, drugs, antibiotics, food additives, and various types of industrial chemicals.

As resources become available, additional programs related to subacute toxicology, biochemical pharmacology and physiological pharmacology will be initiated. Present studies on growth and development will be expanded to

include studies of the potentially harmful effects of environmental chemicals on prenatal growth, the ability of such chemicals to enter the fetus through the placenta, and postnatal effects of prenatally administered chemicals.

Chemistry, cell biology, pathology, and pharmacology scientists will collaborate on the development of a biological model system to relate the chemical structure of environmental agents to their ability to interact to various types of DNA and RNA in both cells grown in tissue culture and cells in the intact host. Chemical studies will include; (1) the mechanism of deposition and metabolism of dietary hydrocarbon in the presence of pesticides and other environmental chemicals in the rat, (2) intermediary metabolism of the main constituents of essential oils of parsley, celery, nutmeg, and other dietary components, (3) aspects of the inhibition and reactivation of enzymes concerned with detoxification by environmental agents including pesticide synergists in various tissues, and (4) studies to permit the characterization of enzyme inhibition resulting from various environmental agents.

Work being initiated in pathologic physiology includes a study of the effect, individual and combined, of a variety of environmental agents. Initially, experiments are planned with trace metals, inhibitors of cholesterol biosynthesis, and several organic phosphate and carbamate pesticides. These studies will emphasize changes in central nervous system irritability, neural and endocrine tissue structure and lipid metabolism. The carcinogenic potential of selected organic phosphate and carbamate compounds will also be evaluated. The principal animal model for these experiments will be the rat and the newborn opossum, a mammal which at birth is approximately equivalent in development to the eight week old human fetus.

Studies initiated in 1968 and concluded in 1969 will provide fresh green vegetables free of environmental contaminants such as organic pesticide residues or microbiological organisms from wild life infestations. By 1970 this program will have progressed so that it will serve as a significant resource in the feeding, husbandry, and care of animals used in Center programs.

During the early half of 1970, it will be necessary to start a large scale animal technician recruiting and training program to provide personnel for the new animal building. It is estimated that the recruiting and training process for sufficient personnel to staff this building will take approximately six to nine months.

The Center's program and engineering staff will continue to provide consultative assistance and information to the Division of Research Services, NIH and DHEW's master site planners for the permanent facilities. Architect/Engineering design work should be initiated by mid 1970. Additional interim facilities will be completed also by mid 1970 which will approximately double the space available for research activities.

A program in the development of specialized scientific instrumentation for environmental research will be initiated late in 1969 and be in full operation in 1970.

The program increase of $1,470,000 and 35 positions would permit the modest planned expansion of most of the ongoing intramural research programs and the initiation of sections within the Cell Biology, Pharmacology and Toxicology, and Pathologic Physiology Branches that were previously planned but not yet activated. The demography area would be expanded with the addition of an Epidemiologic Pathology Branch and the Biometry Branch, initiated at the beginning of 1969 with a staff of two, would be further developed. An increase of $123,000 is requested for annualization of positions new in 1969 and annualization of the 1969 pay increase. There is an offsetting decrease of $703,000 for centrally furnished services financed through the NIH Management Fund.

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	23	$260,000	23	$261,000	---	+$1,000
Other expenses.....	---	180,000	---	182,000	---	+2,000
Total.....	23	440,000	23	443,000	---	+3,000

Introduction

This activity, under the Associate Director for Extramural Research, supports the scientific, administrative, and clerical staffs responsible for the over-all coordination and administration of the Institute's grants program.

Functions for which the staffs are responsible include review and evaluation of fellowships, research and training grant applications for presentation to the Advisory Council; liaison with applicants, grantees, advisory bodies, other components of NIH and PHS, and other interested organizations; maintenance of a continuing review of ongoing research and training programs; and the compilation and reporting of scientific and fiscal information relevant to all transactions.

The net increase of $3,000 requested for this activity includes a program increase of $11,000 to make possible the travel required for additional committee meetings, consultants, and site visits, as well as additional data processing and printing costs for analysis of grant data and information to be made available to committee members or others and a mandatory increase of $1,000 for annualization of the 1969 pay increase offset by a decrease of $9,000 in the cost of centrally furnished services financed through the NIH Management Fund.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	20	$257,000	20	$260,000	---	+$3,000
Other expenses	---	55,000	---	78,000	---	+23,000
Total	20	312,000	20	338,000	---	+26,000

Introduction

This activity supports the Office of the Director, including the administrative, secretarial, and clerical staffs required for the administration, technical direction and coordination of all institute activities; the review of current and proposed programs; the introduction of new knowledge into currently operating programs; and the provision and supervision of centralized administrative services.

Administrative personnel are also concerned with the areas of finance, supply, travel, space utilization, personnel, and management analysis.

The increase of $26,000 requested for this activity includes a program increase of $9,000 to make possible the travel required for the Director and his staff to attend working meetings and conferences at the National Institutes of Health in Bethesda, and at other institutions throughout the country, a mandatory increase of $1,000 for annualization of 1969 pay increases and an amount of $16,000 for the increased cost of centrally furnished services financed through the NIH Management Fund.

New Positions Requested

Fiscal Year 1970

		Grade	Annual Salary
Laboratory and Clinical Research			
(1)	Associate Director of Office	GS-16	$22,835
(1)	Scientist	GS-16	22,835
(1)	Chief of Branch	GS-15	19,780
(2)	Medical Officer	GS-15	39,650
(2)	Scientist	GS-15	39,650
(3)	Medical Officer	GS-14	50,838
(2)	Scientist	GS-14	33,892
(4)	Scientist	GS-13	57,636
(7)	Scientist	GS-12	85,218
(1)	Scientist	GS-11	10,203
(3)	Research Assistant	GS-9	25,386
(2)	Laboratory Assistant	GS-3	9,200
(4)	Animal Caretaker	GS-2	16,924
(2)	Animal Caretaker	GS-1	7,778
	Total new positions	(35)	441,825

WEDNESDAY, APRIL 2, 1969.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

WITNESSES

DR. GERALD D. LaVECK, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
CALVIN B. BALDWIN, JR., EXECUTIVE OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
EARL M. HUBSCHER, BUDGET OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	3,553	3,967	4,442
Positions other than permanent	70	79	89
Other personnel compensation	92	104	117
Total personnel compensation	3,715	4,150	4,648
Personnel benefits: Civilian employees	395	479	532
Travel and transportation of persons	164	179	193
Transportation of things	30	46	52
Rent, communications, and utilities	154	165	180
Printing and reproduction	96	95	107
Other services	5,108	8,818	11,599
Supplies and materials	307	342	385
Equipment	751	642	503
Grants, subsidies, and contributions	55,659	55,884	60,212
Total obligations	66,379	70,800	78,411

PERSONNEL SUMMARY

Total number of permanent positions	478	409	475
Full-time equivalent of other positions	12	16	16
Average number of all employees	368	423	456
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	36,474	41,679	46,564
(b) Fellowships	2,953	4,193	4,027
(c) Training	7,272	10,012	9,621
Total grants	46,699	55,884	60,212
2. Direct operations:			
(a) Laboratory and clinical research	5,754	6,065	6,373
(b) Collaborative research and development	1,299	3,975	6,721
(c) Biometry, epidemiology, and field studies	481	2,022	2,176
(d) Training activities	89	89	85
(e) Review and approval of grants	1,829	1,956	2,037
(f) Program direction	676	809	807
Total direct operations	10,128	14,916	18,199
Total program costs funded [1]	56,827	70,800	78,411
Change in selected resources [2]	9,552		
Total obligations	66,379	70,800	78,411
Financing:			
Comparative transfers to other accounts	445	536	
Unobligated balance lapsing	1,797	1,791	
Budget authority (appropriation)	68,621	73,127	78,411
Relation of obligations to outlays:			
Obligations incurred, net	66,824	71,336	78,411
Obligated balance, start of year	42,155	41,920	54,116
Obligated balance, end of year	−41,920	−54,116	−61,232
Adjustments in expired accounts	−1,298		
Outlays	65,761	59,140	71,295

[1] Includes capital outlay as follows: 1968, $1,028,000: 1969, $642,000; 1970, $503,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $3,934,000; $13,486,000; 1969, $13,486,000; 1970, $13,486,000.

Mr. FLOOD. Now we will take up the National Institute of Child Health and Human Development. We have with us Dr. Gerald D. LaVeck, the Director. How long have you been on board as Director, Doctor?

Dr. LAVECK. Approximately two and a half years.

Mr. FLOOD. We will place your biographical sketch in the record for others who may not know you as well as we do.

(The biographical sketch follows:)

BIOGRAPHICAL SKETCH OF GERALD D. LAVECK, M.D.

Date and place of birth: April 19, 1927, Seattle, Wash.
Marital status: Married, three children.
Present Position and Title: Director, National Institute of Child Health and Human Development.
Education:
1948—B.S., University of Washington.
1951—M.D., University of Washington.
Licensure: Washington, 1952, California, 1957, Maryland, 1965.
Positions held.
1951–1952: Intern, rotating, Vancouver General Hospital, Vancouver, British Columbia.
1952–1953: Resident, Public Health, Seattle King County Department of Public Health.

1953–1955: Senior Assistant Surgeon, U.S. Public Health Service, Epidemic Intelligence Service, Communicable Disease Center, Atlanta, Ga.
1955–1956: Assistant resident, pediatrics, Child Health Center and King County (Wash.) Hospital.
1956–1957: Resident, pediatrics, Children's Orthopedic Hospital, Seattle.
1957–1958: Instructor in pediatrics and fellow in mental retardation, University of Washington School of Medicine, Department of Pediatrics, Neurology and Neuropathology.
1958–1961: Medical director, Rainier School, Buckley, Washington.
1958–1960: Instructor in pediatrics, University of Washington School of Medicine.
1960–1963: Clinical assistant professor of pediatrics, University of Washington School of Medicine.
1963: Clinical associate professor of pediatrics, University of Washington School of Medicine.
1961–1962: Clinical director, Rainier School, Buckley, Washington.
1962–1963: Head, crippled children's service, Washington State Department of Health.
1963–1966: Director, mental retardation program, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Md.
1965–1967: Clinical associate professor in pediatrics, Georgetown University School of Medicine, Washington, D.C.
1966–1967: Acting scientific director, National Institute of Child Health and Human Development.
1966–present: Director, National Institute of Child Health and Human Development.
1967–present: Clinical professor of pediatrics, Georgetown University School of Medicine.

Committee Memberships:
Secretary's Committee on Mental Retardation, U.S. Department of Health, Education, and Welfare 1963–68.
Board of trustees, Rehabilitation Council, Health and Welfare Council, Washington, D.C.
National Institutes of Health Staff Group on Mental Retardation (chairman) 1963–67.
Population Crisis Committee, Washington, D.C.
Federal Panel on Early Childhood.

Professional society memberships:
Diplomate, American Board of Pediatrics.
Fellow, American Academy of Pediatrics.
Fellow, American Public Health Association.
Thurston County (Washington) Medical Society.
Washington State Medical Association.
American Medical Association.
American Association on Mental Deficiency.
American Association for the Advancement of Science.

Awards: Superior Service Award, U.S. Department of Health, Education, and Welfare, April 11, 1966.

Research interests: Genetic, endocrinologic, and clinical aspects of mental retardation; handicapped children; epidemiology of chronic disabilities and infectious diseases; and electroencephalography.

Mr. Flood. I see you have a statement. How would you like to proceed?

Dr. LaVeck. I would like to read the statement.

Mr. Flood. Very well, you may do that.

General Statement

Dr. La Veck. Mr. Chairman and members of the committee, the National Institute of Child Health and Human Development was created and has developed during the 1960's. Our mandate is broad—to unravel the mysteries of human development from the moment of

conception until the end of life. Through knowledge gained by Institute-supported research, fewer infants will die. The number of defects and deficiencies—both biological and behavioral—in our population will decrease. Progress will be made in the control of fertility and the problems associated with aging.

The consequences of the Institute's efforts will be optimal development for many who, without these efforts, would not develop their full potential.

POPULATION RESEARCH

In 1968, a Center for Population Research was established within the Institute. Under its charter, the Center directs, coordinates, and conducts a national program of research and training in the population area. Specific responsibilites include the following: The study of contraceptives; investigation of the social, psychological, and demographic aspects of family planning; and the study of the causes and treatment of sterility.

EFFECTS OF ORAL CONTRACEPTIVES

Studies in Great Britain indicate that the incidence of thromboembolic disease (clotting and blockage of blood vessels) in women is increased for those who use oral contraceptives. In particular, the risk of death from pulmonary embolism or cerebral thrombosis is estimated to be seven to eight times higher in such women. This finding has been validated through a statistical study of mortality rates conducted by an Institute scientist.

This and other possible medical effects of the use of oral contraceptives are being explored by the Institute through contracts. These studies are of a prospective nature, following many women over a period of years.

Mr. FLOOD. Have you heard that the British feel that their own figures on adverse side effects are underestimated by 40 to 50 percent?

Dr. LAVECK. I have not heard that statement, Mr. Chairman. They feel quite comfortable with the data that have been collected, as far as I know.

Mr. FLOOD. But if they were uncomfortable by 40 or 50 percent, that would be rather startling, would it not?

Dr. LAVECK. It would be.

A group of investigators are monitoring the effect of oral contraceptives on metabolic processes, weight, blood chemistry, changes in the breast, and psychological changes. Another group in Los Angeles is primarily concerned with discovering whether use of oral contraceptives increases the incidence of cancer of the cervix, while an investigator in London is investigating the effects of oral contraceptives on carbohydrate and lipid metabolism.

Mr. FLOOD. I was wondering if this thing is as dangerous as it potentially could be, why are we sitting back waiting for the British to tell us all about it?

Dr. LAVECK. I think the history of support for studies on the medical effects of oral contraceptives would be of interest. In 1967 Congress provided our Institute with a million dollars to carry out such studies. At about the same time the FDA received funds to look at the safety of

oral contraceptives. In our Institute as well as in the FDA such studies are underway and the FDA and our Institute coordinate activities to prevent duplication.

The British started somewhat earlier than we did.

Mr. FLOOD. Are you about to produce a report?

Dr. LAVECK. We will be in a position shortly.

Mr. FLOOD. Shortly?

Dr. LAVECK. Within 2 years we will know if the oral contraceptives have an adverse influence on cancer of the cervix. We are supporting a study, which is now in its 3d year, designed to answer that question. We will also be in a position to comment on any effects that the pill may have on chromosome abnormalities, carbohydrate and lipid metabolism, and psychological changes. It seems unlikely that we will be able to determine the relation between the pill and cancer of the breast in the near future. It may take as long as 10 years before that particular question is answered.

In regard to thromboembolic disease, we have completed a study which supports the findings in the British study. The FDA is currently supporting a retrospective study in this country which may further clarify this relationship.

Mr. FLOOD. Are you examining whether it might cause cancer?

Dr. LAVECK. Yes.

Mr. FLOOD. Arteriosclerosis?

Dr. LAVECK. We are interested in a number of adverse effects that might occur including abnormalities in lipid metabolism and their relation to arteriosclerosis. Cancer, thromboembolic disease, and effects on progeny are being investigated.

Mr. FLOOD. Does the hair fall out?

Dr. LAVECK. This is reported as an occasional side effect, that is correct.

Mr. FLOOD. You do not seem to be in much of a hurry.

Dr. LAVECK. I think it is important to recognize that to do these kinds of studies one needs a large population.

Mr. FLOOD. Don't you have that?

Dr. LAVECK. In one of the studies that we are supporting in California, 12,000 women will be followed for a number of years. We need a large population that we can follow prospectively. One cannot simply go back to records and derive data retrospectively to answer some of these questions.

Mr. FLOOD. How long has the pill been on the market?

Dr. LAVECK. Since 1960.

Other Institute studies are exploring the effects of the use of intrauterine devices (IUD's) as contraceptive agents. So far, research has indicated that the IUD's function in a specific and local manner, though investigators have not been able to discover the basic mechanism of action in humans.

What do these findings mean? First, they mean that additional long-term work needs to be done to fully elucidate what oral contraceptives do to women and their progeny. Second, they mean that we do not yet have an ideal contraceptive—one that is safe, effective, reversible, and acceptable to all population groups.

These findings do not mean that women should not be using these contraceptives.

Mr. FLOOD. How many women are using them in the United States?

Dr. LAVECK. In this country approximately 8 million women are using oral contraceptives.

Mr. FLOOD. Is that a lot?

Dr. LAVECK. This is the most common contraceptive used by women at this time.

Mr. FLOOD. That does not answer my question. Is that a lot?

Dr. LAVECK. That represents about 20 percent of women in the reproductive age group.

Mr. FLOOD. Is that a lot?

Dr. LAVECK. That is a lot, yes, sir.

Mr. FLOOD. The Food and Drug people ordered a relabeling because of potential danger.

Dr. LAVECK. That is right; they did.

The relabeling to which you refer was done primarily to draw to the attention of physicians the risk from thromboembolic disease. The package insert lists, in addition, many other adverse effects that can occur. For certain women and populations, the oral contraceptives and the intrauterine devices are the best forms of contraception available. The preliminary findings of these studies do indicate the need for the development of new contraceptives—and this the Institute is planning to do with an expanded contract program.

The Center for Population Research, working with its Advisory Committee, has identified topics in contraceptive development and the social sciences which will make most effective use of its funds. Examples of potential breakthroughs in contraceptive technology include studies of the maturation and fertilizing capacity of spermatozoa. The goal of this inquiry is the development of modern contraceptives which alter normal sperm development in the male reproduction tract, or in the uterus of the female. Also, investigations of corpus luteum function are promising. The corpus luteum is a hormone-producing structure which forms on the ovary shortly after fertilization and is essential to the continuation of the reproductive process. There are now leads to several means of interrupting the function of the corpus luteum through the use of drugs. This approach is particularly attractive, since it would require a woman to take a pill only once a month, at the time of her expected period.

ADVERSE REACTIONS ASSOCIATED WITH USE OF ORAL CONTRACEPTIVES

Mr. FLOOD. Do you have a report of the number, in the United States, of what you would call serious reactions from this pill, including fatalities?

Dr. LAVECK. We do not have such a listing.

Mr. FLOOD. You do not?

Dr. LAVECK. The FDA does.

Mr. FLOOD. I suppose I should have asked them, but they are gone and you are here. Will you borrow it from them?

Dr. LAVECK. We would be happy to get a listing.

Mr. FLOOD. I would like to get a list of what you or they would call serious reactions including fatalities, in the last 2 years.

Dr. LAVECK. We can do this, Mr. Chairman, but I would like to caution you that physicians are asked to report adverse reactions that occur in women taking the pill but there may not be a cause-effect relationship.

Mr. FLOOD. They are?

Dr. LAVECK. Yes.

Mr. FLOOD. I thought only the producer was asked to do that.

Dr. LAVECK. No.

Mr. FLOOD. Are you sure of that?

Mr. CARDWELL. Both physicians and the manufacturer.

Dr. LAVECK. If a woman dies at a time when she is taking the pill it need not mean that her death is caused by the pill. So the information may not be very helpful to you.

Mr. FLOOD. That may or may not be so.

I understand there have been reports from either the producer or the doctor or both attributing deaths directly to the pill.

Dr. LAVECK. We are certain, because of the studies done in Great Britain, that women who use oral contraceptives have greater mortality and morbidity rates from thromboembolic disorders than nonusers.

Mr. FLOOD. Because of studies done in Great Britain.

Dr. LAVECK. Yes.

Mr. FLOOD. I am talking about you. I am very glad the British are doing this because this is a great help, but what about you?

Dr. LAVECK. We also validated these findings which show that women on the pill run a sevenfold increase of dying from thromboembolic disease as compared to nonusers. This means that approximately three women out of every 100,000 on the pill run the risk of dying from a clotting disorder. The risk is not great but it is measurable.

Mr. FLOOD. Do the women who take this thing have the faintest idea of what we are talking about?

Dr. LAVECK. I think it is extremely important that physicians inform women receiving this drug of the adverse effects that can occur and the risks that are involved. Admittedly it is a small risk. It does not approach the risk of pregnancy itself, but it is a risk. I feel that women must be aware of possible harmful effects and inform their physicians when adverse reactions occur.

Mr. FLOOD. You probably will have to get these figures from the Food and Drug people, too, but at the same point we were going to insert the figures on serious fallout, including fatalities, will you also include the figure for the same period of time showing the increase in deaths of women between the age of 20 and 40 as a result of clotting?

Dr. LAVECK. We can supply this from our own data, I believe, but we will work with the FDA to see if we can develop information for the committee.

(The information follows:)

SERIOUS REACTIONS FROM ORAL CONTRACEPTIVES

A. ANALYSIS OF MORTALITY TRENDS

The discussion[1] of a potential increase in risk of mortality from thromboembolic disorders has centered primarily on the causes included in the Seventh

[1] Vessey, M. P., and Weatherall, J. A. C., "Venous Thomboembolic Disease and the Use of Oral Contraceptives." "A Review of Mortality Statistics in England and Wales." Lancet II: 94–95 (July 13), 1968.

Markush, Robert E., and Seigel, Daniel G., "Oral Contraceptives and Mortality Trends From Thromboembolism in the United States." A.J.P.H. 59: 418—434 (March), 1969.

Revision of the "International Classification of Diseases Catagories" (ICD) 460–468, "Diseases of Veins and Other Diseases of Circulatory System." This includes ICD Category 465, Pulmonary Embolism and Infarction.

Table 1 presents the rates for ICD 460–468, for the years 1956–57, for the age group 20–44, for all women, and for white and nonwhite women separately. Also included are rates for men in the same years. The rates for women in recent years appear to be increasing more rapidly than in the years prior to the marketing of the oral contraceptive in 1961. This can be more easily noted from table 2, which presents the average annual increase in these rates from men and women in the time periods 1956–1961 and 1962–1967. For both whites and nonwhites there has been a marked gain in the average annual increase in mortality from these causes.

TABLE 1.—U.S. DEATH RATES PER 100,000 POPULATION, AGE 20-44[1] FOR CAUSES IN THE INTERNATIONAL CLASSIFICATION OF DISEASE CATEGORIES "DISEASES OF VEINS AND OTHER DISEASES OF CIRCULATORY SYSTEM"

	1956	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967
All women	0.96	0.99	1.13	1.05	1.19	1.04	1.32	1.42	1.59	1.82	2.14	2.16
White women	.77	.75	.88	.77	.91	.76	1.04	1.14	1.17	1.45	1.66	1.66
Nonwhite women	2.34	2.76	2.98	3.06	3.23	3.05	3.38	3.43	4.64	4.53	5.66	5.82
All men	.88	.91	.94	1.02	1.02	1.00	1.14	1.23	1.31	1.35	1.42	1.43
White men	.74	.75	.81	.89	.85	.80	.98	1.01	1.06	1.07	1.15	1.12
Nonwhite men	2.00	2.20	2.00	2.03	2.43	2.61	2.38	3.04	3.33	3.56	3.60	3.90

[1] All rates are age adjusted by the direct method to the population of 1967.

TABLE 2.—AVERAGE ANNUAL INCREASE IN MORTALITY PER 100,000 FOR MEN AND WOMEN IN THE YEARS 1956–61 AND 1962–67

	1956–61	1962–67
All women	0.026	0.189
White women	.010	.141
Nonwhite women	.143	.537
All men	.029	.059
White men	.019	.032
Nonwhite men	.106	.273

B. REPORTS TO FOOD AND DRUG ADMINISTRATION

The following tables indicate the number of fatal and serious nonfatal reports to the Food and Drug Administration in the period January 1, 1966, to December 31, 1968. In using these data it should be kept in mind that:

(*a*) The list is undoubtedly incomplete.

(*b*) Many of the reports provide only minimal medical information.

(*c*) It is very difficult to demonstrate that untoward medical events in women using oral contraceptives result from the drug use.

SUMMATION OF FATAL AND SERIOUS, NONFATAL REPORTS RECEIVED FROM JAN. 1, 1966, TO DEC. 31, 1968

	Number of reports	Fatal	Nonfatal
Source:			
Manufacturers	754	83	671
Physicians[1]	154	22	132
Consumers or clinics	12	0	12
FDA district offices	17	6	11
FDA hospital reporting program	83	5	78
Other hospitals	14	2	12
Total	1,034	118	916

[1] Some of these reports attributed to physicians may have come through the firm.

Summation of fatal and serious, nonfatal reports received from January 1, 1966 to December 31, 1968

	Deaths
I. Thromboembolic	87
II. Other Causes	26
III. Unknown Causes	5
TOTAL	118

Distribution of non-fatal events reported in association with the use of oral contraceptives by diagnosis

	Deaths
I. Thromboembolic	466
II. Carinoma	52
III. Hepatitis or Jaundice	38
IV. Pregnancy Associated with congenital Anomalies in Offspring	26
V. Other *	334
TOTAL	916

*Reports of miscellaneous nature or in which there is not enough information to make a definite diagnosis.

MENTAL RETARDATION RESEARCH CENTERS

Dr. LaVeck. Research and research training in mental retardation and related aspects of human development present unique demands in terms of facilities and resources. Recognition of these needs led, in 1963, to legislation authorizing construction grants for facilities in which biological, medical, and behavioral research relating to mental retardation could be conducted. The Institute, which is charged with supporting a major portion of the center's research and research training, expects that the research will assist in finding the causes of and the means of preventing mental retardation, and ways of ameliorating its effects.

Four of the 12 mental retardation construction grant projects have progressed to the point that the centers are functional.

Mr. Flood. Where are they located?

Dr. LaVeck. The four centers that have opened are at the Children's Hospital in Cincinnati, University of Colorado, the George Peabody College for Teachers in Tennessee, and the University of Chicago. The University of Washington now has occupied their new buildings, but they have not had a formal dedication as yet.

Mr. Flood. Why were these centers located there?

Dr. LaVeck. The location of the centers was determined not on geographic spread but on the ability of the particular university to mount a strong program of research in mental retardation. It just so happened that we achieved a good geographic distribution, with centers scattered throughout most of the United States, with the exception of the Southwest.

Mr. Flood. This is not a geographic problem, is it?

Dr. LaVeck. It is not, that is correct.

Mr. Shriver. May I inquire?

Last year funds were included for the University of Kansas.

Dr. LaVeck. Yes, sir.

Mr. Shriver. What has happened to the funds?

Dr. LaVeck. The University of Kansas was slated to open two of their three new facilities during the present fiscal year, 1969. How-

ever, there has been some delay, apparently, in the construction plan and it now appears that they will open after July of 1969.

Mr. FLOOD. Who is responsible for the delay?

Dr. LAVECK. I am unable to say. I can say that with most of our construction programs unforeseen events occur that tend to delay the completion.

Mr. FLOOD. Will you find out for Mr. Shriver where the delay is? Is it in Kansas or is it here?

Dr. LAVECK. Yes, I will be happy to do this.

Mr. SHRIVER. Thank you, Mr. Chairman.

Dr. LAVECK. I might add, Mr. Shriver, that the activities of that center are going on right now even though the buildings are not available, and Dr. Richard Schiefelbush has been conducting research and training in the field.

Mr. FLOOD. Mr. Shriver is interested in the money for bricks and mortar.

Dr. LAVECK. They have the money.

Mr. FLOOD. Is it a planning problem?

Dr. LAVECK. The delays generally occur because of construction problems.

Mr. FLOOD. Look into this and see if you can pin it down a little better.

Dr. LAVECK. We will supply this for the record.

(The information follows:)

KANSAS MENTAL RETARDATION RESEARCH CENTER

The Mental Retardation Research Center at the University of Kansas is administratively one center but has three units which are geographically separated. Each of these units has its own construction schedule independent of the construction of the other units.

Original estimates of completion dates for these three units were as follows:

Lawrence: The middle of fiscal year 1969.

Parsons: Early in fiscal year 1970.

Kansas City: Approximately 18 months after signing of construction contract.

Construction at the Lawrence unit has progressed to the point where interior finishing is now being done. It appears that completion will be within several months of the original target date. The minor delays experienced thus far have been due to construction lags at Lawrence.

The Parsons unit is a cooperative arrangement between the University of Kansas and the State department of social welfare. Construction at Parsons although close to the original schedule has experienced minor delays due to changes in plans at Parsons. Completion is expected during fiscal year 1970.

The Division of Research Facilities and Resources at NIH authorized the advertising of bids for the Kansas City unit as of January 2, 1969. Completion of this unit is called for within approximately 18 months of the signing of the construction contract. Delays in construction of this unit are the result of major changes in program development and planning at the medical center in Kansas City. Subsequent to the construction award of the Kansas City unit, the university made application to the Division of Mental Retardation in the social and Rehabilitation Service for a university-affiliated facility construction grant award. The university plans to integrate the actual construction of the university-affiliated facility with the Mental Retardation Research Center.

Dr. LEVECK. Three more centers are scheduled for opening in fiscal year 1969, four in fiscal year 1970, and all 12 will be operational by fiscal year 1971.

While the biological problems which surround the newborn cause the loss of many human lives annually, the problems of psychosocial

deprivation prevalent in our society contribute heavily to the poor health and subnormal functioning experience of many.

The concentration of three-fourths of those who are mentally retarded in groups disadvantaged by poverty and limited life circumstances places retardation associated with deprivation among our highest priorities.

The planning and construction of the Mental Retardation Research Centers has led to fresh approaches to the problems of mental retardation and psychosocial deprivation.

Mr. FLOOD. Is this retardation acquired by inheritance, or is it acquired because of environmental conditions, or both?

Dr. LAVECK. Both.

I think we have to recognize that heredity plays a role here as well as environmental factors. The North Carolina center is planning a unique research oriented day care center for culturally deprived children. At the University of Kansas, the problem of cultural deprivation has been approached in another novel way. The principal investigator, with Institute support, has developed a program of preschool education, remedial training, and parental guidance at Juniper Gardens, a public housing project. Using positive reinforcement—praise and approval—as a primary tool, the investigators have sought instructional programs for teaching basic educational and social skills to these children. In addition, parents have been taught to use positive rather than negative reinforcement in training their children.

Mr. FLOOD. Positive instead of negative reinforcement?

Dr. LAVECK. This simply means that children are rewarded by praise for carrying out an accomplishment rather than exerting discipline or punishment when they fail to accomplish a given goal.

INTRAMURAL RESEARCH

In 1968, the Gerontology Research Center in Baltimore was dedicated. This is the world's largest and most comprehensive research center for studying aging. In the Center, intramural scientists are pursuing varied and sophisticated programs and are joined by scientists from all over the world who may work there in laboratories identified for collaborative research.

The accomplishments, this year, of the scientists in the Center have been significant. Specific changes in learning capacity with aging have been identified which indicate that older individuals are unduly confused by irrelevant information. Studies on RNA obtained from aged animals support the concept that errors in the synthetic machinery may be the key biological phenomenon in aging.

Mr. Chairman, we do not know why cells die or age. One of the theories concerns RNA.

Mr. FLOOD. Don't all cells reproduce?

Dr. LAVECK. Cells are replaced, but with aging there tends to be a loss in number of certain types of cells.

Mr. FLOOD. It is not peculiar that any thing loses its reproductive faculties with age. Is that surprising?

Dr. LAVECK. It has been demonstrated that when we grow cells in tissue culture, they do not divide forever. They do not continue to reproduce indefinitely. There is a finite limit at which time reproduc-

tion of the cell ceases. Apparently there is loss of cells without adequate replacement of cells during the aging process. One of the possible explanations is a defect in DNA or RNA. That is the point I am making in this statement.

A novel enzymatic pathway for active transfer of glucose across cellular membranes has been discovered by Center scientists. This finding is a possible explanation for the mechanism of glucose resorption into the body.

The special mission of the Institute, relating to maternal and child health, perinatal biology, reproductive biology, and family planning, is receiving special emphasis in programs currently in progress and to be activated in patient facilities and laboratories in the Clinical Center at the NIH. Scientists have identified, documented, and studied the first human example of complete absence of an autosomal chromosome, a unique and important accomplishment.

Previously, absence of an autosomal chromosome was thought to be incompatible with life. A comprehensive study of the electrical characteristics of the fetal heart and brain has demonstrated the sensitivity and usefulness of this method for evaluating fetal distress. A study of alterations in estrogen excretion of subhuman primates has led to the discovery that the peak of estrone excretion is closely related to the predicted time of ovulation by timed observations of the ovaries.

SUMMARY

Mr. Chairman, the Institute's work on population research, mental retardation, infant mortality, growth and development, and aging will provide answers to some of the pressing health and social problems of our time.

ARTIFICIAL INSEMINATION

Mr. FLOOD. You say nothing about artificial insemination at all. Is that in your shop?

Dr. LAVECK. As far as I know we have not been involved in any way in studies of artificial insemination in humans.

Mr. FLOOD. Who is?

Dr. LAVECK. Certainly the Department of Agriculture is working in this area as it pertains to animals.

Mr. FLOOD. I mean in humans.

Dr. LAVECK. I do not know, sir.

Mr. FLOOD. Aren't you curious?

Dr. LAVECK. Some of the research we are conducting would have application to artificial insemination.

Yes, I am curious.

Perhaps I ought to refer this to Dr. Berliner.

Dr. BERLINER. Artificial insemination is done but I am not exactly sure what agencies are involved.

Mr. FLOOD. Will you find out?

Dr. LAVECK. I would be happy to.

Mr. FLOOD. And have them send you a paper indicating how long, to what extent, where, by whom, with what success, and with what prognosis and put that in the record. I do not want a book. I just want something reasonable.

Dr. LaVeck. Yes, sir.
Mr. Shriver. One other aspect: Legality.
Mr. Flood. Yes.
(The information follows:)

ARTIFICIAL INSEMINATION IN HUMANS

As far as can be determined, there has been very little research specifically in the area of artificial insemination in humans. The National Institutes of Health has supported a few projects in this area which deal with methods for the preservation of human sperm. Four such National Institute of Child Health and Human Development extramural research studies are described below; two others were supported by National Institute of General Medical Sciences, but although humans were included, the primary emphasis was on animal subjects.

Grant No. HD–0538: Freund, M., New York Medical College, New York, N.Y. Freezing and Storage of Human Sperm.

This project has been supported since fiscal year 1962, and is due to terminate in July 1969. For the first 2 years it was in the National Institute of General Medical Sciences, but was then transferred to the National Institute of Child Health and Human Development. Annual support of this project has averaged approximately $12,000. It has been concluded from this study that human semen may be successfully and routinely diluted, frozen, and stored provided a sequence of critical steps is carefully followed. These constitute a standardized and repeatable technique for the dilution, freezing, and long-term (up to 39 months) storage of human spermatozoa with essentially complete recovery of motility upon defrosting of a significant number of specimens.

Grant No. HD–0614: Rock, John, Rock Reproduction Clinic, Brookline, Mass. Refrigerant Preservation of Human Spermatozoa.

This grant ran for 5 years, and was also initially supported by the National Institute of General Medical Sciences and later transferred to the National Institute of Child Health and Human Development. Average annual support was approximately $7,000. The grant terminated in April 1968. The purpose of this work was to develop new methods for the refrigerant preservation of human sperm. Comparisons were made of processing the sperm in liquid nitrogen (−196°) and in a Rauce freezer (−70°), controlling for the factor of room temperature.

Grant No. HD–1077: Behrman, S. J., Woman's Hospital, University of Michigan, Ann Arbor, Mich. Biological and biochemical survey of frozen human semen.

This study ran for 2 years, and terminated in March 1967. The average level of annual support was approximately $36,000. The purpose was to examine any deleterious effects of deep freezing and thawing; to study the specific response of human spermatozoa to these effects; to ascertain the optimal protective medium and the best procedure for minimizing possible damage to spermatozoa. Sperm stored in a liquid nitrogen vapor refrigerator were subsequently used for insemination. The results indicated that the capacity of frozen human semen is somewhat less than that of fresh semen from donors, possibly because of loss of sperm motility and other unrecognized damaging effects of freezing.

Grant No. HD–2592: Ackerman, Donald R., Woman's Hospital, University of Michigan, Ann Arbor, Mich. Biochemistry of supercooled and frozen human semen.

This project started in fiscal year 1967, and is to run through May of 1970 at an approximate average cost of $37,500 per year. Its purpose is to study the effects on human sperm cells of continuously decreasing temperatures. A comparative analysis was made of the physiology and metabolic functions of fresh and frozen specimens subjected to continued storage at low temperatures. The investigator is also interested in determining to what extent the cooling process imposes an artificial selection on the various kinds of cells existing in semen samples, as defined by haploid genotype.

The National Institute of Child Health and Human Development also supports a large number of projects concerned with reproductive physiology. Although the emphasis in much of this work is directed toward contraception, research in such areas as sperm metabolism and capacitation and on the process of fertilization is equally applicable to the problems or artificial insemination.

SERVICE PROGRAMS

Heterologous insemination (i.e., using the husband's sperm) is used both by private physicians and in fertility/sterility clinics. Some clinics, such as those of the Margaret Sanger Bureau, provide the service directly. Others, such as Planned Parenthood, would usually refer the patient to a private physician or to an affiliate organization for such treatment. In addition, there are segments of the population for whom the Public Health Service provides full medical care. In such populations, it may be assumed that artificial insemination is used as treatment where indicated.

Heterologous insemination is used when the husband is deficient in sperm or when the husband's sperm is likely to result in a congenitally defective child. We know of no public agencies which are employing the donor method, but some private physicians are using it. Although there are no laws preventing it, there are, in some States and in Canada, widely divergent laws dealing with various aspects of the problem.

Dr. LaVeck. For our activities in the coming fiscal year, the budget request is for $78,411,000, which is $7,611,500 more than the fiscal year 1969 operating level. Of this increase, we are requesting $4,328,500 for grants. For direct operations, which include population research contracts, we are requesting an additional $3,283,000.

RESEARCH ON BIRTH CONTROL

Mr. Flood. The total of your program increases is $8,658,500, and, if I understand this correctly, well over $6 million of this increase is for birth control and closely related research activities. Is there really that much need this coming year for additional research in this area, or do you just simply think it is a very dramatic subject and that is where you can get the money? It is going to be a very tough year, Doctor, and now you want an additional $6 million for research on birth control. Why?

Dr. LaVeck. Excessive population growth is a serious problem that has not received sufficient attention in the past. This has been largely a neglected area.

Mr. Flood. Birth control has been a largely neglected area?

Dr. LaVeck. In the area of research, yes, this is true. Likewise, birth control services have been neglected. These facts were emphasized in the recent report by the President's Committee on Population and Family Planning.

We are concerned with three groups of problems: Those facing the world, those facing the United States, and those facing the individual.

As far as the world problem is concerned, I am sure you are quite aware that in many parts of the world the balance between the numbers of people and the available resources, particularly food, is in jeopardy. The population of the world is growing at the rate of about 2 percent per year. This means by the year 2000 the population for the world will double. There will be 7 billion people rather than 3½ billion.

Even if it were possible to cut the growth rate in half for the entire world we would still expect 5 billion people in the year 2000. The problem in the United States is somewhat less overwhelming but certainly real and important. We anticipate an increase between 1965 and 1985 of 58 percent in the number of women at the ages during which births commonly occur.

Our birth rate at the present time is at its lowest level. 17.4 per thousand population, but because of the additional groups of women

that will be having children in the next 10 to 15 years, even though the birth rate stays low, we are going to see a large increase in the total number of births.

I think it is also important to point out that a significant number of Americans have more children than they want. Of the 5 million women living in poverty, it is estimated each year they have 450,000 unwanted children.

Mr. FLOOD. Is there anything significant in your statistics with reference to multiple births in this country?

Dr. LAVECK. In what respect?

Mr. FLOOD. Anything worth while noticing?

Dr. LAVECK. I know of no particular trends in regard to multiple births. You are talking about twins, I presume?

Mr. FLOOD. Yes; you can go as high as you want.

Dr. LAVECK. The risk to the infants is much greater for twins.

Mr. FLOOD. But there is nothing dramatic or eye catching statistically in reference to multiple births?

Dr. LAVECK. No. Also, the population increase contributes to our high infant mortality rate, our high stillbirth rate, increased maternal morbidity and mortality, criminal abortions, and illegitimacy.

Mr. FLOOD. Maternal morbidity?

Dr. LAVECK. Yes.

Mr. FLOOD. What is maternal morbidity?

Dr. LAVECK. Illness associated with pregnancy. I wish to remind the committee of the problems that we face with overcrowding of our schools and highways, air pollution, and the other social problems that are created by excessive population growth. In regard to the individual, inability to plan and control fertility is associated with a long series of undesirable outcomes, such as poor intellectual performance in offspring, high rates of emotional problems, antisocial behavior, child abuse, and abortions.

Mr. FLOOD. How much did you spend in 1969 on this research?

Dr. LAVECK. In 1969 we will spend $10.8 million on population research.

Mr. FLOOD. Suppose you give us a little detail about what you are doing in this field.

Dr. LAVECK. Yes, sir.

Mr. FLOOD. And what more will you do if and when you get the requested increase next year.

Dr. LAVECK. Our Center for Population Research is concerned with the support of research through contracts in the following three areas: Contraceptive development; the social and behavioral sciences; and the medical effects of existing contraceptives. I think we have made a good deal of progress in launching a contraceptive development program; that is, the development of new methods for contraception. Last year Congress provided us with two and a half million dollars specifically for this purpose.

Mr. FLOOD. What do you mean by new methods?

Dr. LAVECK. New techniques that can be developed. I would like to tell you how we have gone about identifying breakthrough areas. We appointed a population research advisory committee early last year that met with our staff repeatedly to identify those areas that were likely to provide a payoff in terms of products that could be used to

limit family size. Four specific areas were identified. I mentioned two of these, corpus luteum function and the maturation of the sperm.

The other two areas include studies of the oviduct, the passage that connects the ovary and the uterus. The fourth area is the biology of the preimplantation ovum, the ovum before it attaches itself to the uterus.

We then appointed four panels of experts to review applications that we would receive from investigators working in these particular fields. Early in January we sent out 2,000 letters to the leading scientists in the country working in the area of reproduction asking if they had an interest in joining efforts with the NICHD to pursue this line of investigation, and within a matter of a few weeks we had 400 replies to the affirmative. We then sent letters to the most promising of these investigators, well over 300 letters, asking for specific proposals that would lead to the development of new methods of contraception.

They had less than 6 weeks to develop proposals. Still, we received by March 3, 250 research proposals in the area of contraceptive development. The total dollars requested was about 12 million for the first year. Our panels are now reviewing these applications for scientific merit. On April 7 and 8, the Institute will also review the applications. Following this second review, we will launch our contraceptive development program.

Mr. FLOOD. What more are you going to do next year than you are doing now if and when you get the $6 million? That is why you are here.

Dr. LAVECK. Yes. We are asking for an additional $2,850,000 for contracts in this field.

Approximately one and a half million dollars will be used to expand this contraceptive development program.

PSYCHOSOCIAL AND BEHAVIORAL RESEARCH

Mr. FLOOD. Take a look at page 80 of your justifications. You refer to: "Psychosocial and behavioral research." This is in connection with family planning. What does this involve, and why doesn't this belong in the Mental Health Institute?

Dr. LAVECK. Let me say first why it is important. Some believe that all we need is a better method of contraception, and family planning and population control problems will be solved. We know this is not the case. There are other factors that are of extreme importance. For example, during the depression years the birth rate in this country fell to very low levels. Yet we did not have sophisticated contraceptive methods for controlling family size. It was the economics of the situation that resulted in the decision on the part of couples to restrict the number of children they had. Likewise, we had a marked increase in population following World War II with the return of servicemen. So there are many social, demographic and psychological factors that enter in. We are interested in knowing more about motivation. We want to know why families either accept or reject family planning.

I have mentioned one reason, economy.

Mr. FLOOD. How do you find that out?

Dr. LAVECK. This often requires personal interviews.

Mr. FLOOD. The Bureau of the Census is helping you?

Dr. LaVeck. We have worked very closely with the Census Bureau. We want to know reasons for changes in family size preference. For example, in a recent study it was noted that one of the possible reasons for a decrease in the birth rate was the fact that couples had higher aspirations for their children. They want them to go to college. With the increase in cost of education, many couples voluntarily have restricted the size of their families so that they can provide a college education for their children.

Mr. Flood. As the economic status of the family rises from blue collar into white collar stage, down goes the size of the family.

Dr. LaVeck. That is true.

Mr. Flood. You find that in immigrant groups. Two generations ago the immigrant had 10 children, then his son had five, and his grandson has two. The grandson is now a lawyer or a doctor or a businessman.

Dr. LaVeck. There are certain exceptions to this. It has been found through a study we supported that Catholics with more education are having more children than those with less education.

Mr. Flood. But not those in the lower economic group.

Dr. LaVeck. Yes; that is correct.

Mr. Flood. Are you sure of that?

Dr. LaVeck. We are certain of this. The educational factors are reversed from what one would expect, and the reason that is given is perhaps the more educated Catholics are most likely to conform to church teaching and to choose the rhythm method, which is less reliable. This is the interpretation.

Mr. Flood. You say the middle-class Catholic family has more children than the so-called lower class Catholic family.

Dr. LaVeck. The middle-class Catholic family wants more children.

Mr. Flood. I didn't ask you about that. Are they having them?

Dr. LaVeck. They are having more children.

Mr. Flood. How can you tell what they want?

Dr. LaVeck. This can be determined through interviews and surveys. We are also interested in attitudes toward marriage and children. For example, women are marrying at a later age now. This means they are having their first child later in life, and since the reproductive abilities of women diminish as they get older, this may ultimately result in smaller family size.

Mr. Flood. What more are you going to do next year than you are doing today, if and when you get the $6 million?

Dr. LaVeck. We need, Mr. Chairman, to continue to monitor closely trends for family size, family preference, and various motivational factors which change frequently.

For example, Government policy may affect population growth even though it may not be intended to do this. We don't know what effect the present income tax laws have on population change. If the dependency allowance is increased or decreased, it might well have an effect on population growth.

We don't know what effect FHA and VA loans might have on family size, so we plan to assess the impact of Government policies on population dynamics.

FAMILY PLANNING IN FOREIGN COUNTRIES

Mr. FLOOD. Pick out two or three foreign countries. What are they doing about family planning?

Dr. LAVECK. Now, I presume you are moving into the area of services in family planning with which we are not concerned.

One successful family planning program has been in Taiwan where they have used the IUD very widely and seem to have been able to show a significant reduction in birth rate in that country.

Mr. FLOOD. What about Western Europe?

Dr. LAVECK. The situation in Western Europe is similar to this country. That is, the rate of population growth has not been nearly as excessive as in the developing countries.

Mr. FLOOD. Are they doing anything special in any one country there?

Dr. LAVECK. I am not aware of any unique family planning efforts.

Mr. FLOOD. Africa? Any part of it?

Dr. LAVECK. You are asking me questions now that AID is in a better position to respond to.

Mr. FLOOD. Find out for me from them and put something in the record.

Dr. LAVECK. I will be happy to.

(The information follows:)

FAMILY PLANNING IN AFRICA

The status of family planning in the world, a regional overview of Africa and detailed information about Ethiopia, Sierra Leone, and Zambia is described as follows in the September 1968 Report on Population Program Assistance prepared by the Agency for International Development.

Assistance to family planning

There are 26 developing nations now carrying out family planning programs that are government sponsored. In 32 other developing countries family planning activities are being carried on—either intensively or as initial efforts—by voluntary associations. A number of other countries are undertaking preliminary demographic and population studies.

Assistance to these family planning and population efforts is being provided to all of the nations in the first group, and to many in the other two groups, by private nonprofit organizations, by the U.S. Government through the Agency for International Development, by other nations, or by the United Nations. This assistance includes aid to initiate or expand family planning activities, population and demographic studies, medical research, and staff training.

Private organizations and the Swedish Government were the first to identify the great need for assistance to population and family planning efforts in developing nations and to initiate significant programs to supply this assistance. In 1967 the Agency for International Development began to move into a key position in the worldwide battle to help provide an answer to this major problem of our time—slowing the growth of world population to provide for a hopeful future.

AFRICA (REGIONAL)

Although demographic information for much of Africa is lacking or inadequate, birth rates—about 46 per thousand—are among the highest in the world. Death rates are still higher than in any other region, although lower than they used to be. Reported mortality among children is particularly high. However, as public health improves, the population growth rate will undoubtedly increase as mortality declines further. The present growth rate is estimated at 2.4 percent per year.

The rapid population increase is already a major barrier to economic development and improvement in general levels of living. Unless birth rates are reduced along with declines in mortality, economic and social progress may be severely affected.

In response to this situation, several African countries have undertaken family planning programs in recent years and a number are giving new consideration to population problems.

Family planning programs have been launched in Tunisia, Morocco, Rhodesia, South Africa, and the densely populated island of Mauritius. In sub-Saharan Africa, Kenya initiated a family planning effort in 1967.

Other countries are also showing interest. In a number of these, as in Kenya, the family planning activities of voluntary agencies are given some governmental help in the form of facilities and personnel.

In five countries, international or private organizations like the Population Council have provided limited help, although there are no official or private organized activities. These are Botswana, Congo (Brazzaville), Guinea, Mali, and Togo. Three other countries—Central African Republic, Dahomey, and Libya—officially favor large families and have no official or private family planning programs. (In 1965, AID provided funds to assist in conducting a national census in Libya.)

Eleven African nations and territories have no known policy on family planning, nor do they have official programs or voluntary organizations in this field. These are: Angola, Burundi, Congo (Democratic Republic), Gabon, Gambia, Mauritania, Mozambique, Niger, Rwanda, Seychelles, and the Somali Republic.

AID assistance

AID support for population activities in Africa has been limited primarily to support for demographic research and training. AID's worldwide grant to the International Planned Parenthood Federation, to the Pathfinder Fund, and to the Population Council for its post partum program will help support family planning activities in Africa in fiscal 1968. The Agency stands ready to consider proposals for further assistance in Africa, both on a regional and bilateral basis where applicable. AID obligations for population and family planning activities in the Africa region are:

	Fiscal year 1965	Fiscal year 1966	Fiscal year 1967	Fiscal year 1968
Country missions	9,600	8,610	4,050	404,600
Regional			30,000	259,000
Africa total	9,600	8,610	34,050	663,600

Other assistance

Many organizations have contributed to demographic and family planning advances in Africa. Technical assistance for census, vital statistics, and demographic work has been given not only by AID, but by the United Nations, U.S., Census Bureau, France, and others.

The Population Council, Pathfinder Fund, and the International Planned Parenthood Federation have been prominent among the voluntary agencies promoting program development on the Continent. The Ford Foundation and Rockefeller Foundation, and Governments such as those of Sweden, Great Britain, and the Netherlands, have supported population activities through grants to international voluntary agencies and contributions to country programs.

ETHIOPIA

Demographic information

Date of last national census	NA
Population (Jan. 1, 1968 estimate)	23,625,000
Births per 1,000 population [1]	43
Deaths per 1,000 population	NA
Rate of increase (percent of total population)	1.8
Number of years to double population at present rate	40
Infant deaths per 1,000 live births [1]	152
Literacy rate	5
Labor force in agriculture	88
Per capita gross national product (1966)	$62

Population and family planning activities

The Ethiopian Government has no official stated policy on population and family planning. The one clinic devoted entirely to family planning is located in an institution run by the Haile Selassie I Welfare Foundation, a voluntary society sponsored by the Emperor.

After visits by Pathfinder fund representatives beginning in 1964, the Welfare Foundation established a family guidance association in 1966. The executive committee included representatives from the Ministries of Education, Community Development, and Public Health, and from the Addis Ababa municipal government and the University School of Social Work. The association has received support from Pathfinder fund and the International Planned Parenthood Federation for operation of the full-time clinic, at St. Paul's Hospital in Addis Ababa, and for a part-time clinic at Ghandi Memorial Hospital. The Gondar Public Health College also provides limited family planning services. A full-time social worker and part-time consultant trained at the University of Chicago are employed by the association.

The U.N. Statistical Training Center in Addis Ababa includes lectures on population and vital statistics.

AID assistance

AID has assisted a pilot project in birth and death registration to develop reliable estimates of birth, fertility, and infant mortality rates in a number of communities outside of Addis Ababa. Nurses are receiving training in the United States at AID expense, and AID financed the attendance of an Ethiopian family planning leader at the IPPF conference in Santiago, Chile, in April 1967. The AID population officer has given technical assistance to the family guidance association.

Other assistance

The Pathfinder fund has supported its representatives' visits to Ethiopia, contributed funds and contraceptives to family planning clinic facilities, and supported a family planning leader's attendance at a University of Chicago course on family planning in 1965. IPPF has also provided assistance for the clinics and with the population council has provided fellowships for study abroad.

SIERRA LEONE

Demographic information

Date of last national census	1963
Population (Jan. 1, 1968, estimate)	2,459,000
Births per 1,000 population	NA
Deaths per 1,000 population	NA
Rate of increase (percent of total population)	1.5
Number of years to double population at present rate	48
Infant deaths per 1,000 live births	NA
Literacy rate	7
Labor force in agriculture	89
Per capita gross national product (1966)	$157

Population and family planning activities

The Government of Sierra Leone conducts no program in family planning. A planned parenthood association was organized in 1959 and began operating one clinic in a government hospital in Freetown in 1960. It now has its own facilities and operates a clinic twice a week. The association carries on a public information and education program, which includes radio and television broadcasts, lectures, newspaper articles, pamphlets, and posters printed in four languages. Family planning information and supplies have been provided to medical staffs in the Provinces.

AID assistance

AID has provided some commodities for the planned parenthood association, and supported the attendance of family planning leaders at the regional conference of the International Planned Parenthood Federation at Copenhagen in July 1966.

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[1] Based on data obtained from birth and death registration in six roadside towns, 1962–66.

Other assistance

The IPPF made its first grant to the family planning association in 1965. An IPPF medical team traveled throughout Sierra Leone in 1967 to train medical personnel in family planning methods. Supplies for the Freetown hospital clinic were provided by the Pathfinder fund.

ZAMBIA

Demographic information

Date of last national census	1963
Population (January 1, 1968, estimate)	4,010,000
Births per 1,000 population (1963)	51
Deaths per 1,000 population (1963)	20
Rate of natural increase (percent of total population)	3.1
Number of years to double population at present rate	23
Infant deaths per 1,000 live births (1950)	259
Literacy rate	20
Labor force in agriculture	81
Per capita gross national product (1966)	$266

Population and family planning activities

The Zambian Government's policy is to expand the country's population. The Government forbids dissemination of information on family planning through mass media.

A local family planning association has functioned in the past at Lusaka without government support. Plans to reestablish family planning in Lusaka have been studied. Government postnatal health clinics provide family planning information upon request in urban and rural centers, and some individual doctors give advice.

Fifty to sixty maternal and child health clinics are to be built and staffed by 1970. The emphasis in these clinics is on nutrition and child spacing to avoid malnutrition.

Community development and health education training centers provide some instruction in family planning for community development workers and home economists.

AID assistance

Although A.I.D. supports the community development and health education training centers, which give limited exposure to family planning, it does not directly support any population and family planning activities.

Other assistance

The population council has provided fellowship assistance. The Pathfinder fund has sent representatives to Zambia and has donated contraceptives.

MENTAL RETARDATION RESEARCH CENTERS

Mr. FLOOD. You have an increase from $2 million in 1969 to $3 million in 1970 for mental retardation centers. Why is that necessary now?

Dr. LA VECK. The centers are about to open and need support now. As I mentioned, by the end of this fiscal year 11 centers will be in operation. They are all quite different, Mr. Chairman. Some of the centers are very large units that encompass the entire university; not just the medical school, but the departments of psychology, education, speech and hearing and other schools and departments.

The University of Washington is an example of a University-wide center. Other centers are smaller and focus on specific problems such as behavioral research or biological research. A number of the centers are affiliated with institutions for the mentally retarded so that it will be possible to apply new knowledge obtained in the centers to service programs for the mentally retarded in institutions.

I am sure you are aware that there are also university-affiliated facilities for the mentally retarded. That construction program is administered by the Social and Rehabilitation Service.

MENTAL RETARDATION PROGRAMS OF OTHER AGENCIES

Mr. FLOOD. You remind me of something when you mention the Social and Rehabilitation Service. Why isn't this program of yours consolidated with other mental retardation activities? We have a specific appropriation "Mental retardation" in the Social and Rehabilitation Service? Why not put them all together?

Dr. LAVECK. Mental retardation activities are scattered throughout a number of Federal agencies.

Mr. FLOOD. I just said that.

Dr. LAVECK. Not just the Social and Rehabilitation Service, other components of HEW. In each agency the focus is quite different. We are concerned with research and research training. The Division of Mental Retardation in the Social and Rehabilitation Service is concerned with training of personnel for service and the demonstration of clinical services.

We are supporting research and this is not a major function of the Division of Mental Retardation, but we work very closely with that particular group.

MALNUTRITION

Mr. FLOOD. Are you doing anything with regard to malnutrition?

Dr. LAVECK. Yes, we are.

Mr. FLOOD. What?

Dr. LAVECK. We are particularly interested, Mr. Chairman, in the relationship between malnutrition and intellectual development. I think this is a subject that has received considerable attention during the last few months.

Mr. FLOOD. You are concerned about intellectual development?

Dr. LA VECK. What effect does malnutrition have on the developing brain? Is mental retardation caused by malnutrition?

There is an abundance of animal studies that indicate that severely malnourished pregnant animals can have offspring with brain abnormalities and behavioral changes. They don't learn as well as other animals. There are also studies demonstrating that certain young animals, if severely malnourished, will not develop normally.

Now in regard to humans, we know from studies in Africa and in South America that children may die with severe malnutrition resulting in kwashiorkor, a protein deficiency. When their brains are examined, the brains are smaller than normal and there are fewer cells.

Those children that survive this severe type of malnutrition tend to be slower intellectually than well-nourished children. What we don't know is the effect on intellectual development of malnutrition of a lesser magnitude, the type of malnutrition we might see in this country.

The whole problem is a difficult one to tackle because we know that in poverty groups, for example, mental retardation is more prevalent.

Mr. FLOOD. You are speaking now of improper diet as distinguished from lack of food?

Dr. LAVECK. Improper diet or lack of food.

We know that children may be mentally retarded in poverty areas because of a number of possibilities. Malnutrition might be one. It also might be lack of adequate medical care. Disease prevalence is greater and chronic diseases are more frequent in such groups.

It might also be due to poor maternal stimulation; little interaction of the child with his family. He may have limited opportunity to read, for example.

Perhaps there are deficiences in educational opportunities for these children. In carrying out studies it is necessary to control these social variables before one can pinpoint the importance of nutrition as the cause of intellectual maldevelopment.

We are currently supporting a study in Guatemala in which six villages have been identified in the highlands of Guatemala.

Mr. FLOOD. Indians?

Dr. LA VECK. They are native Guatemalans.

Mr. FLOOD. Probably mostly Indians.

Dr. LA VECK. Yes. Mixed Spanish Indian extraction.

These villages have been very carefully selected. Over 100 were thoroughly studied before the six were chosen so that there would be comparability in regard to the social, health, and nutritional aspects in each pair of villages. Individuals in three villages will receive dietary supplementation every day. Supplements will be given to pregnant women, to their offspring, to the siblings of those infants, and all children in the experimental villages under 7 years of age. All six villages receive medical care.

I think from this study in Guatemala, that we will be able to determine within 5 years the extent to which nutrition influences intellectual development.

We are also supporting a study in Bogotá, Colombia, which is quite different.

Mr. FLOOD. In a city?

Dr. LA VECK. This is in the city, in the ghetto areas of Bogotá. Siblings will be studied. One sibling will be diagnosed as malnourished; the other will be well nourished. A dietary supplement also will be provided.

Mr. FLOOD. Have you ever seen the ghetto in Bogotá?

Dr. LAVECK. I have not.

Mr. FLOOD. It is quite a ghetto.

Dr. LAVECK. I presume it is.

This is another approach to the study of malnutrition in that it controls for family environment and genetics. We are now negotiating a contract with Columbia University to carry out a study in Harlem where supplementation of the diet of pregnant women will be assessed to see what effect this has on birth weight of offspring. The smaller the birth weight of the infant, the more likely he is to have certain types of neurological deficits. We also have a new study in the rural South in which a supplement will be given to pregnant women and the benefits for the development of their children will be studied.

VARIATIONS IN BIRTH WEIGHT

Mr. FLOOD. Separate and distinct from this problem, what causes variations in birth weight?

Dr. LAVECK. The causes are multiple, Mr. Chairman.

Mr. FLOOD. Give me one good one.

Dr. LAVECK. Let me first say that of all premature births, we know the specific cause in about 40 percent. Generally, we cannot say why a child is premature.

Mr. FLOOD. What is the variation in weight in a normal birth? Why is one child x pounds and another child y pounds under similar circumstances?

Dr. LAVECK. Some of these differences relate to the health of the mother. For example, a mother with toxemia or premature separation of the placenta, or other similar types of maternal abnormalities, may have smaller infants.

Mr. FLOOD. Normal birth, normal child now.

Dr. LAVECK. Why is there a difference in birth weights in normal pregnancies?

Mr. FLOOD. Yes.

Dr. LAVECK. There are probably two main factors. One is genetic. Large women tend to have large babies. Also, male infants tend to be heavier than female infants.

The second is probably related to intrauterine nutrition. This is a very general answer.

Mr. FLOOD. It was a very general question.

STUDY OF DISADVANTAGED CHILDREN

Now, you are asking for an increase of four people and $55,000 "to study the development of infants and young children in disadvantaged environments." Is that a new program?

Dr. LAVECK. This is in our intramural program. We have a Social and Behavioral Sciences Branch in our intramural program. The main efforts of that Branch have been to study children in Headstart programs in the metropolitan area. Their particular concern is with the various aspects of the Headstart program that may enhance cognition and personality development in the child. The funds and positions we are requesting are to expand these efforts.

As you know, there has been a good deal of controversy about the effectiveness of early childhood intervention programs.

Mr. FLOOD. Indeed there has, but the thing that bother me is, just about every agency I can think of except the Bureau of Mines is studying disadvantaged children. Is this a new program?

Dr. LAVECK. This is not a new program. This program has been underway for the last year and a half.

RESEARCH ON AGING

Mr. FLOOD. In going through these justifications I didn't notice any real progress in regard to research problems on aging. Now, everybody in this room is getting older while we are talking about it. What progress did you make during the last year and how much are you spending in 1969 on aging? This is a problem that everybody is interested in.

Dr. LAVECK. In 1969 we are spending about $8 million. To be more precise, $8,082,000.

Mr. FLOOD. Your justifications aren't very proud of it. You didn't show any real progress in research in connection with aging. You skipped over that one lightly.

Dr. LAVECK. We have made significant progress on many aspects of the problem of aging.

As I mentioned to this committee last year, one of the difficulties is that there are not enough trained investigators in the field of aging to embark on important studies. However, we have greatly increased the amount of money we have spent for training.

For example, in 1964 we spent about $300,000 on the training of scientists to do research in aging. This year we will spend over $2 million.

Mr. FLOOD. How long does it take you to train such a research team?

Dr. LAVECK. It varies from 1 to 3 or 4 years. We have decided to try to get to young people who are in their doctoral training and try to interest them in aging. In June of this year we will have a summer course on the biology of aging which will be held at the University of California at San Diego. Twenty outstanding young people in universities will be participants. We will have a faculty of 25 and the efforts here will be to give these students new information on aging, try to interest them in the field so that they can follow their own disciplines, but delve into the problems of aging.

Mr. FLOOD. I thought the whole spectrum of geriatrics was a red hot operation.

Dr. LAVECK. It is not, sir. Few scientists are interested in this field.

Mr. FLOOD. There is a lot of talk about it.

Dr. LAVECK. There is a lot of talk; that is right. Our greatest contribution has been in the area of training which later will have an impact on research.

Mr. FLOOD. I think that is the answer as far as you are concerned.

Dr. LAVECK. Yes.

Mr. FLOOD. Mr. Michel.

FACTORS INFLUENCING INTELLECTUAL DEVELOPMENT

Mr. MICHEL. Doctor, I read somewhere that either 40 percent or 60 percent of a child's capacity to learn is developed by the age of 4. Is there anything to substantiate that?

Dr. LAVECK. This is quoted in the literature frequently, but there really is nothing that substantiates this.

Mr. MICHEL. Is there something closely akin to that? What is the good professional observation in this area or haven't we studied this sufficiently to know? How much of our capacity to learn is developed, for example, before the age of 4, or before school age? We are interested because of this problem of malnutrition for one thing. We hear, "Well, if you deprive the child in those early, formative, growing years, of proper diet, his capacity to learn has been endangered for life and it can never be recovered."

Dr. LAVECK. You are asking a very important question and one about which we have very little information.

I'd like to call your attention to an article written by Dr. Arthur Jensen which appeared in the last issue of the Harvard Educational Review, in which he assessed the importance of heredity and environment on intelligence. This investigator has concluded that 80 percent of intelligence was determined by heredity and 20 percent by environment.

We can cite other studies that indicate events occurring after birth, environmental effects, are most important in the development of the child. We just do not have the answer. I think this is the important reason that our Institute must be concerned with early development so as to be able to relate these events with later school performance and adult life.

If I might give just one example: We have been supporting a study at Brown University in which visual stimulation is given to infants. A 2 month old child is placed in his crib with a mobile placed above him. He is attached by a string to the mobile so that when he kicks his feet, the mobile moves. This type of visual stimulation offers pleasure to the infants and they kick vigorously much of the time. When they are disconnected they are most unhappy about this.

Other studies indicate that infants respond to visual stimulation.

Now, the reason we are supporting this research is to determine what effect visual stimulation in infancy has on reading ability, for example. We know that the child who reads early tends to be a good reader. Whether children should learn to read at 3, 4, 5 or 6 years of age, we don't know, but we do know that early readers tend to read well. It is possible that this type of visual stimulation during infancy and the early childhood years, may in fact have great importance in preparing a child to read.

I am not sure I have answered your question, Mr. Michel.

Mr. MICHEL. In your studies on why people do or do not have large families or small families, would you go into the matter at all of how wise it is to have what my wife likes to refer to as two families? I was told in the early years of our marriage that we were going to have one family, not two. We have had friends where they have been so spaced out that children were in college and others were being nursed and that my wife didn't want.

But after you have four, as we did, in quick succession, and you have all those problems at once, when they get up to the age of going to college and they are all away at the same time, it leaves a tremendous void. You ask yourself if you shouldn't have had six or eight.

I don't know what effect it really has on one, whether it is good or bad. If you have the resources to have them, I think it is fine to have as many as you can.

ILLEGITIMACY

By the same token, I read a very distressing article in last Sunday's paper entitled "Unwed mothers spurn agency's help." It says "Washington suppliers of services to teenage unwed mothers are shaking their heads and puzzling over a strange new situation: Their lack of customers. While illegitimate births predominantly to teenage mothers continue to increase, fewer and fewer young unwed mothers, or mothers-to-be are coming to the adoption agencies, maternity homes, and social service agencies for help."

And then, going on further, mentioning the fact that 30 percent of the babies born here in the District of Columbia, are illegitimate.

One other striking statistic: Sixty percent of the infants born to the mothers under 21 here in the District are illegitimate.

Do you have anything to do with research in this area at all?

Dr. LAVECK. Not a great deal yet. In fact we currently are not supporting work in this field. I might just comment that the percentage of illegitimate births as a part of all births is about 9 percent for

this country. The percent in Washington, D.C., is much higher. But if one looks at the problem from a different angle and determines the rate of illegitimate births per thousand unmarried women in the reproductive age groups, there has been little change during the past 10 years. The reason we are seeing an increase in the percentage of all births that are illegitimate is because there is a decline in the number of babies born of married mothers. But certainly this is a serious problem and we know that illegitimate birth is frequently associated with prematurity, with mental retardation, and infant mortality. It is a serious problem. From that standpoint we are interested.

Mr. MICHEL. Again, our U.S. infant mortality rate is what?

Dr. LAVECK. For 1968 our provisional infant mortality rate is 21.7 per 1,000 live births and we still rank 13th among the developed countries.

Mr. MICHEL. We haven't made any progress then?

Dr. LAVECK. Not in terms of ranking, that is right. The infant mortality rate has decreased over 12 percent in this country since 1965, which is the greatest drop since the comparable period from 1945, to 1948. We have seen progress but not in respect to other countries.

Mr. MICHEL. Have oral contraceptives been in vogue long enough to give you any kind of an experience factor so far as the effect they might have on limiting of time or extending of time that a woman might bear children?

Dr. LAVECK. No; we have no good information on this particular topic.

DEVELOPMENT OF NEW CONTRACEPTIVES

Mr. MICHEL. I note on page 3 of your testimony that the preliminary findings of these studies do indicate the need for the development of new contraceptives and this Institute is planning to do this with an expanded contract program.

How much of your budget will be going into this expanded contract program?

Dr. LAVECK. For the 1970 budget approximately $1.5 million. When combined with the $1.5 million we will spend this year, it would give us a total of $3 million in this area.

Mr. SHRIVER. Oral contraceptives?

Dr. LAVECK. Not necessarily. We want to develop a variety of new contraceptive methods. Presumably some might be taken orally.

Mr. SHRIVER. How much money on oral contraceptives?

Dr. LAVECK. We are still reviewing our applications and no awards have been made as yet to develop new contraceptives. Therefore, I can't respond as to which of the possible areas might result in an oral medication and which might result in a device or an injectable drug.

Mr. MICHEL. Would these all be limited to the woman?

Dr. LAVECK. No; we are very much interested in new methods for males. Prior to the pill, male contraception was the primary way of limiting the size of the family and we feel there is a need for some type of medication that will limit male fertility.

Mr. MICHEL. Are your applications up to date for both male and female? The applications of those who want to make the studies or go into this area, are they for both sexes?

Dr. LAVECK. Yes.

Mr. MICHEL. I guess that is all, Mr. Chairman.

Mr. FLOOD. Mr. Natcher.

Mr. NATCHER. Dr. LaVeck, I was very much interested in that part of your statement concerning the establishment of your new facility in Baltimore where you having aging research underway.

Doctor, as we go along, you hear from time to time doctors and others say that you are now a certain age and you should limit your activity and you should do thus and so. In this research as far as aging is concerned, Doctor, are we saying to our people and especially men, that when you reach a certain age you shouldn't do this and you shouldn't do that physically? Why not, Doctor?

In other words, am I wrong about this? Your heart is a muscle. Why don't you use it within reason. Are we going too far to the other extreme, Doctor?

Dr. LAVECK. We have no firm evidence that the aging process may be slowed by exercise.

On the other hand, a number of studies indicate that exercise increases general physical fitness and feeling of well-being. It also may exert a beneficial effect on cardiac function and the development of cardiovascular disease. Exercise can aid in weight control. All of these would tend to improve the well-being of the older person, and I think that exercise should not be restricted unless there is a definite medical indication to do so.

Mr. NATCHER. Doctor, do you feel that today we are receiving too much instruction and information to the effect that after we reach a certain age that we should start slowing down and just face the problem of old age? I don't know whether you have answered my question or not, Doctor.

Dr. LAVECK. You raise an extremely important question.

Mr. NATCHER. It is one that we ought to start facing, shouldn't we, Doctor?

Dr. LAVECK. You are absolutely correct.

Really, what you are asking is, what is this retirement period? What does it mean? It is a new developmental stage that older people pass through, a period when they may demonstrate a lessening of vigor, poor physical and mental health, and have less income. They may lose contact with many of their colleagues and friends. Psychological changes occur, as well as physical changes.

We have been very interested in this area and have conducted five different conferences trying to interest investigators to pursue research in this area.

I must admit we have not been very successful in stimulating research on the health and psychological aspects of retirement.

We support one very interesting longitudinal study in which 600 married couples with husbands between ages 60 and 64 are being followed. Data have been collected on health conditions. Medical utilization, finances, personal goals, social participation, family ties and other factors. I think from that study we will obtain more information about the question you have raised. You have identified a problem area that is greatly in need of further exploration.

Mr. NATCHER. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Shriver.

Mr. SHRIVER. Do you anticipate any change in your requests by the new administration? They have emphasized, as I understand, areas of maternal and child health and I wonder if there are any higher priorities that will be requested for them?

Dr. LaVeck. We have had numerous contacts with the new administration in HEW as well as with staff at the White House who have definitely expressed an interest in early childhood development, and malnutrition in particular. These are areas of interest to our Institute and I am not aware of any major changes that might effect our Institute. Perhaps Dr. Marston would care to comment.

Dr. Marston. I don't believe that I can add anything significant to Dr. LaVeck's comment at this time, Mr. Shriver.

CENTERS FOR AGING RESEARCH

Mr. Shriver. On page 86 of the justifications you mention that present funding procedures can be used to encourage support for centers in aging research. Now, what centers are you referring to there? Where are they?

Dr. LaVeck. Because we have had difficulties in stimulating research efforts in the field of aging, we have decided to use the approach that we did in mental retardation. That is we plan to encourage the development of centers in universities that have an interest and have a critical mass of scientists available to carry out interdisciplinary research on aging. We will soon establish such centers, working with our Advisory Council. This plan does not include a new construction program, however. Therefore, we would use our existing funds that are identified for regular research support to establish centers to work on specific problems in aging.

Mr. Shriver. In this request how much is for this new approach?

Dr. LaVeck. There is no increase. This would develop at the expense of some other aspect of research.

Mr. Shriver. When do you anticipate they will be established?

Dr. LaVeck. Early in fiscal year 1970.

Mr. Shriver. You are requesting 57 additional positions or a 26-percent increase for intramural research. Is this on all programs or mainly in a few?

Dr. LaVeck. In all programs dealing with mothers, children, and the aged.

HEADSTART

Mr. Shriver. On page 95 you say that much more precise information is needed than is now available on the type of training offered in the Headstart program. This committee will later hear justifications relating to Headstart. Would you have any recommendation, based on this statement, that we really don't have sufficient information to expand this activity?

Dr. LaVeck. Expand the Headstart activity?

Mr. Shriver. Yes.

Dr. LaVeck. The Headstart program, as you know, focuses not only on preparing children to enter school, but also provides medical and dental services to children; it provides psychological and social services and nutritional programs. That is, Project Headstart is not just an educational program.

Now, if one is to evaluate Headstart only in terms of changes in IQ—that is, what the child's IQ is when he enters the program, what it is after completion, and then 1 year later, there are inconsistencies and disappointment. In many situations one fails to demonstrate a permanent change. What is overlooked, I believe, are some of the other aspects of Headstart which are extremely important and are

difficult to measure, such as motivation and the development of values. It is difficult to evaluate Headstart only on terms of changes in IQ test scores.

Mr. SHRIVER. Your statement that you need more information than is available is what prompted my question.

Dr. LAVECK. I believe we do need more information.

Mr. SHRIVER. As to where we go with this program?

Dr. LAVECK. I think what we need to do is study the preschooler and his environment to be able to identify discrete aspects of intervention programs that indeed do result in a beneficial effect. We really don't know this yet.

Mr. SHRIVER. You are requesting a 69-percent increase in 1970 for collaborative research activities. How much will go to the Center for Population Research?

Dr. LAVECK. All of it.

AID FAMILY PLANNING RESEARCH

Mr. SHRIVER. And in the justifications you mention that emphasis is placed on population problems of a developing nation.

I am on another subcommittee of the Appropriations Committee that has to do with the Agency for International Development. How much of this is really the AID Agency's research program?

Dr. LAVECK. Most of AID funds are used for the provision of services. However, in their current budget I believe they have about $6 million for research, which is primarily for applied research, and most of this, I believe, is spent overseas. However, we have worked very closely with AID. Often they have turned to our Institute for review of domestic research grant applications they receive. That is, we have used our own review panels to determine the scientific merit of proposals submitted to AID. We are now negotiating with them to have an even closer relationship. I don't see that we are going to be confronted with any type of overlap at all since most of their efforts are of an applied type rather than the development of a new contraceptive agent, for example.

Mr. SHRIVER. As I recall, for this year they had $20 million for family planning. Is part of that research?

Dr. LAVECK. Yes. It was my understanding it was more than $20 million.

Mr. SHRIVER. It was originally but they came back and said that this was all that they could use.

Dr. LAVECK. Yes; this must include money for research.

Mr. SHRIVER. That is all, Mr. Chairman.

Mr. FLOOD. Mr. Casey.

MIDDLE AGE

Mr. CASEY. What do you call middle age?

Dr. LAVECK. I am not sure there is a standard definition. It may be a state of mind, but I would suggest 50 might be the start of middle age for men.

Mr. CASEY. Would be the start. How long would it last?

Doctor, a good many years back some experts were in my hometown. They were from out of town so they were experts, according to the chairman's definition, which I accept and agree with. They said that middle age was not a particular year, or number of years after a man's birth, but was when—if he had children—when he had his last child in college. Do you think that would be a pretty good definition?

Dr. LaVeck. I honestly don't have a good definition. One might develop a definition for males and females that might be quite different.

Mr. Casey. What is middle age?

Dr. LaVeck. I know of no scientific definition for middle age. In general terms, 45 to 65 would be a possible age breakdown for that particular category.

Mr. Casey. I was hoping I could get you to agree with those experts. That would make me feel much better.

Dr. LaVeck. I think most individuals who have their last child in college would fall in that age bracket.

STUDIES OF AGING

Mr. Casey. In these studies on the aging, are you just concerned with their health or are you concerned in all aspects of their well-being?

Dr. LaVeck. We are concerned with the health, psychological, and social aspects of their well-being. For instance, at the Gerontology Research Center we have recently completed a study on problem solving and learning in older individuals as compared to young people. With the advance of time, reasoning ability seems to decrease. A very interesting experiment was set up in which a series of nine different foods were identified for young and older subjects, and the subjects were told that one of these foods was poisoned and would cause death. Then, by reasoning, they were to determine which particular food was poisoned. They were given three types of information: Positive information that would help them identify the food; negative information which told them which foods could not be incriminated; and redundant information, which were data they had already received. The old people handled negative and positive information quite well but they were confused by the redundant information in comparison with young people. This reflects our broad interest in aging.

Mr. Casey. How do you disseminate that information?

Dr. LaVeck. We have an excellent method of disseminating scientific information in the field of aging. We have recently put out an experimental edition of a journal which contains abstracts of all the relevant world literature in the field of aging. This abstract journal is sent to all investigators in the field as well as to libraries that would utilize this type of publication. Within the next few months the journal will be published once a month and will be very current. I wish we could disseminate research information in this way for all our programs.

Mr. Casey. A while back we had Dr. Yolles here and we were all concerned about the number of aged people that are placed in mental institutions and in many instances they do not belong there. Are you contributing anything to getting these people out of there and putting them somewhere where they would be more useful or happier?

Dr. LaVeck. No, we are not working in this particular area, but I would agree with Dr. Yolles that the mental institutions do house a number of older individuals who should be in nursing homes or better living situations.

Mr. Casey. I believe that is all, Mr. Chairman.

Mr. Flood. Mrs. Reid?

LINK BETWEEN MENTAL RETARDATION AND CULTURAL DEPRIVATION

Mrs. Reid. On pages 4 and 5 of your statement you speak of mental retardation research in connection with the problem of psychosocial

deprivation. Are you saying that there is a substantial link between mental retardation and cultural deprivation in addition to a biologic one? Would you comment on this further?

Dr. LaVeck. The link between mental retardation and cultural deprivation is indeed very substantial. According to our best estimates, three-fourths of the Nation's mentally retarded are members of impoverished families living in isolated urban and rural slums. The children in these families are 15 times more likely to be diagnosed as retarded at some period in their lifetime than children in higher income families.

A significant proportion of the culturally deprived reach school age without the necessary skills for systematic learning and are functionally retarded in language, reading, and writing. An appalling number fall farther behind every school year and enter the work world poorly equipped for social and vocational independence. Many are rejected by the Selective Service System for mental unfitness.

The culturally deprived are also more vulnerable to certain biologic conditions associated with mental retardation. Mothers in low-income families receive little or no prenatal care, are poorly nourished, and have far more complications of pregnancy and premature births than the more privileged. Neurological and physical disorders are more frequent in premature than full-term babies. Although the retarded come from all classes of society, the overwhelming majority come from the lower socioeconomic group. In some instances the impact of deprivation is expressed in biologic deficits associated with retardation. Often, however, the early and prolonged adversity under which many disadvantaged children live imposes a ceiling on their intellectual growth potentials. The way in which cultural deprivation causes or contributes to mental retardation is not yet fully defined. That it plays a role—and a very vital one—cannot be denied. A successful attack on poverty would undoubtedly help to combat mental retardation.

RELATION OF RESEARCH CONDUCTED IN UNIVERSITY OF NORTH CAROLINA DAY CARE PROGRAM TO HEADSTART

Mrs. Reid. With reference to your North Carolina center providing day care for the culturally deprived children, how does this differ from our Headstart program? From your brief description, they would appear to be very similar. Couldn't the research they are doing be combined in some way?

Dr. LaVeck. The program of day care for culturally deprived children at the University of North Carolina is a major component of their behavioral research program. This program differs from most Headstart activities in a number of significant ways. Unlike Headstart, whose primary objective is the provision of service, this program is concerned with research into the processes of child development—physical, social, emotional and intellectual—and with research on intervention procedures to prevent mental retardation and to promote optimal growth.

Children from deprived environments generally exhibit normal development during the first few years of life but frequently fall behind in their intellectual performance by the time they reach school age. The reasons for this performance pattern are not completely understood, but seem to reflect the interaction of genetic and social environmental factors. The cumulative effects of deprived living conditions exemplified by poor nutrition, lack of appropriate mental stimulation, limited cultural opportunities, inadequate child-rearing practices, and

lack of proper mental and physical hygiene are all thought to be significant contributory elements.

More precise information is needed on the most effective time for intervention, what aspects of the child's life experience need to be modified and what methods are most likely to succeed. Answers to these questions require both short-term and longitudinal studies. The day care facilities at the University of North Carolina will provide a population for these purposes, some of whom will be studied from infancy through the elementary school years. Investigations will be conducted on curriculum development procedures for improving perceptual and verbal skills in preschool children; mother-child interaction patterns; the effects of self-attitudes on intellectual and social behavior; the relation of cultural traditions to behavior; social behavior and self control; disease processes; delivery of health care; genetics of human behavior and mental traits.

In contrast to Headstart, this day care program will include infants, will stress research rather than service and will experiment with a wider range of innovative teaching techniques, health care and environmental modification. The information obtained in this program should have direct application not only to Headstart operations but to broader social engineering concerns. By the same token, research within Headstart settings and evaluation of the outcomes on development of these children would add another dimension to our understanding.

WOMEN INVOLVED IN CHILD HEALTH RESEARCH

Mrs. Reid. Since your Institute deals with child health and women have traditionally been very active in this field, I am curious to know about the number of women pediatricians and technicians involved in such research. Isn't this an area where more could be encouraged?

Dr. LaVeck. Approximately 8 percent of physicians in the United States are women, and among these it is currently estimated that there are about 4,000 women pediatricians. Roughly 900 are engaged in teaching, research, or preventive medicine on the full-time faculties of medical schools, in teaching hospitals including children's hospitals, or in governmental facilities. All of these women pediatricians involved either full or part time in research are working on problems related to child health. A significant number of women pediatricians with part-time medical school appointments engage to a more limited extent in child health related research.

Approximately 1,500 women biologists and about 500 women behavioral scientists are also involved in health related research. Many are engaged in research with direct relevance to child health. Unfortunately, figures are not available on the number of women research technicians who are working on child health problems.

There are a number of obstacles to the entrance of women into these fields and to their remaining there. Lack of day care facilities for children on university campuses or other places where these women might be trained or work, lack of part-time and evening educational opportunities, lack of part-time jobs, misconceptions about opportunities for marriage, are some of these. Child day care centers, tax deductions for child care expenses, assistance in provision of domestic help, part-time residency, postgraduate and retraining programs, better publicity about opportunities for women, and Federal training stipends, are some of the measures which have been suggested to encourage women to enter these fields and to keep them there.

Mrs. Reid. Thank you, Doctor.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Amounts Available for Obligation

	1969	1970
Appropriation	$73,126,500	$78,411,000
Comparative transfer to: "Salaries and expenses, Office of the Director"	-536,000	...
Cutback required by P.L. 90-364	-1,791,000	...
Total obligations	70,799,500	78,411,000

Disposition of cutback:
To be returned to the Treasury $1,791,000

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Grants:						
80	Research		$41,678,500		$46,564,000		+$4,885,500
	General research support grants		(4,082,000)		(4,469,000)		(+387,000)
	Scientific evaluation		(100,000)		(100,000)		(0)
	Categorical clinical research centers		(500,000)		(500,000)		(0)
	Mental retardation research centers		(2,000,000)		(3,000,000)		(+1,000,000)
90	Fellowships		4,193,000		4,027,000		-166,000
92	Training		10,012,000		9,621,000		-391,000
	Direct Operations:						
94	Laboratory and clinical research	222	6,065,000	279	6,373,000	+57	+308,000
98	Collaborative research and development	29	3,975,000	32	6,721,000	+3	+2,746,000
104	Biometry, epidemiology and field studies	22	2,022,000	23	2,176,000	+1	+154,000
105	Training activities	4	89,000	4	85,000	...	-4,000
106	Review and approval of grants	85	1,956,000	88	2,037,000	+3	+81,000
107	Program direction	47	809,000	49	807,000	+2	-2,000
	Total obligations	409	70,799,500	475	78,411,000	+66	+7,611,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions..	409	475	+66
Full-time equivalent of all other positions.....	16	16	...
Average number of all employees.....	423	465	+42
Personnel compensation:			
Permanent positions.....	$3,967,000	$4,442,000	+$475,000
Positions other than permanent...	79,000	89,000	+10,000
Other personnel compensation.....	104,000	117,000	+13,000
Total personnel compensation...	4,150,000	4,648,000	+498,000
Personnel benefits.....	479,000	532,000	+53,000
Travel and transportation of persons	179,000	193,000	+14,000
Transportation of things.....	46,000	52,000	+6,000
Rent, communications, and utilities	165,000	180,000	+15,000
Printing and reproduction.....	95,000	107,000	+12,000
Other services.....	8,818,000	11,599,000	+2,781,000
Supplies and materials.....	342,000	385,000	+43,000
Equipment.....	642,000	503,00	-139,000
Grants, subsidies, and contributions	55,883,500	60,212,000	+4,328,500
Total obligations by object....	70,799,500	78,411,000	+7,611,500

Summary of Changes

1969 estimated obligations	$70,799,500
1970 estimated obligations	78,411,000
Net change	+7,611,500

	Base Positions	Base Amount	Changes to Base Positions	Changes to Base Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay raise	...	...	...	$8,000
B. Program				
1. Research grants	...	$41,678,500	....	4,885,500
2. Laboratory and clinical research	222	4,000,000	57	790,000
3. Collaborative research and development	29	3,938,000	3	2,754,000
4. Biometry, epidemiology and field studies	22	1,965,000	1	189,000
5. Review and approval	85	1,371,000	3	20,000
6. Program direction	47	750,000	2	12,000
Total program increases	...	...	66	8,650,500
Total increases	...	...	66	8,658,500
Decreases				
A. Built-in				
1. Non-recurring equipment	...	...	...	336,000
B. Program				
1. Fellowships	...	4,193,000	...	166,000
2. Training grants	...	10,012,000	...	391,000
Total program decreases	...	...	...	557,000
C. Centrally furnished services from the National Institutes of Health Management Fund	...	2,810,000	...	154,000
Total decreases	...	...	...	1,047,000
Total Net Change Requested	...	...	+66	+7,611,500

Explanation of Changes

Research Grants--The increase of $4,885,500 will provide $3,498,500 for the regular program which includes $3,304,500 to accelerate the Reproduction and Population grants program and $1,000,000 to support research to be conducted in the newly constructed Mental Retardation Research Centers. In addition $387,000 is provided for General Research Support Grants.

Fellowships--The decrease of $166,000 will provide for 207 fellowships in 1970 compared to 252 in 1969.

Training Grants--The decrease of $391,000 will provide for 127 grants in 1970 compared to 142 in 1969.

Laboratory and Clinical Research--The increase of 57 positions and $790,000 will be distributed among the various laboratories and branches of the expanding Intramural Program. Each of the Institute's five major program areas - Reproduction and Population Research, Perinatal Biology and Infant Mortality, Growth and Development, Aging, and Mental Retardation - will be allocated some of the increase. A portion of the increase will also be used to equip newly acquired laboratory facilities.

Collaborative Research and Development--The increase of 3 positions and $2,754,000 will provide for an increased research contract program in the reproduction and population and fertility control areas. The largest portion of the contract increase will be used for the development of new contraceptive devices and techniques. The psychosocial aspects of population and family planning will also receive emphasis under this expanding research contract program administered by the Institute's newly created Center for Population Research.

Biometry, Epidemiology and Field Studies--The increase of 1 position and $189,000 will be used to strengthen the epidemiological research contract program.

Review and Approval--The increase of 3 positions and $20,000 will provide for increased grant management support.

Program Direction--The increase of 2 positions and $12,000 will be used by the Center for Population Research to administer the expanding Population Research Contract Program.

Significant Items in House and Senate Appropriations Committee Reports

Item	
1969 House Report	
(1) The Institute should support research in areas which seem likely to produce significant technological advances (in family planning). (p.26)	(1) Approximately one-third of the program for family planning contracts in 1969 is devoted to the development of new contraceptive methods. In 1970, it is estimated that one-half of the contract increase will be used for this purpose.
1969 Senate Report	
(1) The committee feels that the Institute must accelerate its efforts to solve the many problems that still stand in the way of developing effective, safe, low cost, reversible, and generally acceptable contraceptives. (p.51)	(1) During 1969 the Institute's population research program will use a three-pronged effort in its attack on the problems associated with the "population explosion". The Institute's total program including research grants will be concentrated in the following three research areas: 1) the medical effects of contraceptives, 2) the development of new contraceptives, and 3) the psychosocial aspects of population and family planning. The major directed effort in this program to develop contraceptives meeting all the desirable characteristics is through the contract mechanism.
(2) The committee believes that support of these (Mental Retardation Research) centers at an appropriate level to make their research and training programs a success must be given high priority and therefore expects that future budget requests will make adequate allowances for this important national program (p.52)	(2) The 1970 budget request contains an increase of $1,000,000 for these centers, a 50% increase to support the 11 centers to be in operation in 1970.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act Section 301---Research and Investigation, in general.....	Indefinite
Title IV, Part E ---National Institute of Child Health and Human Development.....	Indefinite

The legislative authority which provides for the award of grants for research, research training, and fellowships is included in section 301 of the Public Health Service Act.

The Public Health Service Act, Title IV, National Research Institutes, Part E, Institutes of Child Health and Human Development and of General Medical Sciences--

"Sec.441. The Surgeon General is authorized, with the approval of the Secretary, to establish in the Public Health Service an institute for the conduct and support of research and training relating to maternal health, child health, and human development, including research and training in the special health problems and requirements of mothers and children and in the basic sciences relating to the processes of human growth and development, including prenatal development."

"Sec. 444. The Surgeon General shall, through an institute established under this part, carry out the purposes of section 301 with respect to the conduct and support of research which is the function of such institute... The Surgeon General is also authorized to provide training and instruction and establish and maintain traineeships and fellowships, in the institute established under section 441 and elsewhere in matters relating to diagnosis, prevention, and treatment of a disease or diseases or in other aspects of maternal health, child health, and human development, with such stipends and allowances (including travel and subsistence expenses) for trainees and fellows as he deems necessary, and, in addition, provide for such training, instructions and traineeships and for such fellowships through grants to public or other nonprofit institutions."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and expenses, Office of the Director," National Institutes of Health.....	$536,000	...	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH management fund.

National Institute of Child Health and Human Development

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)
1965	43,169,000	43,696,000	42,696,000	42,696,000
1966	53,524,000	53,524,000	55,024,000	55,024,000
1967	61,448,000	61,422,000	64,922,000	64,922,000
1968	68,621,000	68,621,000	74,621,000	68,621,000
1969	75,394,000	70,859,000	76,359,000	73,126,500
1970	78,411,000			

National Institute of Child Health and Human Development

Year	Estimate to Bureau of Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)
1965	44,432,000	43,169,000	43,696,000	42,696,000	42,696,000
1966	55,272,000	53,524,000	53,524,000	55,024,000	55,024,000
1967	68,349,000	61,448,000	61,422,000	64,922,000	64,922,000
1968	75,562,000	68,621,000	68,621,000	74,621,000	68,621,000
1969	77,588,000	75,394,000	70,859,000	76,359,000	73,126,500
1970	77,715,000	78,411,000			

Justification

National Institute of Child Health and Human Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	409	$4,629,000	475	$5,180,000	+66	+$551,000
Other expenses	...	66,170,500	...	73,231,000	...	+7,060,500
Total	409	70,799,500	475	78,411,000	+66	+7,611,500

General Statement

Biological and social concerns of the 1960's--mental retardation, family planning, infant mortality, aging--gave rise to the National Institute of Child Health and Human Development in 1963. Its broad mandate to unravel the mysteries of human development from the moment of conception until the end of life-will have a profound effect on our national life. This Institute's research will contribute to the solutions of many of the social problems that face our country. Through knowledge gained here, fewer infants will die. The number of defects and deficiencies--both biological and behavioral--present in our population will decrease. Progress will be made in such diverse concerns as control of fertility and the problems associated with aging. The consequences of the Institute's efforts will be optimal development for many who, without these efforts, would not develop their full potential.

The request of $78,411,000 for 1970 is an increase of $7,611,500 over the comparable 1969 figure.

This increase will be used primarily for four purposes:

1) $3,304,500 to support research grant projects in reproduction and population; 2) $1,000,000 for support of research to be conducted in the newly constructed Mental Retardation Research Centers; 3) $308,000 to support development of the intramural research programs in new facilities; and 4) $2,850,000 to support a contract program in population research directed to a) developing an array of new contraceptive methods suited to a variety of conditions and preferences, b) developing a better understanding of the factors that affect the birth rate, and c) to assist in the world-wide effort to reduce excessive rates of population growth through social and demographic studies.

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Regular projects....	$34,996,500	$38,495,000	+$3,498,500
Special program.....	6,682,000	8,069,000	+1,387,000
Total research grants	41,678,500	46,564,000	+4,885,500

Introduction:

This activity supports regular research grant projects in reproduction and population, perinatal biology and infant mortality, growth and development, adult development and aging, and mental retardation. In addition, funds are provided for general research support grants, scientific evaluation grants, categorical clinical research center grants, and mental retardation research center grants.

Program Plans for 1969 and 1970:

Reproduction and Population Research

The reproduction and population research program has three basic objectives. One, increasing basic information on the biological, behavioral and psychosocial processes of reproduction and contraception in humans and animals. Two, adding to fundamental information concerning population growth, dynamics, change, and regulation. And, three, facilitating the development of population policy and action programs, such as family planning, contraceptive usage, and fertility regulation. Progress toward the attainment of these three objectives will, among other things, contribute to the understanding of, and ability to deal with, problems of excess rates of population growth so evident throughout the world. The program strives to integrate biomedical and psychosocial research with education and training, and with the search for new mechanisms, new goals, and deeper insight into the phenomena of reproduction.

It is becoming increasingly evident that psychosocial and behavioral research is very important to the understanding of reproduction, population dynamics, and family planning. Such research may also be aimed at the development of population policy and action programs which deal with such problems as fertility regulation and family planning. Because of the growing significance of behavioral and psychosocial research, greater emphasis is being given to stimulation and development of such research.

Much more needs to be known about the relation of human fertility to family planning. The Institute is currently supporting studies in this area. Studies are needed on the psychosocial factors involved in the use and in discontinuing the use of contraceptives. The development of attitudes and decisions concerning child bearing and family spacing require careful study. Induced abortion is a pervasive, world-wide problem and the Institute is supporting a study on one important aspect, how to measure accurately the extent of the problem. Greater understanding of the abortion problem must be developed to increase society's ability to deal with it intelligently.

The nature and measurement of population change is receiving attention. The effects of population growth and increased social stress on animals are being studied by Institute grantees. The relationship of reproductive behavior to hormonal activity is also under investigation.

The biomedical component of the program covers investigations of reproductive phenomena from ovum and sperm development to the process of implantation among mammals. It is only by the acquisition of deeper insights into basic biological processes of reproduction that there can be much hope of developing new contraceptives which are compatible with health, effective, and generally acceptable. Reports of the adverse side effects of available oral contraceptives, and the unknown mechanism of action of intrauterine devices (IUD's) are evidence of the need for new contraceptives.

A number of priority areas have been identified in the program for special emphasis: ovulation and gamete transport, luminal fluids of the reproductive systems, immunological aspects of the fertilization process, biology of the corpus luteum, releasing factors and gonadotropic hormones, population genetics, implantation, problems of infertility, and the biology of the male reproductive system. These are areas of investigation in biomedical research which are insufficiently supported and/or where the state of the art lacks sophistication.

Increased attention needs to be given to the development and evaluation of contraceptive agents. The research emphasizes such things as: anti-implantation agents, ovulation inhibitors, secretory stimulators, pharmacologic agents, and spontaneous and induced abortions. Conferences and workshops are being encouraged for the purpose of assessing the state of the art, pointing up gaps in our knowledge, identifying and determining the feasibility of research areas and methods, and to identify effective investigators.

Perinatal Biology and Infant Mortality

A major concern of this Institute is the stimulation and support of fundamental research related to maternal and infant health in general and, in particular, to the reduction of infant mortality. There is an urgent need for new research approaches that will make possible the realization of maximum health and well-being for every pregnant woman and her progeny.

To achieve this goal, the Institute has developed a research program around the following broad areas: 1) pregnancy maintenance, management, and termination; 2) intrauterine fetal survival and well-being; 3) extrauterine adaptation; and 4) disorders of infancy. Since the major causes of infant mortality are prematurity and the respiratory disorders related thereto, the Perinatal Biology and Infant Mortality Program emphasizes a multi-faceted research effort to identify maternal and fetal factors which inhibit fetal maturity, which contribute to the premature termination of pregnancy, and which will determine the adaptive role of lung tissues essential for oxygen/carbon dioxide exchange and of homeostatic mechanisms such as those involved in body temperature regulation.

Each year in this country, about 300,000 infants are born weighing 5 1/2 pounds or less. They must wage an uphill struggle for survival and normal health. For at least one-sixth of these infants the battle is a losing one, and they die during the neonatal period. Should the infant survive these first difficulties and others related to intrauterine life and the process of birth, long periods of expensive hospitalization and nursing care are frequently required before the infant can be cared for at home. Each year, Americans spend an estimated $500,000,000 for such hospital care services, not including continued constant care which is often necessary for infants severely brain damaged or crippled at birth.

To prevent this tremendous waste in human life and the expenditure of millions of dollars yearly, there is a pressing need for research into the nature, causes and sequelae of prematurity, and the patterns of intrauterine growth, both normal and abnormal. These are, for the most part still obscure.

Until more is known about the genetic, environmental and physiological factors that influence fetal growth and development, low birthweight will remain an outstanding child health problem. The National Institute of Child Health and Human Development's Perinatal Biology and Infant Mortality Program, through the development of an integrated program of research and training, is seeking to accomplish four major objectives as part of its efforts to gain new knowledge of, and solutions to, problems associated with low birth weight. These objectives are: 1) a greater understanding of maternal and fetal factors that lead to the initiation of labor, including identification of indices of fetal maturation; 2) identification of those conditions in the premature infant that militate against adaptation to the extrauterine environment; 3) clarification of the effects of changes in the intrauterine environment (i.e., chemical, temperature, pressure) as well as the influence of infectious agents on fetal development through the gestation period; 4) assessment of the factors involved in the complex area of maternal-placental-fetal nutrition.

Studies of extrauterine adaptation will be devoted, to a considerable degree, to research concerning respiratory defects and malfunction, with special emphasis on the respiratory distress syndrome, including hyaline membrane disease. Idiopathic respiratory distress, i.e., unrelated to illness from recognized causes of respiratory problems, occurs in approximately one-fourth of the prematurely born. Of this number over 20 percent die, accounting for between 20,000 and 25,000 deaths each year. Responsible clinicians throughout the country continue to use the best available methods of treating respiratory distress, with disappointing results. The pathogenesis of this disorder remains a mystery and the treatment is essentially empirical. Research pertaining to idiopathic respiratory distress would be greatly enhanced by an appropriate animal model, since some of the most fundamental questions that need to be answered cannot ethically be approached with studies of human infants. Sub-human primates would appear to be the best animal models for in vivo studies of etiologic and predisposing factors in idiopathic respiratory distress.

Conflicting reports on the relationship of maternal nutrition to fetal development, premature birth, and neonatal survival have derived from studies based on different ethnic groups and varying ecological situations. Thus, it is extremely difficult to define at present how nutrition is related to infant morbidity and mortality. More definitive studies using animal models and well designed epidemiologic and demographic studies in man are needed to determine the impact of nutrition on pregnancy outcome. It is mandatory that existing epidemiological data in other countries, and our own, are carefully examined and useful points gleaned. At the same time, key faults and weak areas must be uncovered for future conditions.

Congenital defects represent a group of abnormalities which are present at birth and originate at conception or during intrauterine development. In the broadest sense these congenital abnormalities include metabolic as well as structural defects. In human beings the seventh to tenth week embryo is most vulnerable to teratogenic agents, although teratogenic effects of ionizing radiation can occur after the first trimester of pregnancy. While the effects of teratogenic agents and/or genetic aberrations may result in fetal wastage by the twentieth week of pregnancy, congenital abnormalities may become apparent during later pregnancy, at birth, or still later in life. For example, although only two viral agents, rubella virus and salivary gland virus, have been shown to have true teratogenic effects there are other viruses that may produce intrauterine infections which result in a spectrum of clinical end-results ranging from death, live birth with a severely infected infant usually born prematurely, to a minimally ill infant whose disease may, in fact, be missed entirely. The overall incidence of major malformations is most reliably estimated at greater than five percent of all births, of which approximately half are detected at birth. The problem of congenital malformations is assuming greater absolute importance

because of higher infant survival rates, because of the increasing availability and use by pregnant women of physician-prescribed and non-prescribed pharmacologic agents, and, possibly, because of the increasing levels of radiation in the general environment as well as in diagnosis and therapy. Children born with congenital anomalies often impose a tremendous economic burden, particularly if the parents are young and within the upper-lower or lower-middle income salary ranges. This economic pressure tends to aggravate the parental tensions and anxieties that may be associated with the birth of children with congenital defects.

The sudden and unexpected death of an infant, one that remains unexplained after a complete autopsy and case study, accounts for approximately ten percent of deaths during the first year of life in America and is probably the leading cause of deaths in infants over one week of age. Infectious diseases have long been suspected as a major contributory factor in sudden death syndrome (SDS) because of seasonal distribution (twice as many cases in winter as summer), age factor (most cases occur between five weeks and five months, with a peak incidence between two and four months of age), and the presence of a known minor infection. Information obtained over the last five years by investigators supported by this Institute appears to support the view that SDS is caused by a threshold phenomena surrounding a minor infection. Such an infection might be innocuous in an adult, but could, in an infant, act on the autonomic nervous system in such a manner as to cause the vocal cords to constrict. Constriction of the vocal cords, in turn, closes off the passage of air in the windpipe and death results from asphyxiation. Other known epidemiologic factors in SDS include a higher incidence in males (61 percent as determined in a Seattle study), in low birth weight babies, and in poor families. Although some light has been thrown on this problem, much remains to be learned. Fundamental studies using appropriate animal models appear to be essential to the solution of this infant health problem.

Growth and Development

The Institute-supported research in growth and development is concerned with the period of development extending from birth to adulthood. The ultimate goal is the enhancement of individual capabilities through an understanding of the factors, both biological and behavioral, contributing to human variability and optimal development.

Biological maturation is one aspect of human development which will receive special emphasis in 1970. Current data suggest that children are maturing at an earlier age. Not only is this of considerable interest insofar as physical size and sexual maturation are concerned, but it may be importantly related to questions of physical fitness and of preparation for adult life. Laboratory, clinical and field studies will be conducted to define more precisely the relationships between chronologic age and indicators of biologic age such as bone formation and secondary sexual characteristics. Special emphasis will be given to evaluating how well different groups of children compare against established growth standards to determining what racial, socioeconomic, or medical factors may account for observed variations. Investigations of essential factors in maintaining optimal performance will range from the development of resistance to disease to the need for balanced schedules of rest and exercise and will include the capacity of various organ systems to cope with normal and adverse conditions.

In addition to measuring growth in the whole organism, it is essential to study the physiological mechanisms controlling growth; to explore the events taking place at the cellular level leading to increases in cell size, cell number and the synthesis of tissues; and to establish the mechanisms whereby the substances which make up living matter (such as proteins) are manufactured and regulated within the growing organism. Of particular importance is clarification

of the role of the endocrine glands and their interaction with neural and environmental stimuli. Individual differences in growth, the more serious growth impairments, and deficits in neurological or mental development can only be understood when these processes have been clearly defined. Rational approaches to prevention or therapy of developmental deficits must rest upon a solid basis of knowledge concerning the growth process. Multidisciplinary approaches to these complex problems will be encouraged by this program.

The problem of malnutrition will continue to receive special emphasis in 1970. Interrelated studies will be undertaken with undernourished and disadvantaged children to define the association between nutritional status and intellectual development. Attention will be given to nutritional factors in brain and nervous system development, as well as to those critical periods when improper nutrition may inflict the greatest damage. The synergistic effect between poor nutrition, reduced resistance to infectious disease, and impaired functional development will be another focal area. Definition of the social, attitudinal, and environmental factors contributing to childhood malnutrition will be aggressively sought. Results of these studies will be applicable to improved nutritional intervention programs.

In approaching the complexity of human development from the behavioral standpoint, research on maximizing the capacity of the individual to learn will receive primary emphasis. The success of our society now rests and will continue to rest on the degree to which individuals can learn new skills and adapt to new challenges. This will require expansion of our knowledge concerning how man learns and how the learning process can provide maximal fulfillment for each child. To the extent that functional illiteracy and impaired learning potential prevail, and to the degree to which the gifted persons are not given special opportunities to realize their full potential, our culture will fail to make maximal progress.

It is apparent that impoverished environments inhibit the development of learning and adaptive processes. The mechanisms for these effects are not known. A broader base of fundamental knowledge concerning psychological development and learning is needed. A greater understanding of the role of early stimulation and deprivation on cognitive development will be sought as will the consequences of social deprivation on brain structure and function.

Special emphasis will be given to determining at what age inadequate intellectual development becomes permanent and irreversible. Attention will be given to the development of measures for evaluating present and future improvement of learning ability as new discoveries and techniques improve learning capacities.

Biological and behavioral research will be directed towards a better understanding of the factors contributing to normal development of speech and language functions and the role these skills play in the development of individuals as members of society. With this knowledge, reading and speaking disorders may be prevented or ameliorated and children will be able to acquire greater speech, language, and reading facility than at present.

A second area of concentration in behavioral studies is the problem of youth in a mass society. As the American society becomes more complex, as our cities become more crowded, as schools attempt to face problems of increasingly complex technical education and of heterogeneous student bodies, our understanding of how children and youth develop into contributing members of society must increase. For example, a better understanding is needed of how children respond to diverse and sometimes conflicting social influences arising from parents, peer groups, mass media, schools and other socializing forces. Particular attention will be given to examining ways in which various social institutions combine to influence

the development of skills and values needed to meet, constructively, adult responsibilities. A better understanding will be sought of the factors leading to social and emotional problems among adolescents, particularly as expressed through agressiveness, irresponsibility, and impaired character development.

Adult Development and Aging

This Institute responds to the pressing need to understand the aging process by supporting research in the fields of biological, psychological and social aging. The ultimate goal of this research is to provide man with new levels of health and vigor throughout the span of adult years. Although the impact of the aging process on man has long been acknowledged and often feared, the underlying causes, for the most part, are not known.

A clear consequence of the aging process is man's increased vulnerability to disease as he ages. That vulnerability, as judged by the mortality rate, is lowest at 10 years of age and thereafter doubles every 8.7 years. The cumulative effect of aging is most distressing in persons over 65, of which there are approximately 20 million or 10% of the U.S. population. Lack of knowledge of the aging process stands out in bold contrast to the magnitude of knowledge being gained in related areas, such as research in major diseases. This situation exists in spite of recognition that comprehension of the aging process is essential to the complete and effective understanding of age-associated diseases and maintenance of desirable levels of health throughout the life-span.

To meet biomedical needs directly related to aging, this Institute will support research in the biology, psychology and sociology of aging. Research in biological aging will be encouraged at all levels from molecular and sub-cellular through the whole organism. Studies at the sub-cellular and cellular level include the use of tissue culture systems of normal human cells that age, senesce, and die in the culture environment. This system provides a unique analytic approach to cellular aging that could provide new insight into very basic processes that are reflected in the overt signs of aging in the adult person. Studies of this type will be encouraged through grant support. In addition, because of a possible significance of this model system, development of an organized research effort incorporating contract support will be explored.

Biological research in aging will include continued support and encouragement of research directed toward physiological and biochemical changes at the organismic level with age. Such studies include all the organ systems and the various biochemical systems such as the complex of enzymatic systems. Major changes are known to occur in many of these systems with increasing age, and often these changes are recognized as detrimental to the general health and vitality of the individual. Included in research programs that address questions of this kind are longitudinal studies of humans.

Longitudinal studies follow subjects through extended periods of their life. Because of the magnitude and significance of this research, it receives substantial program involvement. Longitudinal studies involve such complexities as stability of investigators, stability of subjects, sampling of population, uniformity of methodology between different longitudinal studies and special problems of statistical analysis. Optimum utilization and comparability of research data from these investigations is brought about by interaction encouraged through conferences sponsored by this Institute.

It is becoming increasingly clear that many of the older persons in this country do not live in a psychosocially adequate environment. Of concern to this Institute is the lack of an adequate research base for understanding the psychological and social environs of the aging adult person. The factors involved appear very complex and successful pursuit of this research will require recruitment of

highly qualified scientists into the field. It is recognized that after the attainment of maturity the effectiveness of certain psychological functions diminishes with age. However, the accumulation of experience leads to continued improvement of some complex functions until relatively late in the life span. Such positive factors may be negated by some of the current attitudes and practices relative to intellectual challenge throughout adult years, early retirement, family structure, and housing. The environment of man changes as he ages in ways that are not always favorable to continued individual growth.

Particular emphasis will be placed on developing new approaches to support research which will encourage most effective use of resources. This can be partially accomplished by using present funding procedures to encourage support and growth of centers in aging research. Each center would have one or more central substantive interests and an integrated research program designed to study some aspect of aging in depth and breadth. Centers of this type would vary in size and complexity and provide an atmosphere of common purpose and commitment. They would provide an inter-disciplinary structure for graduate training, and a base to attract capable scientists not now intimately involved in aging research.

Conferences will provide a means for stimulating interest and activity in research areas--now inadequately investigated--pertinent to understanding the aging process. Projected conferences range from such subjects as the use of lower-life forms in the studies of the biology of aging to planning and programming for support of organized research. These conferences permit an evaluation of the state of the art of a particular field for relevance to aging research and should lead to support of investigators previously not involved in aging studies.

A summer course in the biology of aging will be supported for the second consecutive year. Recognized as one of the most significant instruments at the Institute's disposal for encouraging well-qualified researchers to move into the field of aging, it is anticipated that a course of this type will be conducted annually. The course attracts a highly qualified and motivated faculty and student body, and confronts extant theories of aging with the latest research concepts in significant branches of science.

Mental Retardation

Mental retardation today afflicts the lives of an estimated 6 million persons in the United States. Its impact is directly felt by the some 20 million family members who share the burden and problems of care of the retarded whose inadequate intellectual development impairs their ability to learn and to adapt to the demands of society. The causes of mental retardation are multiple and involve both physical and environmental factors operating singly or in subtle interactions. Resolution of this complex problem requires the scientific talent from many disciplines--biological, behavioral and social--in a concerted effort involving basic, clinical and applied research over an age span from conception through maturity. The Institute's program of research and research training support represents a major arm of our nation's effort to combat mental retardation which ranks as a major health, social and economic problem.

Congress, in 1964, recognized the limited resources devoted to mental retardation research and the need for centers of research competence with special capability for meeting the research demands of this multi-faceted problem. P.L. 88-164 authorized the construction of mental retardation research centers for the purpose of finding the causes and means for preventing and ameliorating mental retardation.

Implementation of this authority resulted in construction grant awards for 12 research centers to institutions for research and training in 11 different States. Four of the centers were completed and became operational in 1968; 4 will begin operations in 1969, 3 in 1970 and 1 in 1971.

	Mental Retardation Research Centers	Year Completed
1)	University of Chicago Chicago, Illinois	1967
2)	Children's Hospital Cincinnati, Ohio	1968
3)	George Peabody College for Teachers Nashville, Tennessee	1968
4)	University of Colorado Medical Center Denver, Colorado	1968
5)	Albert Einstein College of Medicine Yeshiva University, New York, New York	1969
6)	University of Washington Seattle, Washington	1969
7)	University of California at Los Angeles Los Angeles, California	1969
8)	University of Kansas Lawrence, Kansas	1969
9)	Walter E. Fernald State School Waltham, Massachusetts	1970
10)	Children's Hospital Medical Center Boston, Massachusetts	1970
11)	University of North Carolina Chapel Hill, North Carolina	1970
12)	University of Wisconsin Madison, Wisconsin	1971

The time period between awarding the center construction grant and completing construction has been utilized by the Institute to help the centers to strengthen and expand existing research and research training activities and capability, to plan for new and needed research approaches, and to develope special populations of retarded and potentially retarded patients and research subjects. Under this program the centers have gained and will continue to gain a high state of readiness to carry out their research missions prior to completion of construction.

When fully operational the centers will add significantly to our capability for meeting previously unmet or inadequately met problems of which the following are illustrative: 1) Too little is known of the long-range consequences for development resulting from aberrations of pregnancy, delivery and the neonatal period. The resulting developmental defects often are not expressed until much later in the development of the child. Many data bearing on these events and their later developmental consequences are lost for lack of systematic and coordinated research involving obstetrical and neonatal investigators concerned with studies of longitudinal development. The centers designed to meet these problems will offer a research environment and resources necessary for such long-range studies as well as the teams of investigators composed of members from the different disciplines concerned with these problems; 2) Similarly, coordinated interdisciplinary research in the center settings will permit the assessment of the long-range effects of medical treatment and behavioral training programs on known, biomedically documented subjects.

An overwhelming majority of the retarded (approximately five million) are concentrated in the lowest socioeconomic segments of society. Despite the fact that a significant proportion of this group has no discernable central nervous system abnormality, comparatively little formal study has been undertaken to differentiate those variables, from many, which have etiological significance. Four of the mental retardation research centers plan a major focus on these problems; in addition, the Institute will expand its current, broad efforts to better understand and correct the causes of defects resulting from biological, psychological, and social deprivation.

Malnutrition in mothers and their developing young child is of major concern to researchers concerned with preventing mental retardation. The Institute will give particular emphasis to studies concerned with prevention of retardation by investigations of the role played by malnutrition, a major variable among those involved in conditions of deprivation.

The Institute's current efforts to promote the intellectual growth of children who have been deprived by life have focused on early intervention through preschool enrichment and modification of parent behaviors. The limited success attained thus far by these efforts encourages further studies with an increased emphasis on interventions below preschool age and on the shaping of parent behavior patterns conducive to improved intellectual development for their children.

In recent years there has been an enormous expansion in our knowledge of biology at the molecular level. Newly acquired techniques which permit an extensive study of cellular regulatory processes have not yet been applied to any great extent in the study of mongolism. Mental retardation associated with mongolism represents a major problem of relatively high incidence. The Institute believes it necessary to increase its effort toward resolution of this problem through support for basic studies of the molecular biology of the mongol.

The past decade has seen tremendous strides in cytogenetics. This field of research holds even greater promise for improving our understanding of the causes of mental retardation. New technologies, methods, and increased numbers of cytogenetic researchers permit the Institute to expand its support in this needed area of research.

The Institute is heavily involved in support of research on inborn errors of metabolism. Dietary treatment provides this area of research with the promise of favorably altering the course of subnormal development in children with phenylketonuria, galactosemia, and other metabolic disorders. Continuation and expansion of the Institute's research efforts on these problems is encouraged by the prospects for corrective and helpful applications to victims of these disorders.

Summary:

Increases in research grants in 1970 will be used almost entirely to accelerate research activity in the Reproduction and Population Research program and for the support of the Mental Retardation Research Centers. Of the $4,885,500 increase, $3,304,500 will go to the Reproduction and Population Research program to support grants aimed at developing new contraceptives, evaluating the medical effects of contraceptives, and investigating the psychosocial aspects of population and family planning.

The Mental Retardation Research Centers, constructed with Federal support of over $26,000,000, will receive $1,000,000 of the increased grant funds to support research at the 11 centers to be in operation during 1970.

Distribution of Research Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Noncompeting projects	613	$23,155,500	612	$23,404,000	-1	+$ 248,500
2. Competing projects...	319	11,841,000	352	15,091,000	+33	+3,250,000
3. Subtotal regular program	932	34,996,500	964	38,495,000	+32	+3,498,500
4. General research support	--	4,082,000	--	4,469,000	--	+387,000
5. Scientific evaluation..	--	100,000	--	100,000	--	--
6. Categorical clinical research centers.....	--	500,000	--	500,000	--	--
7. Mental retardation research centers.....	--	2,000,000	--	3,000,000	--	+1,000,000
8. Total research grants..	932	41,678,500	964	46,564,000	+32	+4,885,500

Research Grants Program Analysis

1. Reproduction & Population Research	$7,628,500	$10,933,000	+$3,304,500
2. Perinatal Biology & Infant Mortality.....	8,049,000	8,106,000	+57,000
3. Growth & Development ..	11,234,000	11,314,000	+80,000
4. Aging.....	3,255,000	3,278,000	+23,000
5. Mental Retardation.....	4,830,000	4,864,000	+34,000
6. Subtotal regular program	34,996,500	38,495,000	+3,498,500
7. General research support	4,082,000	4,469,000	+387,000
8. Scientific evaluation...	100,000	100,000	...
9. Categorical clinical research centers	500,000	500,000	...
10. Mental retardation research centers.....	2,000,000	3,000,000	+1,000,000
11. Total research grants....	41,678,500	46,564,000	+4,885,500

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Fellowships.....	$4,193,000	$4,027,000	-$166,000

Introduction:

The primary objective of the fellowship program is to increase the number of scientists qualified to carry on independent research in child health and human development.

Program Plans for 1969 and 1970:

The above objective is carried out through four means: 1) the postdoctoral fellowships are awarded in a wide variety of disciplines to encourage young investigators to obtain research training and experience so that the country's research potential can be maintained; 2) special fellowships are awarded to more mature individuals, often faculty members on sabbatical leave, who find it highly productive to spend a year or two in research laboratories other than their own in which they can improve current skills or acquire new ones; 3) highly successful research career development program supports the younger investigator of demonstrated ability and provides the means whereby the grantee institutions can expand their potential; 4) the research career award provides stable support for the senior investigator.

Funds requested for 1970 will provide for 207 awards, compared to 252 in 1969, a decrease of 45. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	128	$2,556,000	149	$3,075,000	+21	+$519,000
b. Competing	21	421,000	15	301,000	-6	-120,000
2. Supplementals	(10)	10,000	(15)	15,000	(+5)	+5,000
3. New.....	103	1,206,000	43	636,000	-60	-570,000
4. Total fellowships ...	252	4,193,000	207	4,027,000	-45	-166,000

Fellowships by type of program

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral.....	81	$677,000	49	$426,000	-32	-$251,000
2. Special.....	64	812,000	36	486,000	-28	-326,000
3. Research Career:						
a. Career.....	7	218,000	7	220,000	--	+2,000
b. Development awards.	100	2,486,000	115	2,895,000	+15	+409,000
4. Total fellowships...	252	4,193,000	207	4,027,000	-45	-166,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total Training Grants....	$10,012,000	$9,621,000	-$391,000

The training grant programs of the Institute are designed to: 1) attract individuals to careers in the field of child health and human development; and 2) produce investigators who will contribute significantly to the mission of the Institute. In order to achieve these goals, the Institute supports training grants in reproduction and family planning, perinatal biology and infant mortality, growth and development, aging, and mental retardation. The goal of the training is to produce research investigators capable of increasing knowledge of human development not only in terms of physical form and function but also in terms of mental, emotional, intellectual and social development.

Training grants are available to institutions which can provide excellent training programs for both predoctoral and postdoctoral trainees. These programs prepare both research and clinical scientists for careers in the area of child health and human development. The research training prepares future investigators to contribute to the research mission of the Institute. Some of the grants provide clinical training which prepares physicians who are not only skilled clinicians but also specialists, able to evaluate research data critically, translate the results of research for patient care, and keep abreast of their field.

Funds requested for 1970 will provide for 127 awards, compared to 142 in 1969, a decrease of 15. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Training Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuations:						
a. Noncompeting.....	125	$8,514,000	105	$7,843,000	-20	-$671,000
b. Competing.....	11	950,000	13	1,041,000	+2	+91,000
2. Supplementals.....	(2)	80,000	(2)	101,000	--	+21,000
3. New.....	6	368,000	9	536,000	+3	+168,000
4. Scientific evaluation	(1)	100,000	(1)	100,000	--	--
5. Total training grants	142	10,012,000	127	9,621,000	-15	-391,000

Training Grants (By type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Graduate.....	142	$9,912,000	127	$9,521,000	-15	-$391,000
2. Scientific evaluation	(1)	100,000	(1)	100,000	--	--
3. Total training grants	142	10,012,000	127	9,621,000	-15	-391,000

Laboratory and Clinical Research

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	222	$2,410,000	279	$2,886,000	+57	+$476,000
Other expenses		3,655,000		3,487,000		-168,000
Total	222	6,065,000	279	6,373,000	+57	+308,000

Introduction:

Ten laboratories and branches conduct the Intramural Research operations in the program areas of the Institute. These include Developmental Biology Branch, Social and Behavioral Sciences Branch, Reproduction Research Branch, Laboratory of Biomedical Sciences, Behavioral Biology Branch, Children's Diagnostic and Study Branch, and the Gerontology Research Center (Baltimore), composed of the Laboratory of Molecular Aging, Laboratory of Behavioral Sciences, Laboratory of Cellular and Comparative Physiology, and Clinical Physiology Branch.

The funds requested for laboratory and clinical research represent a net increase of $308,000. The increase provides for $790,000 program increase; $5,000 for annualization of the 1969 pay raise; offset by decreases of $336,000 for non-recurring equipment and $151,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Program Plans for 1969 and 1970:

The Office of the Associate Director for Intramural Research is engaged in program development and personnel recruitment to utilize the facilities available to the Institute in the Clinical Center. The mission of NICHD embraces research in reproductive biology, family planning, maternal and child health, perinatal physiology and elements of uterine physiology. The programs under exploration will recognize this mission and establish the basis for comprehensive research in these areas by combining laboratory programs using animals with clinical research involving appropriate patients.

Developmental Biology Branch

The Institute proposes to recruit scientists to fulfill the mission of the Developmental Biology Branch. The programs will include studies of cell division, growth, mitosis and miosis, control mechanism for cell division, growth determinants in embryogenesis, tissue differentiation and cellular individuality as studies through modern immuno-chemical methods.

Social and Behavioral Sciences Branch

Social and Behavioral Sciences Branch concentrates on studying the development of infants and young children from disadvantaged environments. These investigations are aimed at adding to basic understanding of factors in the early environment which facilitate and those which hinder intellectual development, and some aspects of personal-social development underlying the child's attitudes towards learning and achievement. We are particularly interested in the development of autonomy and exploratory behavior, and the kinds of maternal behavior which facilitate and those which hinder the child's development of curiosity and independence in coping with his environment.

There are currently a number of programs, such as Headstart, which attempt to provide children from deprived environment with special experiences in preschool groups to make up for some of the deprivations often found in their homes. To carry out these programs most effectively, much more precise information is needed than is now available on the kinds of learning conditions which promote cognitive development, and the development of feelings of adequacy and achievement in preschool children.

During this fiscal year these studies on preschool environments will be continued. In addition to the descriptive studies of the natural environment, the home and school settings, more focused intervention-type studies are planned in which certain aspects of the environment are controlled, e.g., language stimulation, experiences in delaying gratification.

Reproduction Research Branch

Reproduction Research Branch is committed to a combined clinical and basic research program concerned with the reproductive process with major emphasis on those aspects which may provide new bases for the control of fertility and the correction of infertility.

With the provision of appropriate clinical and community resources, investigations concerning hormonal, nutritional and genetic factors affecting the fertility of men and women are to be undertaken. Effort will be concentrated on such specific problems as menstrual irregularity, gonadal development and pubescence, habitual abortion, sterility, normal pregnancy and contraceptive development and evaluation.

Laboratory of Biomedical Sciences

Laboratory of Biomedical Sciences conducts basic research in molecular genetics, developmental enzymology, intermediary metabolism, physiological controls, and molecular structure. The prime objective of this multidisciplinary investigation is the elucidation of the molecular basis for selected types of mental and physical developmental pathology.

The current topic of interest in the Section on Molecular Genetics is the comprehensive analysis of the mechanism of protein synthesis. The roles of extraneous agents (such as viruses, radiation, and drugs) in the production of physical birth defects and mental retardation will be more fully appreciated when their effects can be described in terms of their interference with the orderly expression of the informational content of the genetic code.

In the Section on Developmental Enzymology primary interest centers on the identification and characterization of pregnancy-associated maternal blood plasmaenzymes and proteins, the characterization of enzymes synthesized by the placenta, and an analysis of some of the factors involved in enzyme induction in the fetus.

Investigators in the Section on Intermediary Metabolism develop laboratory analogs of mental retardation through the use of specific chemical agents and enzyme inhibitors.

The Section on Physiological Controls conducts research on the hormonal regulation of metabolism at the cellular and organ levels of organization, the mechanism of hormonal induction of enzymes, the regulation of cell growth as mediated through deoxynucleotide interconversions, and the developmental effects of inducing alterations of metabolism during specific periods of early development.

The Section on Molecular Structure develops fundamental methods for the elucidation of the primary structure of biologically significant molecules, emphasizing automation of laboratory processes.

Behavioral Biology Branch

The Behavioral Biology Branch will occupy new space which will permit the initiation of several research programs utilizing animal models, with emphasis at the subhuman primate level. The programs will concern both basic research on the neuronal code of the sensory systems and on efforts to develop and understand experimental models of various forms of mental retardation. A substantial portion of the budget requested will be to support these programs. This experimental animal research will be closely related to, and to some extent guided by, the studies now underway on the measurable electrical abnormalities in the brains of children suffering from depressed or delayed nervous system functioning.

Children's Diagnostic and Study Branch

Children's Diagnostic and Study Branch is engaged in research and comprehensive multispecialty evaluation of children with developmental deviation including motor, language, sensory, learning, and behavioral handicaps. The research program is directed toward the promotion of a better understanding of the normal and abnormal processes of human development. The ultimate goal of the Branch is to prevent mental retardation. We plan to investigate the effects of naturally occurring as well as experimentally administered prenatal stimuli on postnatal behavior in infants and infrahuman species, and the effect of auditory feedback on subsequent language development.

Gerontology Research Center

Gerontology Research Center goals are to describe in quantitative terms the biological, biochemical, physiological and behavioral changes that take place with aging and to determine the basic biological mechanisms of these changes with the ultimate aim of improving the health and performance of older people. The new Gerontology Research Center was occupied in June 1968 and the expanded resources are now available for the anticipated expansion of the research program on aging.

Additional funds are requested to expand the guest scientist program and to provide the essential resources and services needed by both intramural and extramural scientists. One of the essential resources is the expansion of the standard rat and mouse colonies and the establishment of the pathogen-free rat, mouse and hamster colonies to provide healthy animals of known ages for scientists and guest investigators. Additional funds are also required to support costs of data analysis, especially for computations required for the longitudinal study of aging in human males.

Laboratory of Molecular Aging

The Laboratory of Molecular Aging is seeking to discover the basic cause of aging by investigating the effect of age on cellular processes at the molecular level. It is concerned with testing hypotheses which assume that aging results from changes in complex large molecules such as DNA, RNA and connective tissue essential for maintenance of cellular functions. We plan to expand the program to include studies of the transport of various substances across cellular and mitochondrial membranes, since this process is essential to the maintenance of cell life.

Laboratory of Cellular and Comparative Physiology.

The Laboratory of Cellular and Comparative Physiology studies the mechanisms

of aging in animals in order to shed light on the process of aging in the human. The effect of environmental factors on mortality and life span in different animal species is being investigated. The biological mechanisms involved in inducing an increase in life span by reducing food intake will be studied in a variety of animal species. Morphological observations on the structure of cellular particulates, cells, and tissues will be made in order to correlate age changes in structure with function.

The requested increase in budget will permit extension of studies on the relations between structure and function in tissues, cells, and cellular particulates. We will initiate a study on the effects of hibernation on life span and thus test hypotheses of aging related to "rate of living" in a mammal.

Clinical Physiology Branch

The Clinical Physiology Branch will study age changes in organ systems and their integration with special reference to the human. In addition to studies on the performance of specific organ systems, such as the cardiovascular, pulmonary, renal and endocrine systems, this Branch will also be concerned with the definition of disease states in the elderly and the development of methods for the early diagnosis and treatment of disease. The major emphasis of the program will be on human studies but identification of the mechanisms of observed age changes will require animal experimentation as well.

Laboratory of Behavioral Sciences

The Laboratory of Behavioral Sciences will investigate the influence of age on behavioral responses including activity levels, speed of response, perceptual skills, cognitive behavior (learning, memory, problem solving) and personality characteristics in animals and man. The mechanism involved in the conditioning of autonomic responses will be investigated. Other studies will relate behavioral responses to physiological conditions. The factors responsible for the slowing of responses with advancing age will be isolated.

Studies of methods to improve learning and memory in the aged have progressed to the point where additional support for the program is essential. A new section on personality changes with age will be established. Studies on the effects of aging on personality characteristics such as attitudes, conservatism, rigidity of behavior, and social participation will be conducted. The effects of environmental differences on these characteristics will be assessed.

Summary

The increase of 57 positions and $790,000 will be distributed among the laboratories and branches as follows: the Office of Associate Director for Intramural Research - 5 positions and $69,000 to conduct clinical research; the Developmental Biology Branch - 5 positions and $70,000 to recruit scientific staff; Social and Behavioral Sciences Branch - 4 positions and $55,000 to study the development of infants and young children from disadvantaged environments; Reproduction Research Branch- 4 positions and $55,000 to conduct research on the control of fertility and the correction of infertility; Laboratory of Biomedical Sciences - 14 positions and $194,000 to conduct basic research in molecular genetics, developmental enzymology, intermediary metabolism, physiological controls, and molecular structure; Behavioral Biology Branch - 16 positions and $222,000 to conduct research on the neuronal code of the sensory systems; Gerontology Research Center - 9 positions and $126,000 to expand the standard rat and mouse colonies and to establish the pathogen-free rat, mouse and hamster colonies to provide healthy animals of known ages for scientists and guest investigators.

Collaborative Research and Development

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	29	$349,000	32	$374,000	+3	+$25,000
Other expenses	...	3,626,000	...	6,347,000	...	+2,721,000
Total	29	3,975,000	32	6,721,000	+3	+2,746,000

Introduction:

This activity serves the important purpose of supplementing and complementing the Institute's research programs. It is one of the most effective ways for coordinating program development in the major areas of interest--reproduction and family planning, perinatal biology and infant mortality, growth and development, aging, and mental retardation.

Program liaison is maintained and furthered through support of interdisciplinary research conferences and symposia and through Scientific Information Centers which are established. In addition, public information activities insure that the Institute's programs and goals are appropriately reflected to interested segments of the public.

The overwhelming majority of funds administered through this activity are assigned to the newly established Center for Population Research. This Center was officially designated by the Department in August to carry out the population research objectives directed by the President's Health Message to the Congress on March 4, 1968. This Center is the organizational entity which administers the new contract funds requested for this activity. The total program increase of $2,754,000 will go entirely to support the population research program. Nearly all of these funds will be used through the contract mechanism to stimulate research in the fields of contraceptive development, social and demographic studies, and evaluation of the medical effects of contraceptives. The three new positions requested will provide additional technical support for Center programs.

Program Plans for 1969 and 1970:

Center for Population Research

Population research deals with three classes of population problems: those facing the world, this country, and individuals. The first class, facing the world as a whole, threatens consequences that fall with particular heaviness on the developing nations. It arises from the inescapable condition that in many parts of the world the balance between numbers of people and the availability of resources, especially food, is in jeopardy. The striking increase in world population growth in recent years is demonstrated in Chart # 1. The population of the world is now about 3.5 billion and the best estimates are that it will nearly double by the end of this century. Indeed, even if it were possible to cut the rate of growth in half right now, there would still be almost 5 billion people by the year 2000.

The population problems facing the United States, though undeniably less overwhelming in their immediate severity than those facing the developing

nations, are nevertheless real and important. One set of problems deals with the fact that a significant number of Americans have more children than they wish partly because they do not have access to adequate medical services. Calculations by Campbell, Polgar and others demonstrate that approximately 5 million American women live below or only slightly above the poverty line and that they have about 450,000 unwanted children each year. Chart # 2 shows that the fetal mortality rate increases markedly with the number of children a woman has. Women who are unable to control the size of their families suffer disproportionately high rates of maternal morbidity and mortality, often due to attempts to end unwanted pregnancies by resorting to criminal abortions. Chart # 3 shows how criminal abortion rates fall markedly once women have more ready access to family planning services.

The ability to control fertility adequately is an essential component of any couple's efforts to achieve and maintain economic independence. More specifically, the prevention of an unwanted birth has two direct economic benefits; it avoids the costs of providing for an additional child, and it enables the potential mother to earn extra money to supplement the family's income. One study has shown that the avoidance of an unwanted child can save a family an average of $7,800. In addition, there are possible benefits of family planning about which only speculative statements may be made, given the present state of knowledge. For example, it seems reasonable to suppose that a healthier emotional environment within the family will reduce problems of school discipline, truancy, and juvenile delinquency.

Chart # 4 relates illegitimacy to poverty. A number of recent studies, particularly one at Yale, have shown how illegitimacy rates will fall when adequate social health services, including family planning, are made readily available.

The third class of population problems deals with individual couples and contains one of special poignancy and concern to those who embrace the American ethic of free individual choice and equal opportunity. A number of recent studies show that inability to plan and control fertility is associated with a long series of undesirable outcomes such as poor performance on intelligence tests, high rates of emotional problems, anti-social behavior, child abuse, abortions, and so on. Presumption is strong that improved capability to choose and limit childbearing reduces these individually and socially destructive developments in the course of family formation. Chart # 5 demonstrates graphically that even in 1965, 58 percent of American married women reported imcomplete success at controlling their fertility.

Objectives of the Center for Population Research

Solutions to population problems briefly described above will come from several sources: 1) the increased dissemination of information concerning population problems and their solutions, 2) the adequate provision of family planning services which will make it possible for couples to achieve their family size goals, and 3)research in contraception and in various aspects of the social sciences. The Center for Population Research is responsible for the third category.

Until 1969 the Center allocated most of its resources to studies evaluating the meidcal effects and the mechanism of actions of various modern contraceptives, particularly the oral contraceptives. Funds for this purpose were specifically appropriated by Congress in 1967.

In 1969, an additional $2.5 million were made available by Congress so that the Center could enter two new fields of investigation: 1) biological research directed toward the development of new contraceptive methods, and 2) population research in the social sciences.

Contraceptive development

The ideal contraceptive is effective, safe, inexpensive,reversible, and acceptable to various population groups. No presently available method fulfills all these criteria. The oral steroids and intrauterine devices represent remarkable improvements in contraceptive technology but it is well recognized that they do not approach the ideal. Probably no single method will be satisfactory in all situations. The goal of the Center for Population Research is the development of an array of methods which would be suitable to a variety of applications. For example, it is generally agreed that modern male methods of fertility regulation are needed, and ways may be developed to alter sperm function or the constituents in semen. New methods for women may act at a local level to affect the processes of ovulation or egg transport; a once-a-month pill is another possibility which is particularly attractive to organizers of family planning programs because of its simplicity.

Population research in the social sciences

Research in this complex field is directed toward a variety of vitally important topics such as 1) the measurement of family size preferences by various population groups and the ways in which such decisions are made, 2) the understanding of various causes and consequences of population trends, and 3) the effects of explicit and implicit governmental population policies. In 1969 the Center for Population Research began an organized research program in this area of concern.

Chart #1

World Population Estimates and Projections, 1920-2000
(in millions)

Projection series	1920	1930	1940	1950	1960	1965	1970	1975	1980	1985	1990	1995	2000
Total	1,860	2,069	2,295	2,515	2,998	3,281	3,592	3,944	4,330	4,746	5,188	5,648	6,130
High							3,659	4,070	4,551	5,096	5,690	6,326	6,994
Low							3,545	3,840	4,147	4,463	4,783	5,109	5,449
1/ Developed Countries													
Total	673	758	821	858	976	1,032	1,082	1,136	1,194	1,256	1,318	1,380	1,441
High							1,102	1,170	1,245	1,322	1,402	1,486	1,574
Low							1,070	1,110	1,153	1,195	1,234	1,266	1,293
Less Developed Countries													
Total	1,187	1,311	1,474	1,658	2,022	2,249	2,510	2,809	3,136	3,490	3,869	4,268	4,688
High							2,557	2,900	3,306	3,775	4,288	4,840	5,420
Low							2,475	2,730	2,994	3,268	3,550	3,843	4,155

1/ Developed countries include Europe, North America, Japan, Union of Soviet Socialist Republics, Temperate South America, Australia, New Zealand

Source: United Nations World Population Prospects as Assessed in 1963, Population Studies #41.

Chart #2

Fetal Mortality by birth order*

Birth Order					
1	2	3	4	5	6 and subsequent
16.0	11.4	13.5	16.7	20.5	30.0

*Average ratios in the United States per 1,000 live births for 1956, 1958, and 1961.

Source: Gordon W. Perkin, "Assessment of Reproductive Risk in Nonpregnant Women," American Journal of Obstetrics and Gynecology, Vol. 101, 1968, pp. 709-717.

Chart #3

Changes in Numbers of Abortions Following Initiation of Family Planning Programs

	N.Y. Metropolitan[1]	Harlem[2]	L.A. County[3]	Corpus Christi[4]
Number Abortions Before Program	1175 (1960)	1185 (1964)	3458 (1965)	374 (1961)
Number Abortions After Program Initiated	805 (1966)	775 (1966)	2357 (1966)	115 (1967)
Percent Decrease	32%	35%	26%	69%

Sources: [1]Gordon W. Perkin, "A Family Planning Unit for Your Hospital?" Hospital Practice, Vol. 2, 1967, pp. 64-72.

[2]Ibid.

[3]Gerald I. Zatuchni, "International Postpartum Family Planning Program," American Journal of Ob. and Gyn., Vol. 100, 1968, pp. 1028-1041

[4]Planned Parenthood-World Population, "Texas: Vignettes of Family Planning Progress," 1968.

Chart #4

Estimated Percentage of Births that are Illegitimate, by Poverty Status of Mother: United States, 1960-65

Poverty status	Percent illegitimate
Total	6.2
Poor and Near-poor	15.7
Non-poor	2.3

Source: Arthur A. Campbell, "The Role of Family Planning in the Reduction of Poverty," Journal of Marriage and the Family, Vol. 30, No. 2, May 1968, p. 244.

Chart #5

Estimated Percent Distribution of Married Women by Reported Success in Controlling Fertility: United States, 1955, 1960, and 1965

Success in controlling fertility	1955	1960	1965
Total	100	100	100
No failures	44	43	42
Some failures	56	57	58
Reported one or more births sooner than wanted	41	37	37
Reported more births than wanted	15	20	21

Source: Estimated by Center for Population Research, NICHD, on the basis of surveys of married women of reproductive age.

Biometry, Epidemiology and Field Studies

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	22	$233,000	23	$241,000	+1	+$8,000
Other expenses		1,789,000		1,935,000		+146,000
Total	22	2,022,000	23	2,176,000	+1	+154,000

This activity supports the Institute's scientific staff in planning and conducting epidemiologic and biometric investigations and conducts research in epidemiological and biometric theory, techniques and methods. It also collects and analyzes program statistics for various programs and executes statistical studies for use in program planning, development and evaluation.

The net increase of $154,000 includes a program increase of $189,000 for staff support and increased epidemiologic research contracts in the Institute's five program areas: Reproduction and Population, Perinatal Biology and Infant Mortality, Growth and Development, Aging, and Mental Retardation.

The increase is offset by a decrease of $35,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Training Activities

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	4	$48,000	4	$48,000	...	...
Other expenses	...	41,000	...	37,000	...	-$4,000
Total	4	89,000	4	85,000	...	-4,000

The direct training program is an effective means of coping with the crucial problem of a lack of sufficient numbers of trained scientists. The program is geared to the needs of the Institute's intramural research operations by providing supplementary or cross-disciplinary training for the Institute's scientific staff members or those who are planning to join the staff.

The decrease of $4,000 is for centrally furnished services from the "National Institutes of Health Management Fund."

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	85	$985,000	88	$1,010,000	+3	+$25,000
Other expenses	...	971,000	...	1,027,000	...	+56,000
Total	85	1,956,000	88	2,037,000	+3	+81,000

This activity is composed of professional and supporting personnel who are responsible for the administration of the Institute's several grants activities. This involves planning and development of programs in research, training, and fellowships that will best serve to accomplish the desired results in the problem areas for which this Institute is responsible; the securing of review and evaluation of research and training grant applications for presentation to the National Institute of Child Health and Human Development Advisory Council; required Council staff assistance; liaison with the applicants, grantees, other components of National Institutes of Health, Public Health Service, advisory bodies, and interested organizations; continued surveillance of scientific activities and progress of the research and training grant programs; and recording and reporting of fiscal and scientific information relevant to all grant transactions.

The increase of $81,000 will provide $20,000 to meet increased staff costs due to added workload in the grant areas, $1,000 annualization of the 1969 pay raise costs and $60,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	47	$604,000	49	$621,000	+2	+$17,000
Other expenses		205,000		186,000		-19,000
Total	47	809,000	49	807,000	+2	- 2,000

This activity includes the Office of the Director, Director of the Center for Population Research, Associate Director for Program Planning and Evaluation, Executive Office, Administrative Office and the Budget Office. These offices are responsible for the general administration, direction and coordination of the Institute programs as well as the review of current and proposed operations.

The net decrease of $2,000 reflects increases of $12,000 to staff the newly established office of the Director, Center for Population Research and $1,000 for annualization of the 1969 pay raise costs offset by a decrease of $15,000 for centrally furnished services from the "National Institutes of Health Management Fund."

New Positions Requested
Fiscal Year 1970

Laboratory and clinical research	Grade		Annual Salary
Medical officer	GS-15		$ 19,780
Veterinarian	GS-14		16,946
Psychologist	GS-14		16,946
Physiologist	GS-13		14,409
(2) Biochemist	GS-13		28,818
Medical officer	GS-12		12,174
Biochemist	GS-12		12,174
Physiologist	GS-12		12,174
Physiologist	GS-11		10,203
(2) Medical officer	GS-11		20,406
Physiologist	GS- 9		8,462
(3) Chemist	GS- 9		25,386
(4) Biologist	GS- 7		27,924
(6) Chemist	GS- 7		41,886
(3) Psychologist	GS- 5		17,196
Secretary	GS- 5		5,732
(5) Chemist	GS- 5		28,660
(3) Biologist	GS- 5		17,196
Biological laboratory technician (Histology)	GS- 5		5,732
(4) Clerk typist	GS- 4		20,580
(2) Biological laboratory technician	GS- 4		10,290
(3) Biological laboratory aid	GS- 3		13,800
Clerk typist	GS- 3		4,600
Electroencephalographic technician	GS- 3		4,600
Physical science technician	GS- 3		4,600
(2) Biological laboratory aid (Animal)	GS- 2		8,462
(5) Animal caretaker	WB		21,238
Dishwasher	WB		3,723
		(57)	434,097
Collaborative Research and Development			
Biologist	GS-15		19,780
Psychologist	GS-14		16,946
Physiologist	GS-13		14,409
		(3)	51,135
Biometry, Epidemiology and Field Studies			
Mathmatical statistician	GS-13		14,409
		(1)	14,409
Review and Approval			
Health scientist administrator	GS-14		16,946
(2) Health scientist administrator	GS-13		28,818
		(3)	45,764
Program Direction			
Program management officer	GS-12		12,174
Program analyst	GS-11		10,203
		(2)	22,377
Total new positions, all activities		(66)	567,782

WEDNESDAY, APRIL 2, 1969.

GENERAL RESEARCH AND SERVICES

WITNESSES

DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT W. BERLINER, DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
DR. THOMAS G. BOWERY, ACTING DIRECTOR, DIVISION OF RESEARCH FACILITIES AND RESOURCES
DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
JOHN W. HAMBLETON, FINANCIAL MANAGEMENT OFFICER, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. ARNOLD W. PRATT, DIRECTOR, DIVISION OF COMPUTER RESEARCH AND TECHNOLOGY
RICHARD L. SEGGEL, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	2,458	2,653	2,754
Positions other than permanent	78	101	101
Other personnel compensation	4	6	7
Total personnel compensation	2,540	2,760	2,862
Personnel benefits: Civilian employees	244	262	276
Travel and transportation of persons	138	150	157
Transportation of things	24	29	32
Rent, communications, and utilities	169	153	158
Printing and reproduction	59	79	87
Other services	4,273	5,687	5,719
Supplies and materials	49	48	51
Equipment	428	116	126
Grants, subsidies, and contributions	57,313	61,401	65,341
Total obligations	65,236	70,685	74,809

PERSONNEL SUMMARY

Total number of permanent positions	253	256	260
Full-time equivalent of other positions	9	11	11
Average number of all employees	237	254	263
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Division of Research Facilities and Resources:			
(a) Grants:			
(1) Research	56,797	60,871	64,831
(2) Fellowships	148	154	146
(3) Training	368	376	364
(b) Direct operations:			
(1) Collaborative research and development	1,193	1,488	1,483
(2) Review and approval of grants	1,123	1,533	1,615
(3) Program direction	471	643	641
2. Division of Computer Research and Technology: Direct operations	3,395	4,611	4,753
3. Engineering development: Direct operations:			
(a) Collaborative research and development		750	750
(b) Program direction	101	259	226
Total program costs, funded [1]	63,596	70,685	74,809
Change in selected resources [2]	1,640		
Total obligations	65,236	70,685	74,809
Financing:			
Comparative transfer to other accounts	11,404	13,580	
Unobligated balance lapsing	4,501	544	
Budget authority (appropriation)	81,141	84,809	74,809
Relation of obligations to outlays:			
Obligations incurred, net	76,640	84,265	74,809
Obligated balance, start of year	55,354	49,556	62,318
Obligated balance, end of year	−49,556	−62,318	−63,645
Adjustments in expired accounts	−1,409		
Outlays	81,029	71,503	73,482

[1] Includes capital outlay as follows: 1968, $246,000; 1969, $116,000; 1970, $159,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $2,756,000; 1968, $4,396,000; 1969, $4,396,000; 1970, $4,396,000.

Mr. FLOOD. Now we have the National Institutes of Health, General Research and Services, and Dr. Robert Q. Marston, the Director of the National Institutes of Health, will be the principal witness.

I see you have a statement on this subject, Doctor. What do you want to do?

Dr. MARSTON. I would proceed to present it, Mr. Chairman.

Mr. FLOOD. Very well.

GENERAL STATEMENT

Dr. MARSTON. Mr. Chairman and members of the committee, this appropriation provides support for three noncategorical areas of activity. These are the Division of Research Resources in the Bureau of Health Professions Education and Manpower Training; the Division of Computer Research and Technology, and Engineering Development. I should like to speak to each of the three elements of this appropriation separately, and to summarize the total request at the end.

DIVISION OF RESEARCH RESOURCES

Mr. Chairman, I propose to address myself first to the programs of the Division of Research Resources. Three of the programs of this Division provide Federal assistance on a nationwide basis for those resources which are vitally interwoven with the individual scientist's quest for medical knowledge. These resources include clinical research centers where laboratory findings are translated into new diagnostic and treatment techniques, primate centers where research on non-

human primates spans a wide range of biomedical science, animal resources where high-quality research animals are developed, and special research resources where complex, highly specialized equipment is made available for the advancement of biomedical knowledge.

GENERAL CLINICAL RESEARCH CENTERS

Ninety-three general clinical research centers, supported by funds from the Division, provide a unique setting for the improvement and intensification of medical research. These clinical facilities are discrete units, small research hospitals within a larger hospital, of from five to 30 beds, with their own well-trained professional, nursing, dietetic, and supporting technical staff. The purpose of these centers is to allow biomedical scientists from many disciplines to carry out intensive studies with carefully selected patients in order to apply the latest in research findings toward the development of new approaches for the prevention and treatment of disease and disability.

In 1960, when the general clinical research centers program was started under a mandate from Congress, it was widely hailed as an important first step in providing the environment necessary for enhanced clinical investigation. Prior to 1960, clinical research had been only haltingly and spasmodically pursued because the kind of resource where sophisticated, controlled clinical investigation could be performed rarely was available.

Today, some 9 years later, there are over 2,400 medical scientists and 2,200 paramedical personnel working at these centers to help abolish serious childhood diseases, to reduce significant illness and suffering, and to make the lives of all Americans longer, healthier, and more productive.

PRIMATE CENTERS

Seven regional primate research centers, supported by this Division, provide facilities, on a nationwide basis, for teams of scientists to conduct intensive research on man's closest animal relatives, subhuman primates, in a coordinated effort to unlock the secrets of many human ailments.

A critical array of today's highly specialized and interrelated scientific talents and disciplines are gathered in these centers. Individual investigators and specialized teams employ the unique resources, where animals, equipment, laboratories, and highly trained support personnel are made available as a unit, in an effort to solve a variety of human health problems.

The 1968 "Report of the President's Committee on Mental Retardation" had the following to say about primate centers as the means for expanding research in the mental retardation field: "There is in existence a national network of centers developed for the purpose of man-related research which cannot be carried out in studies directly involving human beings. We recommend that this network, the regional primate research centers, undertake major inquiries into the relationship to mental development of nutrition, infant stimulation, success-failure patterns, and similar topics." At present, we estimate that approximately 20 percent of primate center research is in the area of mental retardation.

ANIMAL RESOURCES

More than 1.7 billion animals were used for research purposes during 1967, the most recent year for which statistics are available, according to a survey of breeders and researchers conducted by the Institute of Laboratory Animal Resources of the National Academy of Sciences. The survey showed that investigators must utilize a wide range of animals in order to perform effective research. Modern medical science relies heavily upon the opportunity for scientists to select the best animal model for the medical problem at hand.

The Division's animal resources program supports a multifaceted effort to assist institutions in developing the high-quality animals needed for biomedical research.

During 1968, for example, 57 animal resource projects were supported. These included projects for developing and maintaining colonies of special research animals; for defining and elucidating new animal biological models; for developing and maintaining laboratories for diagnosis and study of diseases of laboratory animals; for gathering and disseminating information on laboratory animals; and for providing new knowledge about laboratory animal disease and optimal husbandry of laboratory animals.

SPECIAL RESEARCH RESOURCES

Scientists engaged in biomedical research are utilizing the unique attributes of electronic computers and other highly specialized instrument systems in probing the mysteries of living matter. They have found many uses for these special instruments in helping their research and analysis move forward at a rate not achievable with old-fashioned methods. If man is to add to his store of knowledge about himself and his environment, investigative teams must arm themselves with the most up-to-date technological tools, which, in many cases, are so sophisticated that large-scale institutional resources are required. Many areas of biomedical research today have become enormously dependent upon computer resources, upon unique ensembles of biochemical instrumentation, and on specialized facilities to produce commercially unobtainable biological materials. These special research resources render services to the institutional biomedical community, pursue research and development designed to enhance the capabilities of the resource, and train biomedical scientists in the use of the facility. At present, the special research resources program supports 29 computer resources, eight biomedical instrumentation resources, and two biomaterials resources.

To provide continuing support for these important programs of the Division of Research Resources, $69,080,000 is requested. This includes $38,964,000 for clinical research centers; $10,500,000 for primate research centers; $4,568,000 for animal resources and $510,000 for fellowship and training programs related to animal resources; $10,494,000 for special research resources; $305,000 for scientific evaluation; and $3,739,000 for direct operations, including collaborative studies. These figures remain essentially the same as those in 1969 except for a $3,960,000 increase in the clinical research centers program to meet burgeoning hospitalization and personnel costs at the centers.

I shall be happy to pause here to answer any questions you have on the estimates for the Division of Research Resources.

DIVISION OF COMPUTER RESEARCH AND TECHNOLOGY

Now, Mr. Chairman, I wish to address myself to the Division of Computer Research and Technology. The general categorization of computer applications in the biomedical sciences within the NIH research programs may be thought of as follows:

1. In the traditional analysis of data through statistical and logical techniques
2. In the storage and retrieval of a variety of scientific and medical records essential to future research and education
3. In the mathematical modeling (simulation) and quantitative description of complex life phenomena
4. In the monitoring of clinical and laboratory procedures and experiments
5. In clinical decision-supporting systems
6. And administrative support for the management of the research programs.

To be more specific, computer-dependent projects are underway at the National Institutes of Health which analyze the morbidity of cancer, arteriosclerotic heart disease, arthritis, diabetes, mental retardation, and neurological diseases. Computers are being used to acquire and analyze a vast array of blood chemistry data to determine normal variations of blood components and to establish standard procedures for measuring these components. The electrocardiogram is being automatically analyzed as a screening procedure for heart disease, particularly for the early detection of irregular cardiac rhythms which signal a threat to life and complicate medical management of patients with acute myocardial infarction. The efficiency of prosthetic valves in the heart is being carefully studied and described mathematically as a function of cardiac output and heart rate. Planning of radiation therapy for cancer is being done with the computer insuring that a variety of treatment plans will be considered for each individual patient and the optimal plan selected. The advanced sensing and measuring instruments used in the laboratories and clinics are being coupled to an array of computers for the acquisition and analysis of physical chemistry data for analysis of the primary structure of biologically important chemical molecules such as protein enzymes and the nucleic acids of the basic genetic structures of life.

This list is by no means exhaustive but is representative of the progress being made in biomedical computing at the NIH. We believe this progress is the product of a synthesis between the established biomedical expertise of the NIH and the newly developed interdisciplinary competence in computer science, computer-related engineering and applied mathematics embodied in the DCRT.

The Division of Computer Research and Technology requests $4,753,000 for 1970 which is an increase of $142,000 over the 1969 operating level of $4,611,000. This increase will provide for further implementation of remote terminals and special purpose laboratory computers throughout NIH and thus provide our scientists and administrators with a more responsive access to the computer center.

If there are any questions on the estimates for this Division, I shall be happy to answer them at this point.

BIOENGINEERING

Next, Mr. Chairman, I wish to speak to the request for bioengineering. Bioengineering applies the principles and practice of engineering science to biomedical research and health care. In the health research programs of the National Institutes of Health modern engineering technology has been applied to development of artificial internal organ replacement, automation of hospital laboratories, isolation and containment facilities for both nuclear medicine and cancer virus research, patient monitoring devices and systems utilized in cardiovascular research, and hospital information systems.

Under a current contract, the National Academy of Engineering is attempting to identify and broadly define program opportunities and needs. Subcontracts have been made to develop prototype institutional patterns which would be useful in effecting cooperation among universities, industrial firms, hospitals and Government agencies.

In addition to specific investigations, efforts are directed toward structuring and building an adequate foundation for the successful realization of this program, which would require a major expansion. Assessment of the "state of the art" and determination of the best organizational structure for implementation of this program are being discussed with interested officials both inside and outside the Government.

For this activity we are requesting $976,000, a decrease of $33,000 from the 1969 operating level of $1,009,000. This request provides for continuing the 1969 program level. The decrease relates to the formula redistribution of the estimates for providing centrally furnished services from the NIH management fund.

CONCLUSION

In conclusion, Mr. Chairman, the request for the general research and services appropriation is for $74,809.000. This is an increase of $4,124,000 over the 1969 operating level of $70,685,000. Of the total, $69,080,000 is for the Division of Research Resources, including an increase of $4,015,000; $4,753,000 for the Division of Computer Research and Technology which is an increase of $142,000 over the 1969 operating level, and $976,000 for bioengineering, a decrease of $33,000 from the 1969 operating level.

Thank you. I shall be happy to answer any questions.

ENTERTAINMENT

Mr. FLOOD. You ask a small increase of $2,500 for a very, very sensitive item, entertainment. Why do you need this increase and what would happen if you did not get it? Would the Heavens fall?

Dr. MARSTON. The purpose of these funds is entirely for the Fogarty International Center.

Mr. FLOOD. That is a good answer. That will take care of that.

GENERAL CLINICAL RESEARCH CENTERS

The only large increase you have is $3,960,000 for general clinical research centers. How much of this is just for the increased cost of doing business?

Dr. MARSTON. I would like to check with Dr. Bowery, but I think this is entirely due to the increased cost of doing business.

Dr. BOWERY. Basically it is entirely for the increased cost of doing business. We expect that hospitalization costs will rise an additional 12.5 percent.

Mr. FLOOD. What is the balance for?

Dr. BOWERY. About 90 percent of the center's operational cost falls in hospitalization and personnel costs. Both of these tend to rise each year. Including hospitalization and personnel costs, the overall cost is rising about 10 to 11 percent.

DRUG ADDICTION

Mr. FLOOD. Take a look at page 174. There you have a paragraph on drug addiction and you say: "Research on narcotic addiction initiated 5 years ago has led to the first successful program for treatment of hard core criminal addicts."

What does "successful" mean in this instance?

Dr. BOWERY. That, I think, is the ability to take some of these individuals and by utilizing a different method of approach——

Mr. FLOOD. A different method of approach?

Dr. BOWERY. Yes, using a compound called methadone.

Mr. FLOOD. There is nothing new about methadone, is there?

Dr. BOWERY. It was reported, I think, at least last year.

Mr. FLOOD. What do you mean by "successful"?

Dr. BOWERY. I think "successful" is the ability to not necessarily take hard core criminal addicts but others in the addictive stage and return them to a reasonably productive life.

Mr. FLOOD. I am quoting from your justifications, and you say your research has led to the first "successful" program for treatment of hard core criminal addicts. What do you mean?

Dr. BOWERY. Successful in getting them off narcotics such as heroin.

Mr. FLOOD. You have been successful in that?

Dr. BOWERY. In some cases.

Mr. FLOOD. Successful in taking hard core criminal addicts off the stuff? How successful are you 7 days after they are out?

Dr. BOWERY. I am not sure, sir.

Mr. FLOOD. You are not very successful, are you, in treating hard core criminal addicts?

Dr. BOWERY. In the particular study that is referred to here there has been a pretty high success in keeping them off heroin.

Mr. FLOOD. How large a program is this?

Dr. BOWERY. This is a program in New York, I think.

Dr. MARSTON. Yes.

Mr. FLOOD. If it is that good, why is it not universally used?

Dr. BERLINER. The program has been somewhat controversial because they substitute one addiction for another. That substitute addiction is methadone, which has a mild influence and is less destructive on the functions of these individuals. Some of them have become more or less rehabilitated socially.

Mr. FLOOD. Is there much success in substituting the mild for the bad?

Dr. BERLINER. It has encountered resistance in the medical profession.

Mr. FLOOD. Why?

Dr. BERLINER. I am not certain why.

Mr. FLOOD. I think we should have a statement in the record showing why there should be resistance in the profession to treating these hard core addicts by the substitution of this milder drug.

Dr. BERLINER. We shall be glad to put in a statement on that.

(The statement follows:)

STATUS OF METHADONE PROGRAM

The use of so-called methadone blockade as a method for the treatment of heroin addiction was developed by Drs. Dole and Nyswander of the Rockefeller University of New York. Beginning in 1964, they conducted detailed studies of the pharmacology of substitute narcotic drugs given in high doses over extended periods of time to individuals with a long history of narcotic addiction. The methadone blockade technique represents an effort to swamp the metabolic system with sufficient drug to permit the extinction of both narcotic craving and the euphoric reaction to acute incremental doses of narcotics. In theory, patients thus treated, are maintained in a steady state of normal function analogous to the insulin-treated diabetic. Dole and Nyswander demonstrated the potential of this form of treatment for rehabilitating addicted individuals and the method has been extended to the treatment of some 1,200 addicts in New York City and perhaps an additional 1,000 patients in other cities.

The method remains experimental and requires further evaluation of its full potential for the effective treatment and rehabilitation of opiate addiction. It should be remembered that the treatment method is not a cure and does not involve drug withdrawal. Rather, a longed-and-smoother-acting drug with predictable dose-response effects is substituted as the addicting agent for illegally procured heroin with its erratic purity and fluctuating effects. Rather than being allowed to continue the pattern of wide swings of mood and general physiological functioning between extremes of drug craving and drug euphoria characteristic of the street addict, the methadone "blocked" patient is maintained on an even keel by steady and continued dosage of the drug.

Methadone may be a very useful tool in the social and occupational rehabilitation of drug addicts It does not represent an attempt to reverse the state of addiction itself. Criticism of the method is in part based on this defect, that the method represents acceptance of addition as the future of the addict under treatment rather than attempting a withdrawal of all drugs as is the goal of other treatment methods. Additionally, rehabilitation can rarely be accomplished without the active and motivated cooperation of the addict himself. Many of the current methadone studies have been conducted with addicts selected for their motivation to change and who do not necessarily constitute a representative sample of the addict population.

Thus, in summary, the method has been shown to be effective within somewhat limited goals. Controversy remains as to the adequacy of the treatment goals and the general applicability of the study conclusions. Extensive further application and evaluation of this method would be necessary before it could be recommended as the treatment method of universal choice for narcotic addiction.

Mr. FLOOD. I thought drug addiction treatment belonged to the Institute of Mental Health.

Dr. MARSTON. Yes, sir.

Mr. FLOOD. Why is this item here?

Dr. MARSTON. Well, this is a utilization of the clinical research centers which allow one to do research on the whole broad array of health problems, and mental health is included in this. A general clinical research center is a facility that makes available to the investigator

the resources to carry out careful clinical research, and all patients with problems in every area of illness are treated.

Mr. FLOOD. Does the Institute of Mental Health do that?

Dr. MARSTON. The Institute of Mental Health does not provide these clinical research centers. This study on drug addiction was carried on in facilities provided by the general clinical research centers program.

SPECIAL RESOURCE CENTERS

Mr. FLOOD. On page 177 you say:

It is anticipated that approximately four new life science computer resources, one new analytical biochemistry instrumentation resource, and one new biomaterial resource will be established.

In language that even Congressman Flood can understand, will you define each of these three types of resources and tell us why they are so important.

Dr. BOWERY. A life science computer resource is normally made available to all biomedical scientists at an institution to allow access to this sort of computation instrumentation.

An analytical biochemistry instrumentation resource is a broad name applied to such things as nuclear magnetic resonance and mass spectrometry equipment which gives precise determination of the constituents of compounds.

And a biomaterial resource is one which gives the biomedical scientist the ability to obtain or upgrade laboratory-scale amounts of enzymes, micro-organisms, cells, and other biomaterials to semipilot plant quantities.

Mr. FLOOD. How many of these are already established, and where are they?

Dr. BOWERY. We support three biomaterial resources, the American-type culture collection here in Rockville, Md., the New England Enzyme Center at Tufts University, and one at Wisconsin University. We have approximately nine analytical biochemistry instrumentation resources.

Mr. FLOOD. Will you list these for the record?

Dr. BOWERY. Yes.

(The information follows:)

ANALYTICAL BIOCHEMISTRY INSTRUMENTATION RESOURCES

INSTITUTION AND PROJECT TITLE

Cornell University, high resolution mass spectrometer facility.
Michigan State University, mass spectrometry facility.
Massachusetts Institute of Technology, mass spectrometry facility for biomedical research.
Mellon Pittsburgh Carnegie Corp., nuclear magnetic resonance facility for biomedical studies.
Ohio State Research Foundation, a nuclear magnetic resonance facility for biomedical research.
University of Pittsburgh, mass spectrometric facility for biomedical research.
Purdue University, mass spectrometry center for biomedical research.
Research Triangle Institute, mass spectrometry center for research.
Yale University, physical sciences instrumentation resource facility.

Mr. FLOOD. What is the cost of each unit or resource?

Dr. BOWERY. They range in cost from approximately $20,000 to $300,000. Some of the computer resources go much higher.

Mr. FLOOD. Will you list for the record the spread in cost from top to bottom for each one?

Dr. BOWERY. Yes.

(The information follows:)

SPECIAL RESEARCH RESOURCES—RANGE OF OPERATING COSTS DURING FISCAL YEAR 1969

Type	Minimum	Maximum
Life science computer	$76,110	$2,073,000
Analytical biochemistry instrumentation	25,000	242,000
Biomaterials	20,000	325,000

USE OF COMPUTERS

Mr. FLOOD. A year ago you were having trouble with a hardware manufacturer who was behind in the delivery of material. I believe it was IBM.

Dr. MARSTON. I think this was in Dr. Pratt's area.

Mr. FLOOD. Was it not IBM?

Dr. PRATT. Yes, sir.

Mr. FLOOD. We put something in the report last year to the effect it was holding up important activities. What have you done about this?

Dr. PRATT. We did quite a bit, with your help. You helped us in getting these special programs which the executive and legislative branches support. Our own people, with IBM, have generated a very advanced computer capability, one I think you can admire.

Mr. FLOOD. Yes, we had some testimony as to the extent to which you have used this hardware and I understand it is the best in the business.

Dr. PRATT. I hope so.

PRIMATE CENTERS

Mr. FLOOD. On page 178 you say: "The Primate Centers are functioning at about 75 percent of planned initial capacity."

Why is that true and how does that affect the program?

Dr. BOWERY. It is true because with the launching of this program back in 1962 and the last dedication of a center in 1966, there is now a physical plant and an intellectual resource available to move forward very rapidly, but fiscal constraints have limited the ability of the Government to keep up. We have not kept pace.

Mr. FLOOD. Why don't you close two of them and operate the rest at full capacity?

Dr. BOWERY. We have a basic investment of approximately $2 million per center in initial construction as well as yearly core support. The understanding we have with the universities is to maintain them, and it would be detrimental to close them out.

Mr. FLOOD. Somebody will ask me and want to know what in the world has happened in the operation of these centers that is worth $10.5 million. Well, I am asking you.

Dr. BOWERY. We have quite a bit happening in reproductive biology at the Oregon center where we have the opportunity to work in the

areas referred to in earlier testimony by Dr. La Veck on nonhuman primates. In the Wisconsin center we have a good deal of work going on in the field of mental retardation, social interaction and social development.

Mr. FLOOD. I want you to develop a half dozen good examples on that.

(The information follows:)

The nonhuman primates, on the evolutionary scale, are more similar to man, both biologically and behaviorally, than any other animals. They are afflicted, sometimes uniquely, with many diseases similar to those of man. Therefore, the probabilities of successfully applying information gained from nonhuman primates to man are in many cases higher than with any other animal. The use of nonhuman primates in medical research requires specialized facilities, appropriately trained professional and supporting personnel, an adequate selection of animals and a variety of distinctive resources.

The regional primate research centers Program, administered by the division of research facilities and resources, National Institutes of Health, was initiated in early 1960 as a coordinated effort on the part of the Federal Government and a number of major universities to establish a resource for conducting biomedical research using the nonhuman primate. The goal of this program is to provide the complete research environment, as well as research support, so that scientists will be able to perform investigations with nonhuman primates as test subjects. Seven centers have been constructed with Federal funds at a total cost of $14.1 million. They each have developed a research orientation and well established research programs, providing research opportunities for resident and visiting scientists and a large number of collaborators from many universities. These centers are located at the University of Oregon, Tulane University, Emory University, University of Washington, University of Wisconsin, Harvard University and the University of California at Davis. The operation of the centers is supported by base grants which totaled $10.5 million in fiscal year 1969.

A number of areas of biomedical investigations are underway at present, including, but not restricted to the following: reproductive biology and population control, infectious diseases, environmental health, behavioral sciences, heart disease, dental health, trachoma and other eye diseases, nutrition, mental retardation, carcinogenesis and organ transplantation. The following are some of the research accomplishments.

Spontaneous disturbances of the ovarian cycle, like those induced by antifertility drugs, are accompanied by marked alterations in the pattern of endocrine secretions and by changes in character of reproductive behavior.

When the ovarian rhythm is disturbed, reproductive behavior tends to be unpredictable; also, the normal pattern of progesterone secretion is irregular. When, during the early phase of the cycle, progesterone is present in abnormally high amounts, ovulation is delayed. This is also what happens with antifertility drugs which have a progestin base: behavior is deficient and the length of the menstrual interval abnormally lengthened. The source of the naturally occurring abnormally high level of progesterone is not yet known, but the alternatives are the adrenal cortex and the ovarian interstitial gland. If it is found that the adrenal cortex of primates secretes amounts of progesterone capable of inducing abnormalities in ovulation, behavior, and menstruation, the results may have profound implications for psychiatric theories of infertility and menstrual disturbances, on the one hand, and for "stress-induced" reproductive abnormalities on the other. An attack on this critical problem through the use of the nonhuman primate as the test subject is possible and underway at a center.

The chimpanzee has proven to be an unique experimental model for organ transplantation studies. Many of the antigens important in compatibility studies in man are present in the nonhuman primate. These antigens, if properly matched, allow successful organ transplantation; and because of their complexity are responsible for most of the rejection problems in organ transplants between unrelated individuals. Current studies with drugs indicate a slowing or abolishing of the rejection mechanism. The chimpanzees permit a type of experimentation in this area which would be morally or ethically impossible with humans.

The oviducts of monkeys, like those of man and other mammals, are lined with millions of microscopic hair-like structures called "cilia". These cilia beat

rhythmically, and thereby create fluid currents that are essential for the transportation of both egg and sperm. Without these currents, fertilization would not be possible. A scientist at one of the centers has discovered that growth of cilia is totally dependent upon estrogen sex hormones secreted by the ovary. In monkeys, cilia disappear and then regenerate at regular intervals. This phenomenon is now so well understood by this investigator, that he can control the growth of cilia at will. Extending these studies of ciliary growth to human oviducts, he has obtained strong evidence that here too cilia depend upon estrogen levels for their growth. He has developed a method of growing monkey oviducts in organ cultures which permits the study of ciliary growth in an artificially controlled environment. In this system, he is studying the effects of certain drugs on growth in the hope of finding a reliable means to inhibit the growth of cilia. The aim of this program is to devise a new and better way of controlled conception by controlling and preventing the growth of cilia. This technique has considerable promise as a new method of birth control.

Investigations have shown that it is possible to produce monkeys which show abnormalities in learning and social behavior similar to that reported in children suffering from phenylketonuria. This disease was produced in newborn monkeys by feeding excessive amounts of essential amino acid phenylalanine to the mother. This elevates the blood and body fluid levels of this compound to a greater extent in the fetus than in the mother, indicating for the first time that the placenta plays a role in concentrating this substance. Investigators are seeking the biochemical causes of this disease and are assessing the intellectual and social defects produced by the faulty metabolism of this amino acid.

In summary, the primate centers are well established and are producing a great deal of scientific information directly applicable to human health. For example, the 155 professional staff members produced a total of 524 publications last year. The research programs of the centers are assisting in solving a number of medical and sociological problems facing society today, including the development of new drugs for malaria control, new techniques for correcting orthodontic problems, the development of a vaccine for trachoma and methods to accelerate the recovery from stroke.

HEURISTICS

Mr. FLOOD. One of the items of computer research mentioned on page 184 is heuristics, which I take it is the development of artificial intelligence. Will you tell us something about that?

Dr. PRATT. Heuristics is a specialty of applied mathematics in computer science. There is a great need for heuristics. The name implies learning through the ability to deduce, i.e. logical deduction. You are quite right; heuristics is called artificial intelligence or machine intelligence. What NIH is attempting to do here can be explained in the following way: There are existing very fine data bases. The previous NIH witnesses have told you about the many studies and the data that are being compiled. The important thing here is that with the computer it is possible to query, to ask questions, of the data bases and obtain the answers. What is also important, each of these answers involves many variables. A complete answer requires that all the variables be logically structured together via the deductive process.

Heuristics is that part of mathematics which will allow us to develop in the computer a precise deductive process in that we can give to the computer certain rules of the concepts that man can understand. These rules are incorporated in the computer program. We are well

fixed to handle numerical data but we are hard put to handle the nonnumerical data. It is the world of heuristics that gives us hope.

Mr. FLOOD. We will hear a great deal more about this, will we not?

Dr. PRATT. Yes; there is no question about that.

Mr. FLOOD. Put a good statement on this in the record.

(The information follows:)

DIVISION OF COMPUTER RESEARCH AND TECHNOLOGY.

HEURISTICS LABORATORY

Heuristics is a branch of applied mathematics and comprises a growing set of formal, rigorous mathematical procedures. Heuristics arises from the need to solve intellectually complex problems, usually involving nonnumerical data, which are otherwise poorly handled by the deterministic or stochastic mathematics utilized in evaluating numerical data.

The adjective "heuristic" is defined in the dictionary as "serving to discover." The goal of heuristics is to get a computer to simulate (behave like) an intelligent human. This leads immediately to the notion of artificial intelligence in contrast to the natural intelligence of the human. Heuristic programing is indeed an approach to artificial intelligence. Intelligence is here defined as the ability to apprehend interrelationships of presented facts in such a way as to guide action or decision toward a desired goal.

Heuristics, while old as a concept, is still an emerging discipline stimulated by the recent availability of computers. Considerable progress has been made. Heuristic programs exist which play checkers, chess or some card games. Some programs can deduce answers to questions from given facts and axiomatic rules. Still others prove theorems in mathematical logic and geometry. From the successes to date, one can conclude that heuristics accurately simulates human performance in solving well-formulated problems such as theorem proving or the playing of simple games. One is encouraged to believe that what has been learned in the solution of well-formulated problems may be extended to the less well-formulated problems of the real world. It is for this reason that heuristics competence has been incorporated in the computing environment of the NIH.

The tenet of modern medicine assumes that the complex life phenomena can be explained in the context of the laws of physical science. Implicit in this assumption is the need to recognize and define the multiplicity of interrelationship always characteristic of life functions. The human can comprehend the most complex of concepts but the range, number and variety of the constituent relations greatly exceeds the mechanical processing ability of the human. It is natural then that the research worker attempt to exploit the rapid and accurate symbol processing capability of the computer in the processing of data. The heuristic program and the computer offer immense potential for extending and expanding a human's ability to process his data; the effort in heuristics is an attempt to transfer man's intelligence to the computer.

In summary, the Heuristics Laboratory of the Division of Computer Research and Technology, at the NIH, performs research in artificial intelligence. The Laboratory is attempting to make computers exhibit behavior that we call intelligent behavior when we observe it in human beings. The Laboratory devises and studies methods (heuristics) which help a computer to discover the solutions to very complex problems. The long-term goal is to apply exteremely intelligent computers to the solution of very important problems that are so complex as to be beyond the capabilities of any human. The short-term goal of the Laboratory is to apply moderately intelligent computers to the solution of some current biomedical research problems. Currently, the Laboratory is concerned with automatic pattern recognition and with deductive question-answering capabilities. Significant progress is being made. A computer has been programmed to make fairly accurate diagnosis on patients complaining of abdominal pain or to

answer simple questions about chemical analysis and synthesis and about the effects of lesions in the human visual system.

IMAGE PROCESSING PROJECT

Mr. CASEY. On page 185 you refer to the image processing project. Would you briefly describe what is involved in this project and why you think it is so important.

Dr. PRATT. Image processing is a vernacular name for a larger set of problems known as pattern recognition. Consider, if you will, in the nervous system, beginning at the highest cortical level and progressing to the spinal cord, there is an array of anatomical structures. These do not all conform to the textbook rules. The most important application in image processing is in collaboration with the National Institute of Neurological Diseases and Stroke. We are attempting to provide the technology and mathematical basis so that we can identify with computer technology the variations that occur in the nervous system structures, and particularly see if we can identify subtle changes.

Can we indeed identify subtle but nevertheless real derangements of structure so they can be correlated with disease or mental retardation?

A second application could be the recognition in peripheral blood preparations of abnormal cell forms-leukemic cells or breakaway tumor cells that represent potential tumor metastases.

Is that adequate, sir?

Mr. CASEY. I think so.

GENERAL CLINICAL RESEARCH CENTERS

Dr. Marston, on these General Clinical Research Centers, these are highly staffed, I would say, is that correct? In other words, these centers you refer to here are used in some of your transplant cases for postoperative as well as preoperative studies?

Dr. MARSTON. They are staffed differently from a general hospital because the purpose is to support research activties, and this requires a certain amount of special training. Especially, in some areas, you would have more backup people for these than for general hospital service.

Mr. CASEY. These centers are not for any particular studies, are they?

Dr. MARSTON. No, they are general purpose research centers.

Mr. CASEY. And they are clinical centers?

Dr. MARSTON. They are clinical centers.

Mr. CASEY. That is where the action is?

Dr. MARSTON. Yes, sir, and they require a screening by a local committee. There is an application procedure that is carried out in each institution to assure that only the most worthwhile studies are carried out in the clinical research centers.

CLINICAL USE OF ANIMALS

Mr. CASEY. Doctor, I have been getting a lot of mail lately—somebody is generating mail on the use of animals in clinical research. Those animals that are used in your shop are attended, as I understand from previous testimony, by trained veterinarians?

Dr. MARSTON. Yes, I think we have been looked upon as being somewhat of a model in the care of animals in the intramural program. I think that in all the controversy one has heard about animal research, NIH's intramural program has not been the subject of criticism. Is that right, Dr. Berliner?

Dr. BERLINER. Anything that uses animals is subjected to criticism, but I do not think there has been any criticism of the NIH facilities for the care of the animals.

Mr. CASEY. As I understand it, you want good healthy animals?

Dr. MARSTON. Yes, we do. It is necessary to have healthy, well treated animals to make the research worthwhile. In the last session of Congress, NIH supported the Rogers-Javits bill which was moving in the direction of providing even better care for the animals, and the programs we are talking about today are to provide funds to give the best animal care possible.

Mr. CASEY. I believe that is all. Mr. Michael?

SHORTAGE OF VETERINARIANS

Mr. MICHAEL. Thank you, Mr. Chairman.

Following closely on that subject, did I read somewhere in the justifications that there is a shortage of veterinarians to conduct this kind of research?

Dr. MARSTON. I think the shortage is specifically in the area of the care of research animals, those who specialize in that area. Dr. Bowery, I think, can better answer that.

Dr. BOWERY. I think a survey by the National Academy of Science indicates the area is short by about 1,000 individuals.

Mr. MICHAEL. I just got a communication this past week, and this might be a good place to bring it out, coming from my good friend, Dr. Cliff McGinnis of Peoria, who makes much of the fact that in 1968 the Health Manpower Act was amended to make veterinary schools eligible for participation in the moneys provided by the Department of Health, Education, and Welfare in the following three categories: (1) Basic improvement grants; (2) scholarship grants for students; and (3) special educational project grants to improve teaching.

He says that under the original Health Manpower Act, only schools of medicine and dentistry were eligible for these special educational support programs and that, under the amendments, money for the other newly covered professional schools could come

only from funds approporiated in excess of those previously available to schools of medicine and dentistry.

Dr. McGinnis says that therefore schools of veterinary medicine and the other medical science professions will not benefit from the revised Health Manpower Act of 1968 unless the Committees on Appropriations provide additional funds to the Department of Health, Education, and Welfare for disbursement under the Health Manpower Act of 1968.

And he goes on to say that this is important to the residents of the State of Illinois because of its College of Veterinary Medicine at Urbana-Champaign and other schools in Illinois training students in the medical science professions besides medicine and dentistry. He says that actually our State Board of Higher Education for Illinois has recommended that the College of Veterinary Medicine double the number of veterinarians graduating by 1980 and that it triple the number of graduate students in the college by the same date. Then he goes on to say these graduates are sorely needed to protect animal and public health not only within our own State of Illinois but throughout the country.

Do you have any comment on that?

Dr. MARSTON. Yes; I think one minor correction might be made. The previous law did include medicine, dentistry, optometry, osteopathy, and podiatry, and with the passage of legislation which goes into effect on July 1 of this year, veterinary schools were added. This becomes effective the 1st of July and you have before you and will be hearing, in the discussion of health education and manpower training, testimony on that. There is in the budget before you $12.5 million for veterinary medicine and pharmacy in the basic improvement grants, and they will be eligible for special education grants beginning the 1st of July.

I think there is one point in his letter that is important. There is, as a part of the law, a provision that no institution shall receive less dollars from the basic improvement grant in fiscal year 1970 than they did in fiscal year 1969. The budget you have before you does take this into account and it does have additional funds so that one can have the basic improvement grant for these other schools and can also include schools of veterinary medicine and pharmacy.

Perhaps Dr. Fenninger can add something to that.

Dr. FENNINGER. I think Dr. Marston has covered it. They do compete. They are on a competitive basis.

DRUG ADDICTION

Mr. MICHEL. What do we have in this budget for narcotics addiction? I guess there is mention of the research that has been going on for 5 years.

Dr. MARSTON. That research was instituted in a clinical research center, which provided the resource, and this was an example of the kind of research carried on in a clinical research center in New York.

Dr. BOWERY. The research protocol was reviewed and approved by the universities' screening committee. We do not have that specific function.

Mr. MICHEL. Where does most of the activity take place in regard to the Government's interest and research activities to cope with the problem of drug addiction?

Dr. MARSTON. The Mental Health Institute carries the largest responsibility in this area.

Mr. MICHEL. I think that is all.

REPLACEMENT OF AUTOMOBILES

Mr. CASEY. What are your foreign activities?

Dr. BOWERY. We have none, sir.

Mr. CASEY. What about this station wagon in Pakistan that you want to replace?

Mr. SEGGEL. This is the appropriation in which we request authority to replace motor vehicles. This is a replacement under GSA standards. When a vehicle has gone over 60,000 miles, under GSA standards we ask for a replacement.

Mr. CASEY. Who is using the station wagon?

Mr. SEGGEL. In Pakistan? The SEATO laboratory. But that does not relate to any one program.

Mr. CASEY. You just get stuck in this budget for the automobile?

Mr. SEGGEL. Yes, we have to ask for it in one place.

Mr. CASEY. They seem to run longer in Pakistan than here. You have over 100,000 miles on it.

REMOTE TERMINALS

Mr. MICHEL. I have one further question. In expanding your computer facilities, I read somewhere you were including remote terminals. How much do you intend to spend on this project in the coming years?

Dr. PRATT. Generally what is involved is the ability to bring the computers into the laboratories and clinics. Our remote terminals range from typewriters which link to the facility. In some of the laboratories and clinics where there is a need to process data in a physical-chemical sense, the remote terminal can be a small computer. We are at the moment installing six computers in various laboratories. In one application, for example, 10 large physical-chemical instruments are speaking directly to a computer.

Mr. MICHEL. Is this fully funded with Federal funds?

Dr. PRATT. Yes, sir. This is entirely an intramural activity in NIH.

Mr. MICHEL. Is there any reason why those six you speak of should not be identified in this record?

Dr. PRATT. Not at all. We shall be delighted to supply that.

(The information follows:)

NEW SMALL COMPUTER INSTALLATIONS AT NIH

Activity	Make and model of computer	Probable installation date	Purpose of system
NIAMD	Honeywell DDP-516	June 1969	Acquisition, reduction, and display of physical chemical data from laboratory instruments.
NIDR	Honeywell DDP-516	do	Acquisition, reduction, and display of biochemical data from laboratory instruments.
NINDS	Digital Equipment Corp. LAB 8/I-C	May 1969	Acquisition of data, real-time computations, and display of data in conjunction with research studies on physiology of the eye.
NINDS	Digital Equipment Corp. PDP 12 (2 installations).	December 1969	Support of research programs in experimental neurophysiology.
NHI	Digital Equipment Corp. PDP-8	May 1969	Calculations of chemical molecular structure data in conjunction with mass spectrometers.
NICHD	Digital Equipment Corp. PDP-12	December 1969	Support of research programs in experimental neurophysiology.

Mr. MICHEL. Can you give me a figure of what is involved in this expansion of activity? Obviously once it starts it builds from that point, does it not, the more terminal outlets you have, and if it is worthwhile information it is a two-way street, information going out and coming back in?

Dr. PRATT. Yes, it is. The center facility is maintained on a service basis, it pays for itself. The equipment in the center is rented because we did not want to buy it. It would involve a huge expenditure. On the contrary, the equipment going in the peripheral sites is usually purchased and from that hardware my colleagues built into it the systems for particular applications. We think there is considerable saving in buying it. It is a one-time cost.

Another aspect is that these very talented scientists are at work already and they are having to find ways to deal with these masses of material. They can handle more data at less cost.

The other thing I would say here, and I know Dr. Berliner has considered this with me, I would say in the near future we are not going to be going through the same rate of growth as you see now. The reason the rate of growth is high at the moment is that we had, as Mr. Flood mentioned, a very difficult time building the newer technology. In your own State, Illinois is the source of a considerable investment in this development technology. We had a considerale period of difficulty, 2 years, in building up a modern central computer facility. As such we thought we could not invest in the peripheral devices until we could support them.

We are now able to support them and indeed we are supporting our scientists. At this moment this looks like a jump. The rate will fall off, because these computers will support, more than one investor. We are searching for the economist. What I believe we are seeing is replacement costs. We are seeing a new and more modern technology replacing those activities which could not be made official.

Dr. MARSTON. The figure is $105,000 out of the $142,000 increase.

Mr. CASEY. Thank you.

We will reconvene at 2 o'clock.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

General Research and Services

Amounts Available for Obligation

	1969	1970
Appropriation	$84,809,500	$74,809,000
Comparative transfers to:		
"Salaries and Expenses, Office of the Director"	-441,000	
"National Institute of Allergy and Infectious Diseases"	-10,328,000	
"John E. Fogarty International Center for Advanced Study in the Health Sciences"	-2,811,000	
Cutback required by P.L. 90-364	-544,000	
Total obligations	70,685,500	74,809,000
Disposition of cutback:		
To be returned to the Treasury	544,000	

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
173	Division of Research Facilities and Resources:						
	Grants:						
	Research.....	--	$60,871,000	--	$64,831,000	--	+$3,960,000
	Fellowships.....	--	154,000	--	146,000	--	-8,000
	Training.....	--	376,000	--	364,000	--	-12,000
	Direct Operations:						
	Collaborative research and development.....	2	1,488,000	2	1,483,000	--	-5,000
	Review and approval of grants.....	104	1,533,500	108	1,615,000	+4	+81,500
	Program direction.	36	643,000	36	641,000	--	-2,000
183	Division of Computer Research and Technology:						
	Direct Operations...	112	4,611,000	112	4,753,000	--	+142,000
186	Engineering Development:						
	Direct Operations:						
	Collaborative research and development.....	--	750,000	--	750,000	--	--
	Program direction.	2	259,000	2	226,000	--	-33,000
	Total obligations.....	256	70,685,500	260	74,809,000	+4	4,123,500

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	256	260	+4
Full-time equivalent of all other positions	11	11	--
Average number of all employees	254	263	+11
Personnel compensation:			
Permanent positions	$2,653,000	$2,754,000	$+101,000
Positions other than permanent	101,000	101,000	--
Other personnel compensation	6,000	7,000	+1,000
Total personnel compensation	2,760,000	2,862,000	+102,000
Personnel benefits	262,000	276,000	+14,000
Travel and transportation of persons	150,500	157,000	+6,500
Transportation of things	29,000	32,000	+3,000
Rent, communications, and utilities	153,000	158,000	+5,000
Printing and reproduction	79,000	87,000	+8,000
Other services	5,687,000	5,719,000	+32,000
Supplies and materials	48,000	51,000	+3,000
Equipment	116,000	126,000	+10,000
Grants, subsidies, and contributions	61,401,000	65,341,000	+3,940,000
Total obligations by object	70,685,500	74,809,000	+4,123,500

Summary of Changes

1969 estimated obligations	$70,685,500
1970 estimated obligations	74,809,000
Net change	+4,123,500

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay raise	--	--	--	$+7,000
B. Program				
1. Research grants --				
General clinical research centers	--	$35,004,000	--	+3,960,000
2. Review and approval of grants	104	1,479,000	4	+29,500
3. Computer research and technology	112	4,537,000	--	+105,000
Total program increases	--	--	4	+4,094,500
C. Payment to the "National Institutes of Health management fund" for centrally furnished services	--	205,000	--	+42,000
Total increases	--	--	--	+4,143,500
Decreases				
A. Program				
1. Fellowships	--	154,000	--	-8,000
2. Training	--	376,000	--	-12,000
Total program decreases	--	--	--	-20,000
Total net change requested	--	--	--	4,123,500

Explanation of Changes

Research grants--The program increase of $3,960,000 will provide funds for the General Clinical Research Center program to support the rising costs for hospitalization and technical personnel in the continuing and activated centers.

Fellowships--The program decrease of $8,000 will result in no change in the number of grants awarded, however, the average amount of each grant will be diminished.

Training grants--The program decrease of $12,000 will result in no change in the number of grants awarded, however, the average amount of each grant will be diminished.

Computer research and technology--The program increase of $105,000 will enable the division to enter the implementation phase for more powerful and efficient programming tools to exploit the new remote terminals and special purpose computer systems now being acquired by NIH laboratories.

Review and approval--The program increase of $29,500 and four positions will provide for the scientific administration, processing, and fiscal management of grant programs.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1969 Senate Report	
No significant items.	None.
1969 House Report	
No significant items.	None.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act Section 301--Research and Investigation, in general.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Title III -- General Powers and Duties of Public Health Service

PART A -- RESEARCH AND INVESTIGATION

In General

"Sec. 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man, including water purification, seqage treatment, and pollution of lakes and streams. In carrying out the foregoing the Surgeon General is authorized to--.....

(c) Establish and maintain research fellowships in the Service with such stipends and allowances, including traveling and subsistence expenses, as he may deem necessary to procure the assistance of the most brilliant and promising research fellows from the United States and abroad;

(d) Make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for such research or research training projects as are recommended by the National Advisory Health Council....."

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Salaries and Expenses Office of the Director".....	-$441,000	--	To provide funds covering expenses of the Office of the Director which were previously funded through the NIH Management Fund.
"National Institute of Allergy and Infectious Diseases".....	-10,328,000	--	For the programs and functions of the Office of International Research transferred to the National Institute of Allergy and Infectious Diseases.
"John E. Fogarty International Center for Advanced Study in the Health Sciences".....	-2,811,000	--	For the programs and functions of the Office of International Research transferred to the Fogarty International Center.

29-867 O—69—pt. 4——58

General Research and Services

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$28,974,000	$36,404,000	$49,585,000	$45,994,000
1961	47,260,000	52,600,000	104,405,000	83,900,000
1962	95,341,000	119,275,000	140,000,000	127,637,000
1963	147,826,000	155,826,000	161,826,000	159,826,000
1964	164,674,000	163,869,000	164,674,000	163,869,000
1965	163,715,000	162,959,000	164,759,000	164,759,000
1966 1/	58,719,000	59,969,000	60,469,000	60,469,000
1967	67,821,000	68,534,000	68,534,000	68,534,000
1968	81,141,000	81,141,000	81,141,000	81,141,000
1969	87,000,000	82,719,000	94,823,000	84,809,500
1970	74,809,000			

1/ Excludes the "National Institute of General Medical Sciences" established as a separate appropriation in 1966.

Justification

General Research and Services

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	256	$2,760,000	260	$2,862,000	+4	+$102,000
Other expenses.....	--	67,925,500	--	71,947,000	--	+4,021,500
Total.....	256	70,685,500	260	74,809,000	+4	+4,123,500

General Statement

The appropriation for General Research and Services finances the Division of Research Facilities and Resources, the Division of Computer Research and Technology, and the Engineering Development activity. Each of these is described individually in the following justification.

Division of Research Facilities and Resources

Research Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
General clinical research centers	$35,004,000	$38,964,000	$+3,960,000
Scientific evaluation	305,000	305,000	--
Special research resources	10,494,000	10,494,000	--
Animal resources	4,568,000	4,568,000	--
Primate centers	10,500,000	10,500,000	--
Total research grants	60,871,000	64,831,000	+3,960,000

Introduction:

The primary mission of the Division of Research Facilities and Resources is to provide the Nation's academic and scientific institutions with the research resources and facilities essential for sustaining and advancing the National biomedical research and research training program leading to the improvement of the health of the Nation. The Division's programs underpin a broad spectrum of institutions by supporting critical resources that are essential to the total panorama of individual as well as team biomedical research activities.

The programs administered by the Division provide support for clinical research centers where physicians and scientists can study human disease; for computer centers and other special research resources that form a most important technological base for modern biomedical research; for critically important laboratory animal facilities and resources essential to a wide variety of specialized biomedical research efforts; and for several other types of major biomedical research resources. The grants of this Division help to sustain the Nation's educational and training institutions. These institutions are the stage upon which the biomedical research and educational projects sponsored by the Institutes and Divisions of the National Institutes of Health are executed.

General Clinical Research Centers

The broad objective of the program is to create and sustain, on a stable basis, highly specialized institutional resources in which the Nation's clinical investigators; can observe and study human diseases; define their characteristics; devise ways of exploring clinical phenomena in laboratory situation; apply, where possible, fundamental biological concepts to patient care; and study the biological characteristics of the normal human subject. Within the physical and conceptual confines of these resources, a number of patterns of research activity have emerged which are identifiable and can be projected. One pattern is intense investigation centering around the management of diseases, such as cancer, cardiovascular-renal diseases, infectious diseases, the process of aging and diseases contributing to high infant mortality rates. A second pattern is training of all classes of personnel who will conduct and participate in clinical investigation in the years ahead, which includes medical and scientific as well as ancillary health-professional personnel. "Graduates" of these programs will be in the "pool" from which the faculties of medical schools now in prospect will be drawn. The third pattern is the increasing inter-change between research activity of the Center and local organizations concerned with the practice of medicine. Such interaction facilitates communication and expeditues application of new methods of diagnosis and treatment of disease at the community level.

Each center is a self-contained research ward devoted to intensive medical research in human patients. An "average" center can accommodate 12 patients, is supported by its own scientific director and ancillary staff and has a complement of laboratory and dietary facilities. The facilities and resources provided are a vital link in translating the results of laboratory research into new diagnostic and therapeutic tools for the management of human disease. Research in major disease areas includes renal diseases, cardiovascular, infectious diseases, allergy and immunology, dermatology, cancer, and diseases contributing to high infant mortality rates.

The following are a few of the many projects conducted in General Clinical Research Centers during the past year:

Transplantation: The transplantation of the human heart has become a reality during the past year. This procedure has captured the imagination of the world, has offered hope to many and has redefined thoughts about life and death. Many of the transplants in this country have used Clinical Research Centers for the pre- and post-surgical study of these patients.

The Clinical Centers have been active in all areas of transplantation. They were used in the early days of kidney transplantation for the development of this almost standard procedure. Presently the Centers are being used for work on the early detection of rejection of transplanted organs, for work on the means for prolonging organ survival, and for studies on alternative means of therapy for transplant recipients.

Transplantation immunology: The success of transplantation rests on the extensive efforts made over the years in the field of immunology. While the area of transplantation immunology has achieved the widest publicity, immunologists have used the Centers to study the role of the immune system in arthritis, cancer, gastrointestinal disorders, blood diseases, congenital defects, leprosy, tuberculosis and many other infectious processes.

Radiation therapy for abdominal and pelvic cancer: Radiation therapy is often the treatment of choice for abdominal and pelvic cancer. One of the limitations of such therapy is the danger of radiation-induced kidney damage that might prove fatal to the patient. A method for protecting the kidney by the intra-arterial injection of epinephrine during radiation has been demonstrated successfully at one Center after years of animal research. Such a drug program will allow for far better treatment of certain tumors.

Drug addiction: Research on narcotic addiction initiated five years ago has led to the first successful program for treatment of hard core criminal addicts. This program, reported to the Committee three years ago, has been extended to over 1,000 patients in the New York City area and approximately 1,000 other patients in various cities of the United States, Canada, and Europe. A system has been developed for routine urine monitoring on patients to detect narcotic drugs, barbiturates, tranquillizers and amphetamines. An ambulatory method of treatment now saves approximately $2,500 per patient each year. In addition, it has been shown that prisoners selected by purely random processes can be brought into the methadone treatment program and the majority converted into more useful citizens.

Program Plans in 1969 and 1970

The 1970 estimate of $38,964,000 provides for an increase of $3,960,000 over the 1969 level of $35,004,000. This increase is vital and necessary for (1) the protection of the Nation's current investment in a network of resources that bring clinical research even closer to clinical application, and (2) a modest extension into a few of the medical schools without such resources.

The increase requested in 1970 will allow the maintenance of the number of beds now in use and the present rate of occupancy, in the face of rapidly rising hospital costs, largely as the result of pay raises for nurses, technicians, and other paramedical personnel. During 1969 centers were permitted the option of releasing up to 25% of the available beds for general hospital use in order to help defray the fixed operating costs of these centers. It is estimated that current operating costs will rise some 12% by 1970. The 1970 estimate will provide hospitalization funds for 62% occupancy or the approximate equivalent of 645 of the 1,040 beds available, and will provide personnel for 2,080 of the 2,540 currently approved positions.

The need to accelerate the closing of any gap that might exist between research findings and application to the hospitalized or ambulatory patient is becoming acute in many of the 40 medical schools without such centers. Modest assistance in this effort in medical schools with newly demonstrated excellence in clinical research will allow additional citizens to benefit from more modern medicine.

Scientific Evaluation

The $305,000 requested for 1970 will support the study sections, and preliminary review committees used by the Division to provide scientific merit review of grant applications.

These study sections and committees, composed of outstanding authorities in the various fields of medical research, are responsible for the scientific peer evaluation of all research grant applications and forward their recommendations to the appropriate National Advisory Council.

Special Research Resources

This program provides institutional support to enhance the capability of individuals and research teams in our medical schools and universities through application of large-scale equipment and instrument oriented resources to disease problems demanding major multidisciplinary research endeavors. Many research areas, such as understanding enzyme structure and function and the relationships between living tissue and toxic compounds, depend very heavily upon computer resources, specialized instrumentation and/or commercially unobtainable biological materials. Since facilities to fulfill these needs are usually too costly or too extensive to be managed by a single investigator, a Special Research Resource is established for use by a community of scientists.

While the exact nature of each computer resource varies, the program cuts into almost every facet of bioscience. The program supports very large centralized machines at regional general-purpose centers, and also helps to build computing devices consisting of discrete modules of hardware capable of performing specific logical functions that may be quickly assembled into sets to meet the special demands of a researcher.

Over the past few years high-resolution mass spectrometers and nuclear magnetic resonance spectrometers have been adapted for the analysis of biological compounds. These instruments can be used to distinguish molecules and their fragments by the precise determination of either the particle's mass or their nuclear magnetic properties. An expert team is needed to use these elaborate and sophisticated machines effectively. Centralization of analytical biochemical instrumentation resources contributes to the economic utilization of instruments and assures high quality investigative work through the efforts of permanently available, highly-trained manpower.

Biomaterials resources are varied in nature. Currently we have one type that acts as a central large-scale laboratory for the use of scientists at different academic institutions within a geographic region, while another type serves as a repository for the maintenance and preservation of viable biologic materials for national distribution.

The following are a few of the many projects conducted in Special Research Resources during the past year:

Testing organs for compatibility before transplantation is of vital importance and is conducted for several of the Nation's transplantation centers at the Division supported Health Sciences Computer Facility at the University of California, Los Angeles. These investigators employ the computer to classify (or type) the white blood cells of a subject. They use a remote display terminal and take advantage of the system's time-sharing capabilities in monitoring the results of their computations and in effecting alterations in the subsequent course of their analyses. This type of research and computer application is essential if the transplantation of organs is to be placed on firm scientific ground. While at present the change of a non-related kidney transplant surviving one year is about 50 percent, this figure might be considerably raised as a result of such research. Moreover, a computer might be used to maintain a Nation-wide list of typed possible recipients in order to have donor organs rapidly delivered to a compatible recipient.

Investigators at the Massachusetts Institute of Technology and nearby Beth Israel Hospital are conducting a collaborative program in order to develop mass spectrometric-computer integrated techniques for the rapid identification of drugs ingested (accidentally or attempted suicide) by humans. Drug identification is based on automated analysis of mass spectral data obtained on the drug and its metabolites present in the patient's blood. A previously recorded file of mass spectral data on common drugs, poisons, and their metabolites is stored on magnetic tape and, by use of a computer program developed at this center, identification is established.

The Mass Spectrometry Center for the Research Triangle Region of North Carolina has provided a very essential service to the biomedical research community situated in the southeast. This contribution has been made through support of a number of medicinal chemistry research programs that are currently in progress. Potential additions to the drug armamentarium of the clinical physician are being explored through the isolation of chemicals from natural sources. In general, isolation of a new biologically active constituent is followed by structural elucidation, chemical synthesis, adequate biological evaluation. Modificiations of the natural substance are usually performed in order to develop more effective and safer drugs. The Research Triangle Facility has participated in programs involving the structure elucidation of promising tumor-inhibitory and anti-leukemic agents from natural sources, the identification of drug metabolites reflecting the fate of drugs in biological systems, and the identification of naturally occurring physiologically active substances.

Program Plans in 1969 and 1970:

The $10,494,000 available in 1969 will provide support for a program currently composed of 39 centralized resources of which 29 are life science computer resources, eight analytical biochemistry instrumentation resources, and two biomaterial resources. It is anticipated that approximately four new life science computer resources, one new analytical biochemistry instrumentation resource and one new biomaterial resource will be established.

The same amount requested for 1970 will provide continuing support for the established resources.

Animal Resources

The rapid growth of biomedical research in the Nation's academic and research institutions have imposed a substantial requirement for institutional laboratory animal resources that facilitate the development and carefully controlled use of animals of the quality and in the quantity needed for all aspects of medical research. The specific goals of the Animal Resources Program are to: (1) Provide for the development and maintenance of special strains of laboratory animals which are unique and highly valuable to research but are not available commercially. This includes highly inbred and isogenic stocks, mutant bearing stocks, institutional primate colonies, and colonies of exotic species. (2) Study anatomic, physiologic, and behavior characteristics of selected animal species to elucidate their usefulness as models to study human disease and basic biologic phenomena. (3) Provide for the development and support of laboratories for the diagnosis and control of laboratory animal diseases. (4) Strengthen institutional animal resource programs through grants to institutions to improve animal care equipment, facilities and personnel. Thus, many institutions are assisted in meeting the requirement of the Laboratory Animal Welfare Act (PL 89-544). (5) Support research projects focused on improving health and well being of laboratory animals. These include projects on animal diseases and environmental requirements. (6) Disseminate information on laboratory animals.

A diagnostic laboratory has been established at the Medical School of Yale University under an award from this program on the premise that the effective control of laboratory animal disease is essential to their total research effort in biology and medicine. The laboratory provides diagnostic services for investigators throughout the university, supports an institutional animal receiving/conditioning program and conducts an independent research program. One notable accomplishment of this laboratory is that mortality of certain species of research animals has been reduced from 30 percent in 1967 to less than eight percent in 1968. Facilities for diagnosis of diseases of laboratory animals are essential for all laboratory animal resources. Some of the diagnostic laboratories serve many institutions within a geographic area. Benefits to be derived from such laboratores are the identification and subsequent control of outbreaks of disease that may decimate colonies vital to continued study of the health problems of man.

The Animal Resources program has emphasized the development of new animal biological models both through studies to establish previously unavailable physiological, anatomical, or behavioral baselines, and through development of optimal methods of husbandry and breeding for specific animal strains and species. An example of this phase of the program is the development of biological profiles for the baboon. This biological model is being used extensively in research programs involving studies on arborviruses, cardiovascular diseases, reproductive biology, and basic immunological studies associated with transplantation. Studies of the normal physiology

of this animal have made it one of the best understood and scientifically documented primates available for research.

Program Plans in 1969 and 1970:

The $4,568,000 available in 1969 will provide support for a program currently consisting of 45 ongoing resources and enable the establishment of approximately ten new resources. The same amount requested for 1970 will provide continuing support for 50 resources and an estimated seven new grants for animal resources.

Primate Centers

Since this program's inauguration in 1962, the Primate Research Centers program has organized, constructed and initiated operations in seven centers. On the average these units are functioning at about 75 percent of planned initial capacity. The orginal program concept emphasized meeting the needs for suitable facilities and resources for conducting biomedical research on nonhuman primates and for establishing methods and facilities for breeding and maintaining healthy animals over a long period of time. While this concept is valid today, there has been an evolution of the centers toward research centers focused on special biomedical problems.

The knowledge and research instrumentation now available are capable of leading to the answers to basic biologic questions in many disease areas. However, often times the major deterrent to progress is the lack of suitable biological models for investigation. In order to study many of the serious health problems, the most suitable research animal is the nonhuman primate. The homologies between the nonhuman primate and man are very direct, and the probabilities of successfully applying information gained from studies on the nonhuman primate to man are higher than with any other animal. Some of the important research areas where nonhuman primates are being used are: (a) tissue and organ transplantation; (b) reproductive biology and population control; and (c) behavioral sciences, mental health, and mental retardation. With the increased interest in these areas and many others the need for nonhuman primates will continue to grow.

The following are a few of the many projects conducted at the Primate Centers during the past year:

1. Techniques have been devised for monitoring the exchange of drugs and other chemical substances between the mother and fetus. The transfer of essential growth material, as well as potentially dangerous materials, can be measured during pregnancy, permitting observations of the developing fetus which were not heretofore possible.

2. Studies of the development of behavior from birth to maturity are yielding a better understanding of the origin of behavioral defects and abnormalities. The complex adjustments of primates to their natural habitat and to experimentally altered environmental conditions are being studied. The factors which permit adjustments to alternate conditions are being analyzed to gain a comparative perspective of human needs and behavior.

3. Greater apes are being utilized for studies involving transplantation and the associated immune response. Tissue antigens have been identified by immunologic procedures. Immunization of chimpanzees with these

extracted tissue antigens resulted in accelerated rejection of skin from the specific antigen donor. These experiments provide background data on the feasibility of similar experiments in human volunteers. The chimpanzee is also being studied as a potential donor of kidneys to the human.

Program Plans in 1969 and 1970:

The $10,500,000 requested will provide continuing support for operation of the seven primate centers. The ongoing programs include the establishment of methods of breeding and of maintaining health stocks of nonhuman primates of all ages over a long period of time; the determination of the suitability of various species for different kinds of investigations; and the continuing evolution of the proper research resources environment to undertake these studies.

Plans for 1969 and 1970 provide for continuing support of the seven primate centers as follows:

	1969 Estimate	1970 Estimate
Regional Primate Research Centers:		
1. Medical Res. Found. of Oregon Portland, Oregon	$2,050,000	$2,050,000
2. University of Washington Seattle, Washington	1,400,000	1,400,000
3. University of Wisconsin Madison, Wisconsin	1,600,000	1,600,000
4. Emory University Atlanta, Georgia	1,250,000	1,250,000
5. Tulane University New Orleans, Louisiana	1,350,000	1,350,000
6. Harvard University Boston, Massachusetts	1,300,000	1,300,000
National Center for Primate Biology:		
7. University of California Davis, California	1,550,000	1,550,000
Total	10,500,000	10,500,000

Fellowships

	1969 Estimate	1970 Estimate	Increase or Decrease
Total fellowships	$154,000	$146,000	-$8,000

Introduction:

The increasing sophistication of animal resources for health related research requires personnel with highly specialized training. It is the purpose of the fellowships program to provide this training. The goal of the program is to provide an adequate number of specialists for research in laboratory animal science and medicine. The Division anticipates that people with demonstrated ability in laboratory animal medicine will be given

fellowships in special areas such as surgery, anesthesiology, pathology, virology, primatology, biochemistry, etc.

Program Plans in 1969 and 1970:

The $154,000 available in 1969 will provide support for 15 fellowships at the postdoctoral level. The $146,000 requested for 1970 will provide continued support for the 10 existing fellowships and five new fellowships.

Distribution of Fellowships

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Continuation:						
a. Noncompeting.....	11	$113,000	10	$101,000	-1	-$12,000
2. New.....	4	41,000	5	45,000	+1	+4,000
3. Total fellowships.....	15	154,000	15	146,000	--	-8,000

Fellowships (by type of program)

	1969 Estimate		1970 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Postdoctoral.....	12	$123,000	12	$116,000	--	-$7,000
2. Special.....	3	31,000	3	30,000	--	-1,000
3. Total fellowships.....	15	154,000	15	146,000	--	-8,000

Training Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Total training grants.....	$376,000	$364,000	-$12,000

Introduction:

The increased use of animals in medical research programs, not only in total numbers, but also in the variety of species, and the necessity of using animals raised under controlled conditions, have resulted in a great demand by medical research institutions for professional support by specialists in laboratory animal medicine.

Studies by the Animal Resources Advisory Committee of the Animal Resources Branch of this Division indicate that while approximately 500 veterinarians and PH.D.'s are now employed in laboratory animal care activities, an additional 1,100 are needed. These estimates are based on requirements of 1,600 institutions which use animals, including some 400 institutions with major animal colonies. Thus, a large number of medical schools and research institutions which are actively seeking veterinarians with a special competence in laboratory animal medicine are having great difficulty in finding suitable candidates.

Program Plans in 1969 and 1970:

The $376,000 available in 1969 will provide for nine training grants at the graduate level in the field of laboratory animal medicine. The $364,000 requested in 1970 will provide continued support to the nine grants.

Distribution of Training Grants

Graduate	1969 Estimate No.	1969 Estimate Amount	1970 Estimate No.	1970 Estimate Amount	Increase or Decrease No.	Increase or Decrease Amount
1. Continuations:						
a. Noncompeting	7	$300,000	7	$284,000	--	-$16,000
b. Competing	1	40,000	--	--	-1	-40,000
2. New	1	36,000	2	80,000	+1	+44,000
3. Total training grants	9	376,000	9	364,000	--	-12,000

Collaborative Research and Development

	1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
Personnel compensation and benefits	2	$37,000	2	$37,000	--	--
Other expenses	--	1,451,000	--	1,446,000	--	-$5,000
Total	2	1,488,000	2	1,483,000	--	-5,000

This activity supports research in collaboration with Federal and non-Federal institutions through contracts. No program increase is requested in 1970 to carry out this research.

Program Plans in 1969 and 1970:

The funds available in 1969 and 1970 will be used to support research contracts in the areas of Pharmacology-Toxicology, special research resources and laboratory animal care.

Emphasis will continue in the area of the Chemical/Biological Information Handling program of the NIH Pharmacology-Toxicology program primarily for the development of computer-based techniques for manipulating chemical and biological information so as to accelerate the realization of systems for handling numerical and other data related to interactions between living systems and exogenous drugs and poisons as well as endogenous chemical compounds.

There is a decrease of $5,000 for centrally furnished services from the "National Institutes of Health management fund".

Review and Approval of Grants

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	104	$1,199,000	108	$1,229,000	+4	+$30,000
Other expenses	--	334,500	--	386,000	--	+51,500
Total	104	1,533,500	108	1,615,000	+4	+81,500

This activity supports the scientific and administrative staff of the Division's special research grant programs, General Research Support programs and the Health Research Facilities construction program. This includes program planning and development; review and evaluation of grant applications for presentation to the National Advisory Research Resources Council, the National Advisory Council on Health Research Facilities and the National Advisory Health Council. Other duties of this activity include liaison with applicants, grantees, other components of the NIH and DHEW, the advisory bodies, and interested organizations.

The increase requested will provide 4 positions and $29,500 for assistance in program management.

Included in the net increase are mandatory increases of $4,000 for the annualization of cost of 1969 pay raise. There are also increases of $48,000 for centrally furnished services from the "National Institutes of Health management fund".

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	36	$487,000	36	$487,000	--	--
Other expenses	--	156,000	--	154,000	--	-$2,000
Total	36	643,000	36	641,000	--	-2,000

This activity is responsible for the overall direction, administration, planning, evaluation and data analysis of the several programs of the Division of Research Facilities and Resources. No increase in funds is requested.

There is a decrease of $2,000 for centrally furnished services from the "National Institutes of Health management fund".

Division of Computer Research and Technology

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	112	$1,253,000	112	$1,361,000	--	+$108,000
Other expenses.....	--	3,358,000	--	3,392,000	--	+34,000
Total.....	112	4,611,000	112	4,753,000	--	+142,000

Introduction

The Division of Computer Research and Technology provides a central scientific and computational resource for the NIH. To carry out this role, the Division plans and conducts a broad inter-disciplinary research and development program in which the concepts and methods of computer science, engineering and mathematics are applied to biomedical investigations. These research efforts provide a solid technical foundation for computational efforts at NIH and create new tools with which to attack biomedical problems.

Program Plans in 1969 and 1970

This Division was authorized in 1964 and became operational in 1966. Its early days were characterized by a period of recruiting, staff development and the exploration of its new role. Almost simultaneously, NIH upgraded its computer equipment to provide a hardware base for the computational power needed in this effort and there followed an involved and troublesome period of conversion.

Staffing and conversion problems encountered earlier in the Division's history have been largely overcome and has brought together the several kinds of specialists needed to give it a broad base of computational expertise and to provide an interdisciplinary bridge to other biomedical sciences. This bridge includes complete computational support to NIH investigators and building an innovative research base which produces the new tools, techniques and concepts needed in the rapidly developing field of biomedical research. DCRT continues to provide faster and more efficient computer services using third generation equipment. It offers new and powerful computer languages and a library of ready-to-use programs designed for the most frequent computational needs of NIH.

During 1969, a selected set of remote terminals are being provided for users of the central computer. These installations proved eminently successful as the first steps in providing NIH scientists with the ability to work from locations appropriate to their laboratory environment. The Division of Computer Research and Technology now exists as a powerful combination of hardware and people, broadly and solidly based, and focused on the entire spectrum of biomedical computation--from conceptual formulation of a problem solution to machine execution of the results.

The developmental efforts of DCRT will, during the remainder of 1969 and 1970, provide a much greater variety of remote access capability for NIH users. Division engineers are in the midst of critical projects involving several special-purpose computer systems in selected complexes of NIH laboratories. The hardware components of three such systems will be delivered late in 1969. Division staff, in collaboration with Institute personnel, will be involved in these and similar systems implementations through next year.

The first of these projects is in the National Institute of Dental Research. This project will involve the development of a medium-sized computer system linked directly to at least ten automated laboratory instruments. A second project, similar to that planned for the Dental Institute will involve the development of a computer system which will collect, analyze, and make immediately available biochemical laboratory data for the National Institute of Arthritis and Metabolic Diseases. It will initially link five quite advanced laboratory instruments to a central laboratory computer. Eventual expansion to 12 instruments is planned. The third project involves the installation of a small computer system in the National Heart Institute to collect and analyze data taken from two mass spectrometers. This equipment, combined with new analytical techniques developed by the Division allows an entirely new approach to the study of molecular fragmentation.

The growth of computation in the central computer facility, the installation of remote terminals linked to that facility, and the evolution of special-purpose computers in a number of program areas will bring into existence by 1970 a potential network of computers, terminals and users on the NIH reservation. The Division has therefore undertaken an ambitious but necessary project--to link these computers and all remote terminals into the central computer facility. A special control and scheduling interface, or common boundary, between the laboratory computer systems and the central facility will permit access by the remote terminals to whichever computer in the central facility is most appropriate for a given problem. This system can serve as a model to other biomedical areas throughout the nation who have needs similar to those found at the NIH.

In addition to providing NIH with central computational and data processing services and computer engineering systems design support, the Division conducts research in mathematics, mathematical statistics, heuristics (the development of artificial intelligence), physical chemistry, mathematical biophysics and computer programming. The main thrust of the program is carried out in collaboration with scientists in other Institutes, where mathematics and computer sciences play a productive and sometimes indispensable role. These collaborations make use of the Division's interdisciplinary base and develop specific techniques or computer programs to solve future problems both within and outside of NIH.

Examples of this role include applications of computer science and mathematical methods in heart surgery and surgical neurology. These tools include two large mathematical programming systems which have been fully documented and catalogued for routine use. The first of these analyzes measurements of internal heart pressures, blood flow, and the corresponding cardiogram signals. The system has been supplemented by an extensive array of automatic graphic outputs to enable the scientists to see results quickly. These programs have enabled researchers to measure heart valve efficiencies. They also offer promise of a more precise calculation of coronary artery blood flow.

The second tool which is available is a package of programs for "time series analysis". This kind of analysis has wide applicability to serial measurements of biomedical phenomena ranging from the better known clinical EKG and EEG to laboratory studies of cell division in cancer. The repertoire of these time series techniques will be made available to users via remote terminals supported by the central system.

The studies of the Division and its collaborators at NIH can be seen more clearly in some cases as directly affecting the provision of health care to the Nation. The mathematical and statistical programming staff have worked for some time in research study of clinical blood tests from normal volunteers and patients in the NIH Clinical Center. Data are available from approximately 2,500 Clinical Center patient admissions and from 78 normal volunteers. In 1968, basic analyses of the normal control data have been completed, as have many auxiliary analyses testing age, race, sex difference. Factors related to laboratory quality control and to the validity of various statistical estimates have been studied. A series

of reports concerning the results of these analyses and their significance for clinical medicine is in final preparation. These studies are expected to add substantially to existing information on the normal behavior of blood constituents and to enable development of standards for the increasing use of automated clinical laboratory techniques in comprehensive health care systems.

The development of processing and display of biological images has progressed with the installation of a specially designed computer system. This work was initiated as a collaborative effort with the National Institute of Neurological Diseases and Stroke and involved the computer analysis of the normal and pathological anatomy of brain and nerve tissue. However, the ultimate objectives of the image processing project are much broader than this, and once again show that a specific application of computers may have great general potential. New techniques and devices should ultimately permit study of any biological images with a view toward determining significant characteristics of these images, where the images are too complex or too profuse for the human mind to comprehend successfully. A "natural language" control system will be developed to ease the three-way scientist-microscope-computer interactions in image processing. Another goal of this project is the creation of computer programs to permit semi-automatic and fully automatic processing of large volumes of biological images. With today's powerful electron microscopes, these images can extend down to the smallest parts of living cells or virus particles. This long-range project will continue to apply state of the art computing devices and techniques to an important segment of biological investigations.

Other research in the Division is concerned with automatic deductive question-answering. In this process a computer is programmed to select certain facts from a sometimes unmanageably large (by human standards) data base and apply this "knowledge" in a mathematically logical way to obtain a solution to a specific problem. This program learns from experience in that it uses its attempts at answering previous questions to improve its question-answering ability.

Many areas of medicine and biology have reached a stage where the introduction of knowledge and skills from the areas of physics and mathematics can add immeasurably to their progress. A number of projects are aimed at such an integration of knowledge. For example, by "marrying" mathematical physics to physiology, a deeper understanding has evolved regarding the excitation mechanisms of nerve membranes. Another project has led to successful application of techniques of physical chemistry to obtain knowledge concerning the manner in which biological molecules change their conformations in response to changes within the liquid environment of cells.

Other studies have been directed towards quantitative understanding of the physical basis of molecular transport across biological barriers; still others have led to extended theoretical bases for the use of physical probes in the measurement of molecular and cellular activities. Finally, a project has been undertaken to develop computational programs for determining molecular structure. If the latter is successful, computers will be used to correlate the function and predict the activity of drugs and other pharmacological agents.

The increase of $142,000 for 1970 includes a program increase of $105,000 which will be used to develop the programming tools necessary to exploit the capability of new remote terminals and special purpose computer systems being acquired in NIH laboratories, $3,000 for annualization of the 1969 pay raise and $34,000 for the Division's share of centrally furnished services from the NIH management fund.

Engineering Development

Obligations by Activity

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Collaborative research and development.....	--	$750,000	--	$750,000	--	--
Program direction.....	2	259,000	2	226,000	--	-$33,000
Total obligations.....	2	1,009,000	2	976,000	--	-33,000

This activity supports centralized efforts in the evaluation of the potential contributions to health and medicine from advances in the physical sciences and the application of the principles and practice of engineering science to biomedical research and health care. These contributions can range from the development of new, natural and synthetic materials, sophisticated and minaturized instrumentation and electronic devices, to computer technology and systems analysis concepts.

Throughout the health research programs of the National Institutes of Health there are investigations of the specific application of modern engineering technology to medicine and health, including artificial internal organ replacement, automation and its integration into the hospital environment, isolation and containment facilities, patient monitoring devices and systems, and hospital information systems. The orderly and effective development of this new and complex field of biomedical engineering requires an evaluation of broad questions such as determining the optimum institutional and functional arrangements for the effective exploitation of technological innovation.

The 1969 and 1970 plans for this activity include the exploration of selected, well-defined areas of concern. A current contract with the National Academy of Engineering (NAE), serving in an advisory capacity to program management, is attempting to identify and broadly define program opportunities and needs on the basis of current engineering theory and practice and the application of these to problems of biology and medicine. Various subcontracts have been made to develop prototype institutional patterns which would be useful in effecting cooperation between diverse groups such as universities, industrial firms, hospitals and government agencies; to explore specific areas such as the impact of engineering on surgery; and to determine those factors influencing industrial participation in the United States and abroad.

In addition to these specific investigations, efforts are directed toward structuring and building an adequate foundation for the successful realization of this program, which would require a major expansion. This includes the continuous assessment of the "state of the art" for making the vital determination of when a field or particular biomedical problem has reached the optimal point for exploitation. This assessment and the determination of the best organizational structure for implementation of this program are being discussed with interested officials both inside and outside the government.

The decrease of $33,000 was a result of a reduction in centrally furnished services from the "National Institutes of Health management fund".

New Positions Requested
Fiscal Year 1970

Division of Research Facilities and Resources	Grade		Annual Salary
Review and approval of grants			
Scientist	GS-14		$16,946
Administrative staff assistant	GS-13		14,409
(2) Secretary	GS-6		12,642
Total new positions		(4)	43,997

29-867 O—69—pt. 4——59

WEDNESDAY, APRIL 2, 1969.

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

WITNESSES

DR. MILO D. LEAVITT, JR., DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GEORGE E. PRESSON, EXECUTIVE OFFICER, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (In thousands of dollars)

	1968 actual	1969 estimated	1970 estimated
Personnel compensation:			
Permanent positions	535	630	680
Positions other than permanent	23	25	25
Other Personnel compensation	1	2	2
Total personnel compensation	559	657	707
Personnel benefits: Civilian employees	75	80	84
Travel and transportation of persons	195	219	228
Transportation of things	19	41	41
Rent, communications, and utilities	68	88	93
Printing and reproduction	9	62	68
Other services	163	748	309
Supplies and materials	10	65	74
Equipment	18	128	136
Grants, subsidies, and contributions	1,607	1,786	1,720
Total obligations	2,724	3,874	3,460

PERSONNEL SUMMARY

Total number of permanent positions	51	52	58
Full-time equivalent of other positions	3	3	3
Average number of all employees	52	52	57
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Operations:			
(a) Grants:			
(1) Research	229	150	150
(2) Fellowships	1,378	1,636	1,570
(b) International center	1,106	1,588	1,740
2. Facility planning and construction		500	
Total program costs, funded [1]	2,713	3,874	3,460
Change in selected resources [2]	11		
Total obligations	2,724	3,874	3,460
Financing:			
Comparative transfers from other accounts	−2,724	−2,774	
Unobligated balance available, start of year		−500	
Unobligated balance available, end of year	500		
Budget authority (appropriation)	500	600	3,460
Relation of obligations to outlays:			
Obligations incurred, net		1,100	3,460
Obligated balance, start of year			705
Obligated balance, end of year		−705	−1,640
Outlays		395	2,525

[1] Includes capital outlays as follows: 1968, $11,000; 1969, $128,000; 1970, $142,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $443,000; 1968, $454,000; 1969, $454,000; 1970, $454,000.

Biographical Sketch of Principal Witness

Name: Milo David Leavitt, Jr.

Position: Director, John E. Fogarty International Center for Advanced Study in the Health Sciences, NIH.

Birthplace and date: June 24, 1915, Beloit, Wis.

Education: 1933–38, University of Wisconsin, B.A.; 1938–40, University of Pennsylvania, M.D.; 1945–48, University of Minnesota, M. Sci.; 1958–59, Harvard University, M.P.H.

Experience:

1968–present, Director, John E. Fogarty International Center for Advanced Study in the Health Sciences, NIH.

1967–68, Acting Director, Office of Program Planning, NIH.

1967, Deputy Director, Office of Program Planning, NIH.

1966–67, Deputy Assistant Secretary for Science and Population, DHEW.

1966, Science Policy Coordinatior, OS–AHS, DHEW.

1962–66, Head, Special International Programs Section, Office of International Research, NIH.

1960–62, Assistant Chief, Perinatal Research Branch, National Institutes of Neurological Diseases and Blindness, NIH.

1959–60, Chief, Project Services Branch, Collaborative Research, NINDB, NIH.

1958–59, Postdoctoral Public Health Trainee, Harvard School of Public Health, Boston, Mass.

1949–58, Clinical Assistant Professor Medicine Woman's Medical College of Pennsylvania, Philadelphia, Pa.

1945–49, Fellow, Internal Medicine, Mayo Clinic, Rochester, Minn.

1942–45, Captain, U.S. Army Medical Corps.

1940–42, Rotating Internship, Philadelphia General Hospital, Philadelphia, Pa.

Association memberships:

American Medical Association.

Philadelphia County Medical Society.

Society of the Sigma Xi.

American Diabetes Association.

Association of American Medical Colleges.

New York Academy of Sciences.

American Association for the Advancement of Science.

Industrial Medical Association.

Alumni Association of the Mayo Foundation.
American Heart Association.
American Public Health Association.
American Society for Public Administration.

Mr. FLOOD. Now we have the John E. Fogarty International Center for Advanced Study in the Health Sciences, and as our witness we have Dr. Milo D. Leavitt, Jr., the Director. Will you introduce your people, please? This is your first budget hearing, is it not?

Dr. LEAVITT. Yes, sir, Mr. Chairman.

May I introduce my executive officer, Mr. George Presson.

Mr. FLOOD. I see you have a statement, Doctor. How do you wish to proceed?

Dr. LEAVITT. With your permission, Mr. Chairman, I would like to read it for the record.

Mr. FLOOD. Very well.

GENERAL STATEMENT

Dr. LEAVITT. Mr. Chairman and members of the committee, it is a pleasure to appear before you to present the budget of the John E. Fogarty International Center for Advanced Study in the Health Sciences. This Center will be a lasting memorial to Congressman John E. Fogarty, who in 1963 proposed the establishment of a center dedicated to international cooperation and collaboration at the National Institutes of Health. It represents the continuing effort of the NIH to encourage and foster the maximum effectiveness of scientific research. The establishment of this Center marks the beginning of a new dimension in the advancement of research on an international scale.

First, I would like to report to you on our progress with the physical establishment of the Fogarty International Center. In 1968, both this committee and the Senate Appropriations Subcommittee, in commending the proposal to establish a center for research in biology and medicine dedicated to international cooperation and collaboration, appropriated funds for the planning and design of a building in which to house the Fogarty International Center.

After approval by the Bureau of the Budget of the proposed plans and requirements of this Center, a contract was made with the architectural firm of Hellmuth, Obata & Kassabaum of St. Louis, Mo., for the design of the building. This organization, which was chosen after extensive review and evaluation of several architectural firms by the NIH and the General Services Administration, enjoys an excellent reputation. We are most pleased with its selection. The design plans are scheduled for completion in the spring of 1970.

In addition to the planning funds for a new facility, approval was given for the release of funds for the restoration of Stone House. The restoration is scheduled for completion by July 1969.

Secondly, I wish to report on the programs of the Center. You may recall that last year the Director, NIH, stated that with the establishment of the John E. Fogarty International Center he would reorganize the international activities of the NIH. On July 1, 1968, certain programs and functions of the Office of International Research were transferred from that Office to the Fogarty International Center. Other programs of the Office of International Research, such as the United

States-Japan cooperative medical science program, the international centers for medical research and training program and the international research career development program were transferred to the National Institute of Allergy and Infectious Diseases.

UNITED STATES-JAPAN COOPERATIVE PROGRAM

Mr. FLOOD. What do you know about the United States-Japan cooperative program?

Dr. LEAVITT. Sir, I was privileged to be a part of its early planning in 1965.

Mr. FLOOD. That was after Mr. Johnson and the Prime Minister of Japan had their meeting?

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. Do you know it is controversial? One of your colleagues here yesterday was not aware there was controversy about it.

Dr. LEAVITT. I had not been aware of any real controversy, Mr. Chairman.

Mr. FLOOD. Real? Some? Didn't you hear it was called just a publicity stunt by some people; that these same people said that it wouldn't do anything that would not be done by the Japanese and the Americans anyhow; that it was only a paper program with no real organization or central direction?

Dr. LEAVITT. No, I hadn't.

Mr. FLOOD. I want to make it clear that I wasn't among these critics, but I certainly heard this, and I am amazed that some people administering the program haven't heard this.

How much money have the Japanese put into this? Nobody knew when the question was asked yesterday. Isn't it odd that in a cooperative enterprise you wouldn't know how much your cooperator put in in dollar value? We don't know. That is not much cooperation, is it?

Dr. LEAVITT. No, sir.

Mr. FLOOD. Don't you think we should know?

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. But we don't know how much the Japanese put in. Isn't that odd?

Dr. LEAVITT. Insofar as the Japanese support of specific research projects is concerned, I believe their investment has been, as you say, a modest one.

Mr. FLOOD. I do not know if it is modest. We have no idea. I said to your colleagues, how much is the United States putting into this program, and he told me to the dollar. If the Japanese ask you, you would tell them to the dollar. Then I said to him, "How much are the Japanese putting in?" He did not have the faintest idea and neither do you. Isn't that odd?

Dr. LEAVITT. I believe the cooperative efforts, Mr. Chairman, primarily involved conferences and meetings.

Mr. FLOOD. What about that one flat question? Here we are spending x dollars under a cooperative agreement and we don't even know, approximately, what our partner is contributing. Why?

Dr. LEAVITT. There has been perhaps a disproportionate investment by the United States.

Mr. FLOOD. Why?

Dr. LEAVITT. Because for our own selfish interests, we were interested in some of the areas that the United States-Japanese cooperative program encompassed.

Mr. FLOOD. The Japanese are not selfish? Even they would be surprised to hear that.

Dr. LEAVITT. This is for our own interest.

Mr. FLOOD. Yes, I know, but this is a cooperative program.

Dr. LEAVITT. I believe the real cooperative efforts took the form of joint conferences and seminars which each country supports.

Mr. FLOOD. I will tell you what you do. Will you try to find out for me what Japan has been contributing.

Dr. LEAVITT. I will be very pleased, indeed.

Mr. FLOOD. Just put it in the record.

(The information follows:)

UNITED STATES-JAPAN COOPERATIVE MEDICAL SCIENCE PROGRAM

During fiscal years 1966, 1967 and 1968, the Japanese contribution has been in dollar equivalents, $138,800, $245,000 and $178,900 respectively. It must be recognized that these amounts cannot be compared to U.S. figures due to differences in methods of funding and recording. An accepted way of judging the capabilities of different countries to participate is to use as a common denominator a factor derived from the Gross National Product (GNP) times total population.

In 1967 the Japanese GNP and population were $115 billion and 100 million, and those of the United States were $811 billion and 199 million. This results in a U.S. capability 14 times that of Japan. Applying the 14:1 formula to the Japanese 1967 expenditure, its comparability would be $3,444,000 to the U.S. expenditures of $4,137,000. Adding the fact that most Japanese scientists are paid by their universities and therefore this amount is not included in the Japanese total, the proportionate amount of effort of each country is quite similar.

For the year 1968 the Japanese comparison is not quite as favorable. The Japanese GNP and populations were $135 billion and 101 million, while those for the United States were $891 billion and 202 million. This results in a comparison factor of 13.2:1.

Another aspect in making comparisons is to consider the relative size and state of development of the scientific base of each country. The United States has not only a larger proportion of scientists and scientific institutions, our scientific base is broader and more diversified. As a result, the U.S. scientific community is capable proportionately of a larger and more sophisticated participation in a program of this type.

Mr. FLOOD. You may proceed.

Dr. LEAVITT. The Fogarty International Center is a focal and coordinating point for the international activities of the National Institutes of Health. It is responsible for the administration of the International postdoctoral fellowship program, the NIH portion of the special foreign currency program (Public Law 480), the NIH overseas offices located in Rio de Janeiro, Brazil; Paris, France; Tokyo, Japan; and New Delhi, India, the scholars-in-residence program and the conference and seminar program.

CENTRALIZATION OF INTERNATIONAL ACTIVITIES

Mr. FLOOD. That is exactly what this committee thought. That is what we were led to believe when the Fogarty Center was created, that these programs would all be collected under your center, and that would be the purpose and the jurisdiction of the Fogarty Center.

Of course, it is not at all. You only have a fraction of your patrimony. It is scattered all over the lot. I doubt if you can do anything about it. I know you do not have the responsibility for determining how these things are organized.

You do not have half the programs that you should have.

I would not reply to that. There is nothing you can do about it especially. Go ahead.

INTERNATIONAL POSTDOCTORAL FELLOWSHIP PROGRAM

Dr. LEAVITT. The international postdoctoral fellowship program provides an opportunity for the two-way exchange of research capability and knowledge between American scientists and scientists from other countries in the attack on problems which affect the health of the American people. These foreign scientists bring to our laboratories in the United States a first-hand working knowledge of diseases and health situations which provides a base for future international scientific collaboration.

This program is conducted on a highly competitive basis. Applications of each of the candidates from the 40 participating countries receive extensive scientific and merit review. At this time, there are 152 fellows representing 33 countries. Funds requested for this program for fiscal 1970 will support 104 new fellows or one-half of the number whose applications are recommended by selected country committees.

SPECIAL FOREIGN CURRENCY PROGRAM (PUBLIC LAW 480)

The Fogarty International Center has the coordinating and operating responsibility of the NIH special foreign currency program. This program began in 1961, as an extension of the NIH domestic research interests. Its purpose is to utilize resources and unusual research opportunities through collaborative efforts of NIH scientists and foreign investigators. In 1965, the Public Health Service, recognizing the interests of other elements of the Service, assumed administrative responsibility for the program and now presents a coordinated budget. The NIH program is now financed with an allocation from the PHS Public Law 480 appropriation.

Collaborative research proposals considered for support under this program must meet the usual NIH standards of merit, must be relevant to domestic research objectives and must show promise of productivity. An unusual aspect of this program is the requirement for collaboration between an American scientist and a foreign investigator. No proposal is submitted for review unless this collaboration exists. Although there is a disapproval rate of over 50 percent, we now have nearly 100 active projects.

CONFERENCE AND SEMINAR PROGRAM

The objectives of the Conference and siminar program are to:

(1) Promote advanced study in the health sciences by conducting international conferences, seminars and workshops within the scope of the NIH mission, that is, advancement of knowledge for the Nation's health.

(2) Identify the legal, ethical, social and economic problems that may arise from new findings of biomedical research.

(3) Advance our understanding and insight into these problems confronting us by holding cross-disciplinary conferences and seminars.

(4) Stimulate research in particular fields by holding training seminars and workshops drawing on the international and biomedical research community for participants and faculty.

During 1969, the following conferences will be held at the Center:

(1) A symposium on "Reform of Medical Education in Advanced Countries."

(2) "Family Planning and the Status of Women."

(3) "Environmental Influence on Genetic Expression."

(4) The 6th International Symposium on Pupillography in collaboration with NINDS and NEI.

Conferences have long been recognized as an effective medium for encouraging creative and speculative thought. Despite the value of scientific meetings, many are randomly selected, are of diverse character, and all too frequently are of questionable utility or value. They lack coordination and effective management. Thus, the need for a deliberately organized, carefully planned program of scientific conferences devoted to major problems, opportunities, and developments in the biomedical sciences. The Fogarty International Center program will fulfill this need.

SCHOLARS-IN-RESIDENCE

The primary objective of this new program is to provide an environment conducive to the discussion, expansion and evolution of ideas. Within this environment the program will promote fruitful exchange of ideas between distinguished leaders in science, scholars in other disciplines and other creative individuals. In conjunction with an advisory committee we propose to select outstanding scientists and scholars from the United States and abroad who will focus their attention on important issues of biomedical research. While in residence at the Center the scholars will be encouraged to consider broad problems. The unique environment at the NIH offers an unusual opportunity for scholars to meet with large numbers of intramural staff scientists for discussion—focusing attention on important health problems, holding small conferences, workshops and, on a group basis, assessing the state-of-the-art in many disease areas. It is anticipated that scholars will provide not only inspiration to others but will also assume leadership in delineating important areas of research where group discussions by leading scientists should result in more rapid advancement in the solution of disease-related problems of man.

Mr. Fogarty devoted his life to improving the health of the American people. It is our intention to carry on his great work by adding a new dimension to the research programs of the National Institutes of Health, for which we are requesting an increase of six positions and a budget of $3,460,000.

I shall be happy to answer any questions on the Fogarty International Center.

CHAIRMAN'S GENERAL COMMENTS ON FOGARTY CENTER

Mr. FLOOD. Doctor, as, of course, you know, this Center is the brainchild of this committee. This is our favorite project for very obvious reasons. We are both happy and unhappy with the situation as it exists today at the Center.

First, I will say the nice things. I am very glad to hear what you have to say today on the progress in establishing the Fogarty International Center, because this committee is deeply interested in your office and its program.

We are interested in it because it is a memorial to a congressional colleague we all loved, a man who did so much for the health of the world, but we are also interested because the mission with which you are charged is extremely important in itself for the effects it will have in the international medical community.

I am glad to see you are making progress in getting the Fogarty International Center underway. I am looking forward to the time that you will have it operational and will be able to bring foreign scientists to Bethesda to work in the research institutions out there. These scientists will be able to make contributions to our research and the results of our research will enable them to bring back to their own countries knowledge they could not get in any other way.

I think the time may have arrived, Dr. Leavitt, for you to begin to do some planning on the operational details of your project. Next year when you testify, it might be well for you to be prepared to tell us how you think the Center should work and how you look for it to develop over a period of years.

Keep the committee informed of your thinking on a formal basis as you are doing when you testify today, and feel free to keep in touch with me and other members of the subcommittee as you find it in the interest of the Fogarty Center. If you have an idea which you feel will contribute to making the Center better, don't hesitate to get in touch with me at any time. I will always be glad to receive any ideas that will help this project to reflect well on the memory of the man for which it is named and so will the other members of this committee and of the entire House of Representatives.

FUTURE DEVELOPMENT OF THE FOGARTY CENTER

Now that I have said these very nice things to you, we want to probe a little deeper because there are some things with which we are unhappy.

We have mentioned a few specific activities in the field of international health and medical activities, and we are not just a little surprised, but very surprised and disappointed that they have not been transferred to the Center, as I mentioned a couple of minutes ago. Could you and Dr. Marston give us some idea of what you see as the probable—not possible, but probable—future of the Center. Let us begin with you.

Dr. LEAVITT. I have viewed the Center's development in phases. The initial phase would include the development of the scholars-in-residence program and the conference and seminar program. These would provide the academic environment which was originally conceived to be a major function of the Center. With time and with ex-

perience in getting these initial programs underway, it is my hope then that we may expand our activities to include additional programs.

I believe Dr. Marston might wish to speak further on it.

Dr. MARSTON. The focus has been on the title of the Center, a Center for Advanced Study in the Health Sciences. One of the first questions that had to be addressed, and which Dr. Shannon addressed in his comments last year before this committee, was how NIH could carry on the operational responsibilities without overloading the Fogarty International Center, particularly in the early phases. As he promised the committee last year, he would be reorganizing the international activities of NIH, moving to the Center those activities that would permit it to get on with its work of developing a major center for advanced study, but at the same time not loading it down with operational activities. So the activities of the Office of International Research, which had been a part of the Director's Office, were transferred in part to the Fogarty Center, and the remainder to the NIAID.

The role of the Fogarty Center already has been to draw together, in a way that was not previously possible, all the activities concerning international affairs at NIH. Dr. Leavitt and his staff have been meeting personally with all of the Institutes all of whom have demonstrated a type of enthusiasm that we have never seen before.

Mr. FLOOD. They do not think that you are the white-haired boy of this committee and resent you over there on that campus, do they?

Dr. LEAVITT. No, sir; I do not believe so.

Mr. FLOOD. We have heard some mutterings about this.

Dr. LEAVITT. The NIH scientists are delighted that for the first time there will be a focal point on the campus where a series of conferences can be held and where they and their scientific counterparts from U.S. and abroad can meet.

INTERNATIONAL HEALTH ACTIVITIES NOT INCLUDED IN THE FOGARTY CENTER

Mr. FLOOD. Suppose you list for the record the international health and medical activities that are not under the Fogarty Center, along with the funding level for 1968, 1969 and what is proposed for 1970.

Dr. LEAVITT. Yes, sir, I will be pleased to do so.

(The information follows:)

INTERNATIONAL HEALTH AND MEDICAL ACTIVITIES, NATIONAL INSTITUTES OF HEALTH

(Not under Fogarty International Center)

Visiting scientists (activity)

Activity involves appointment of outstanding or promising foreign scientists to NIH positions for research purposes. There is no central funding for this Program. All salaries and expenses related to the appointment are provided by the Institute in which the scientist is employed.

Funding level:

Fiscal year 1968	$1,405,000
Fiscal year 1969	1,400,000
Fiscal year 1970 (proposed)	1,400,000

Training of foreign nationals under domestic training grants (activity)

Activity involves employment of foreign scientists by NIH Grantees with approval of the NIH Institute funding the grant. Funding for this activity is by individual Institute through training grants.

Funding level:

Fiscal year 1968	$1,800,000
Fiscal year 1969	1,800,000
Fiscal year 1970 (proposed)	1,800,000

International centers for medical research and training (program)

These Centers promote collaborative research and research training between U.S. universities and selected foreign institutions and investigators. Five International Centers now in operation derive their financial support from research grants awarded by the National Institutes of Health.

Funding level:

Fiscal year 1968	$2,360,000
Fiscal year 1969	2,400,000
Fiscal year 1970 (proposed)	2,400,000

U.S. fellows training abroad (activity)

Fellowship awards made by Institutes to individual U.S. applicants who wish to undertake research training abroad. Funding for activity is through Institutes fellowship appropriation.

Funding level:

Fiscal year 1968	$1,724,000
Fiscal year 1969	1,973,000
Fiscal year 1970 (proposed)	2,250,000

International research career development program

This program, utilizing commissioned officers of the Public Health Service, is a career development program in medical research in foreign countries where unusual or unique opportunities exist for pursuing studies of importance to medical science.

Funding level:

Fiscal year 1968	$160,000
Fiscal year 1969	160,000
Fiscal year 1970 (proposed)	160,000

United States-Japan cooperative medical science program

A cooperative program between the United States and Japan focusing on diseases of mutual importance.

Funding level:

Fiscal year 1968	$4,094,000
Fiscal year 1969	5,269,000
Fiscal year 1970 (proposed)	6,500,000

Gorgas Memorial Laboratory (program)

This Laboratory, the research arm of the Gorgas Memorial Institute of Tropical and Preventive Medicine, conducts broad studies of tropical diseases. It collaborates with the Pan American Health Organization and the World Health Organization.

Funding level:

Fiscal year 1968	$500,000
Fiscal year 1969	500,000
Fiscal year 1970 (proposed)	500,000

SEATO-Pakistan Cholera Research Laboratory (activity)

This Laboratory is engaged in extensive studies on cholera in Southeast Asia. The NIH is responsible for scientific direction of the program, but program support is shared by the SEATO members.

Funding level:

Fiscal year 1968	$99,000
Fiscal year 1969	100,000
Fiscal year 1970 (proposed)	100,000

Foreign research grants (activity)

Research grants for studies in foreign countries are administered by individual NIH Institutes according to categorical program areas involved. Appropriations for such support are included in the total grant appropriations for each Institute.

Funding level:

Fiscal year 1968	$6,199,000
Fiscal year 1969	5,250,000
Fiscal year 1970 (proposed)	6,000,000

Foreign training grants (activity)

Training grants to foreign institutions are administered and funded by individual Institutes according to program interest involved. Appropriations for such support are ncluded in the total grant appropriation for each Institute.

Funding level:

Fiscal year 1968	$289,000
Fiscal year 1969	160,000
Fiscal year 1970 (proposed)	160,000

Foreign research contracts (activity)

Foreign research contracts are administered by individual Institutes according to program area involved.

Funding level:

Fiscal year 1968	$1,325,000
Fiscal year 1969	1,700,000
Fiscal year 1970 (proposed)	1,900,000

(NOTE.—The term "program" has been used when the support is specifically identified in the budget. The term "activity" has been used when the support is fragmented or carried by more than 1 institute.)

REDUCTION IN BUDGET FOR THE FOGARTY CENTER

Mr. FLOOD. The increases in the budget for the various Institutes have been held down to less than enough to cover increased costs in most instances. But here, after all these glowing things that you said, here you are actually cutting below the dollar level of 1969 by $414,000, or a little over 10 percent.

The new Eye Institute was opposed by our friend Dr. Marston and NIH. But despite that, the Eye Institute has an overall increase of 50 percent. Now is the Fogarty Center actually low man on your totem pole over there, as these facts would indicate?

Dr. LEAVITT. No, sir.

Mr. FLOOD. How do you put that one together? That is a nasty question, but I meant it to be.

Dr. LEAVITT. The reduction in budget actually represents a nonrecurring item, the planning funds of $500,000 for the new building.

Mr. FLOOD. I want you to know that big brother is looking over your shoulder on the Fogarty Center.

COORDINATING ROLE OF THE FOGARTY CENTER

On page 202, you say "The Center serves as a focal point for the international activities of the National Institutes of Health." Those are very high sounding words. In view of the facts they are just rhetoric.

Dr. LEAVITT. No, sir.

Mr. FLOOD. Semantics.

Dr. LEAVITT. Other than program responsibilities, the Fogarty Center does conduct a final review of all of our foreign awards to insure that they are consistent with departmental and U.S. foreign policy.

Mr. FLOOD. Do you know what the U.S. foreign policy is?

Dr. LEAVITT. The State Department provides information and policy guidance.

We attempt to be sure that our awards are consistent with administration policy. We also conduct an overall review and surveillance of all NIH expenditures overseas. We maintain and administer the Bureau of the Budget ceiling of our expenditures overseas.

We coordinate NIH participation in East-West exchanges with designated Communist bloc countries.

Mr. FLOOD. Who designates the Communist bloc countries?

Dr. LEAVITT. The State Department. We maintain a close working relationship with HEW and the State Department concerning all of our awards to foreign institutions and the development of any new exchange agreements.

We provide program direction and guidance to the NIH oversea offices. In addition we provide to NIH and other interested organizations, an information service on international activities.

RESULTS OF RESEARCH IN FOREIGN COUNTRIES

Mr. FLOOD. For the record would you list several of the worthwhile results of biomedical research performed in other countries during the past 20 years?

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. Tell us about one now. Pick out a good one.

Dr. MARSTON. You mean supported by us, Mr. Flood, or regardless of support?

Mr. FLOOD. Regardless of the source of support.

Dr. LEAVITT. I think something for which we are all grateful to the United Kingdom was the development of penicillin by Florey and his associates at the time of World War II.

Mr. FLOOD. That is a little obsolete.

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. What have they done recently?

Dr. LEAVITT. There is some very excellent work going on in Israel having to do with central nervous system disease and diseases affecting the neurillema that may lead us into a fuller understanding of degenerative diseases of the brain and spinal cord, such as multiple sclerosis.

Mr. FLOOD. What about the Germans?

Dr. LEAVITT. Excellent work is underway in molecular biology and cancer at the Max-Planck Institute, Tübingen, West Germany, under the direction of Dr. Werner Schafer.

Mr. FLOOD. Suppose you develop a few for the record in each hemisphere.

Dr. LEAVITT. Yes, sir.

(The information follows:)

SIGNIFICANT BIOMEDICAL RESEARCH PERFORMED IN OTHER COUNTRIES

WESTERN HEMISPHERE

Argentina

Bernardo A. Houssay, M.D., Director of the Instituto de Biologia y Medicina Experimental in Buenos Aires, Argentina, shared the 1947 Nobel Prize in medicine and physiology for his studies of the hormone of the anterior pituitary lobe in the metabolism of sugar. The work for which Dr. Houssay received the prize helped clarify normal sugar metabolism, paving the way for an understanding

of the cause of diabetes. Dr. Houssay has conducted research into the role of endocrine glands in regulation of metabolism and the cause of certain pathological conditions—diabetes, hypertension, and tumorigenesis for nearly 50 years.

Peru

Dr. Alberto Hurtado, Peruvian University, Lima, Peru, is considered one of the world's foremost high-altitude physiologists. He is currently conducting research on the effects of chronic hypoxia (oxygen insufficiency) on man. Chronic insufficiency of oxygen and its consequences are problems related to innumerable diseases of man such as chronic diseases of the heart valves or coronary arteries, hypertension, lung diseases of many kinds, shock and certain blood conditions. In order to better understand these problems, Dr. Hurtado is studying Peruvian natives who live at altitudes about 12,000 feet who are chronically exposed to low oxygen tensions.

Uruguay

Dr. Roberto Caldeyro-Barcia at the University of the Republic in Montevideo, Uruguary, is making measurements of newborn infants EKG, EEG and blood components during the process of the delivery of the child. He is working out the mechanisms involved in fetal distress and compressive force acting on the brain during birth. Information of this type is most urgently needed in order to assess the condition of the infant during birth and calculate the risk to which the infant is exposed in particular instances. Until such information becomes available, remedial and preventive measures cannot be improved.

EASTERN HEMISPHERE

Australia

Dr. Gustav J. V. Nossal, the Director of the Walter and Eliza Hall Institute in Victoria, Australia, is engaged in research aimed at understanding the cellular and biochemical basis of antibody production and other aspects of immune reactivity. Using an animal model system employing rats and various purified Salmonella antigens, Dr. Nossal hopes to answer the question of whether antibody production rests on the same principles of genetics as the production of enzymes and other proteins of defined structures, and if so, how antigen controls the antibody production rate. The work of Dr. Nossal is a part of the much larger picture of transplant immunology and the problem of rejection of transplanted organs. The antigen-antibody reaction must be fully understood before measures can be taken to effectively suppress antibody formation following organ transplants.

England

Dr. Peter Medawar, C.B.E., M.A., D.Sc., F.R.S., an outstanding British biological scientist, University of London, England, has been engaged in research on the problems of tissue transplantation since 1943. The greatest obstacle to a more widespread use of tissue and organ transplantation is the frequent rejection by the recipient's boby. Dr. Medawar has introduced the concept that tissue rejection is essentially an actively acquired immunity of the recipient's body to the foreign tissue. Dr. Medawar is now extending his immunological studies, and, especially, is probing into the chemical nature of the cell substances which are responsible for the acceptance or rejection of the tissue or organ. Knowledge of the chemical identity of these substances will open up the possibility of rational chemotherapy to prevent the rejection of transplants.

Sir Hans A. Krebs, M.D., M.A., F.R.S., Oxford University, Oxford, England, German by birth, and British by citizenship, has been engaged in cell metabolism research for more than 30 years. He is the discoverer of the tricarboxylic acid cycle, also known as the Krebs cycle, which is one of the processes by which cells create and use energy for bodily processes. Numerous specific enzymes are needed for this cycle. Each is vital to the well functioning of the system, and a defect in or lack of just one enzyme may prevent a cell from functioning normally, and may result in metabolic disease. Before such diseases can be cured, they must be understood. Dr. Krebs received the Nobel Prize for physiology and medicine in 1953 for this important piece of knowledge.

France

The 1965 Nobel Prize for psysiology and medicine was awarded to a three-man team of researchers at the Pasteur Institute in Paris. Microbiologist Dr. Andrew Lwoff, biochemist Dr. Jacques Monod, and geneticist Dr. Francois Jacob

discovered a class of genes, called operons, that regulates all chemical activity within a cell. This work may have a great bearing on the conquest of cancer. These operons are normally inactive because of repressor substances sent out by other genes within the cell. Drs. Lwoff, Monod and Jacob have postulated that it may be possible that cancer virus particles may cause the biochemical conditions necessary to activate the operons and begin uncontrolled multiplication of cancerous cells.

Germany

Dr. Feodor Lynen, the Director of both the Max Planck Institute and the University of Munich's Biochemical Institute was awarded the 1964 Nobel Prize in medicine and physiology for discoveries about the mechanism and regulation of cholesterol and fatty acid metabolism. During recent years cholesterol has become a word of common usage in relation to the lively discussions of the relation of arteriosclerosis to dietary and blood cholesterol. The fact that cholesterol is necessary for the living human cell and is the compound from which the adrenal cortical hormones and all the sex hormones are formed has almost been obscured.

Israel

Dr. Harry Heller, Tel-Hashomer Government Hospital, Tel-Aviv, Israel, has more than 40 years of experience in research on metabolic diseases. He has been recently interested in Familial Mediterranean Fever (FMF), a genetic disorder which affects mainly, if not exclusively, people of Mediterranean origin. Many Americans fit this genetic picture and the disorder is not uncommon in the United States. Nowhere in this country, however, does a population concentration suitable for FMF research exist comparable to that which exists in and near Tel-Aviv. Dr. Heller and his associates have made considerable progress on the development of a reliable diagnostic test for FMF. Presently, only characteristic clinical cases can be diagnosed. Moreover, other disorders are sometimes misdiagnosed as FMF. The new test is based on the detection of an abnormal protein fraction in the serum of patients with the disease, a protein which Dr. Heller's group originally discovered. Such a test is expected to be of great vaue in the United States.

Japan

Dr. Takeshi Yonezawa, Kyoto Prefectural University of Medicine, Kyoto, Japan, is one of the few people in the world able to establish and maintain long-term cultures of human nerve tissues. He is presently studying the process of myelinating and demyelinating of nerve tissue. The myelin sheath is a fatlike insulating substance which forms a protective sheath around certain nerve fibers. When this sheath disintegrates, nerve impulses go askew, and one of a number of diseases may occur, the most common being multiple sclerosis. Dr. Yonezawa is studying myelin formations in vitro (in living laboratory animals) as it is affected by vitamins, hormones, glucose (sugar) and toxic substances. Once factors causing demyelination are fully understood, appropriate remedies may be found for such diseases as multiple sclerosis.

Dr. Setsuro Ebashi, University of Tokyo, has probably contributed more than any other worker to our knowledge of the molecular mechanisms of muscle relaxation. Dr. Ebashi and his coworkers have discovered several proteins which are important in maintaining the physiological contraction-relaxation cycle in muscle. These proteins are being investigated in detail so that the role of each in the contraction-relaxation process will be clearly understood. Work of this nature may have great relevance to muscular diseases wherein muscular control is damaged.

South Africa

Dr. John F. Brock, Chief of the Department of Medicine, University of Cape Town, South Africa, and his coinvestigators are studying human protein malnutrition, particularly the disease, Kwashiorkor, which is caused by severe protein malnutrition in the postweaning phase of early life. Although malnutrition is not as severe in the United States in epidemic proportions, it is found in this country, but because of its relative infrequence, American practitioners require information from abroad for proper diagnosis. Kwashiorkor, for example, was found to have been the cause of diarrhea in Negro children in Louisiana in 1958, and in Navajo children in Arizona in 1960 and 1961.

Mr. FLOOD. Mr. Michel.

SELECTION OF FOREIGN PARTICIPANTS

Mr. MICHEL. Doctor, what mechanism is there in foreign countries for participation in this overall program? Did our State Department issue a memorandum of any kind to all governments that we have this International Center and in the spirit of international cooperation we would be happy to see any of their scientists participate. How does the thing get aired abroad? How do you get the participation?

What are the ground rules for the scholars from abroad participating? Take me through the steps, if you can, briefly.

Dr. LEAVITT. The State Department has not been involved in publicizing the Fogarty International Center. Our own overseas offices in four locations do assist here. However, the activities of the Fogarty Center are primarily based in Bethesda. We expect to draw upon the expertise of foreign scientists by bringing them to Bethesda.

We carefully select a conference topic with the assistance of an advisory committee.

This committee, the International Advisory Committee—Fogarty International Center, met for the first time Monday, March 31, 1969, at which time the Conference and scholars-in-residence programs were discussed. Among the many items we considered were the appropriate types of conferences for us to hold, and the appropriate invitees to participate in both programs.

Mr. FLOOD. Who named the advisory committee?

Dr. LEAVITT. Dr. Marston, Dr. Berliner and I.

Mr. FLOOD. Will you list them at this point in the record?

Dr. LEAVITT. Yes, sir.

(The information follows:)

INTERNATIONAL ADVISORY COMMITTEE

Chairman, Dr. Milo D. Leavitt, Jr., director, Fogarty International Center, National Institutes of Health, PHS, Bethesda, Md.

Dr. John C. Eberhart, director of intramural research, National Institute of Mental Health, Health Services and Mental Health Administration, PHS, Bethesda, Md.

Dr. Karl Frank, chief, laboratory of neutral control, National Institute of Neurological Diseases and Stroke, National Institutes of Health, PHS, Bethesda, Md.

Dr. Donald S. Fredrickson, director, intramural research, National Heart Institute, National Institutes of Health, PHS, Bethesda, Md.

Dr. Richard C. Greulich, director of intramural research, National Institute of Dental Research, National Institutes of Health, PHS, Bethesda, Md.

Dr. A. McGehee Harvey, director, Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, Md.

Dr. William B. Jakoby, chief section on enzymes and cellular biochemistry, laboratory of biochemistry and metabolism, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, PHS, Bethesda, Md.

Dr. Ronald W. Lamont-Havers, associate director for extramural research and training, National Institutes of Health, PHS, Bethesda, Md.

Executive secretary, Dr. Arthur H. Furnia, program analyst, program analysis and development branch, Fogarty International Center, National Institutes of Health, PHS, Bethesda, Md.

INTERNATIONAL FELLOWSHIP REVIEW COMMITTEE

JANUARY 1969

Dr. Sanford S. Elberg (1970), dean, graduate division, University of California, Berkeley, Calif.

Dr. Wilhelm R. Frisell (1971) (Chairman, IFRC), associate dean of the graduate school, University of Colorado, School of Medicine, Denver, Colo.

Dr. Walter R. Guild (1972), professor of biophysics, Department of Biochemistry, Duke University Medical Center, Durham, N.C.

Dr. Harper K. Hellems (1972), professor and chairman, Department of Medicine, Medical School, University of Mississippi, Jackson, Miss.

Dr. Frank M. Huennekens, Jr. (1970), chairman, Department of Biochemistry, Scripps Clinic & Research Foundation, La Jolla, Calif.

Dr. William Insull, Jr. (1972), assistant professor, Department of Medicine, University Hospitals, Case Western Reserve University, 2065 Adelbert Road, Cleveland, Ohio.

Dr. C. Frederick Kittle (1970), professor of surgery, head of the section of thoracic and cardiovascular surgery, University of Chicago Clinics, 950 East 59th Street, Chicago, Ill.

Dr. Sidney C. Madden (1971), professor and chairman, Department of Pathology, University of California, School of Medicine, Los Angeles, Calif.

Dr. Douglas S. Riggs (1972), professor, Department of Pharmacology, State University of New York, 122 Capen Hall, Buffalo, N.Y.

Dr. Morris F. Shaffer (1970), professor and chairman, Department of Microbiology, Tulane University, School of Medicine, New Orleans, La.

Dr. James M. Sprague (1970), chairman, Department of Anatomy, University of Pennsylvania, School of Medicine, Philadelphia, Pa.

Dr. John B. Stanbury (1969), professor of experimental medicine, Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, Mass.

Dr. Robert R. Omata, Head, International Fellowships Section, Fogarty International Center, NIH, Bethesda, Md.

Dr. LEAVITT. We expect to have under study at the center two or three major themes or problems for consideration over a period of time.

This might be from 3 to 5 years. As an example, we are interested in medical education. The NIH now has the additional responsibility for professional education. We are well aware of the situation in which American medicine now finds itself, particularly as it relates to medical schools. They are having financial difficulties. There has been student unrest and dissatisfaction with the traditional curriculum. As a result, we are going to have a small colloquium next week, April 9, 10, and 11, with 25 invited participants—13 from the United States and 12 from abroad. These have been very carefully selected from France, Germany, England, Japan, and Australia.

We are interested in the countries which have been experiencing problems similar to our own, and we hope to call on their expertise, working in the proper mix with our authorities from the United States to discuss some of the problems and perhaps their solution.

This is just a beginning.

Mr. MICHEL. Are those participants from the foreign countries brought to your attention because of any publicity that has been given to their activities and their expertise over a period of years?

Dr. LEAVITT. Our own group of scientists at NIH are intimately acquainted with many of these persons personally and do assist us in tendering the invitations to the people.

Mr. MICHEL. Of course, the time actually spent in this country varies depending on whether or not they are just coming here for a seminar or an extended period for some cooperative research activity.

Dr. LEAVITT. Yes, sir.

We would like to maintain program flexibility, if you will, in the Fogarty Center. Our next week's conference is only of 3 days duration. It could be that later this year we may sponsor a conference of a full week's duration involving a greater number of participants.

As a beginning it was thought a small colloquium was most appropriate. It is quite possible that a year from now, with clearer direction based upon our prior conferences and consultations, we may wish to mount an international conference involving perhaps 150 persons. This will vary. We would like to have medical education as one of our general concerns in the center for a period of perhaps 5 years. We are not going to solve the problems overnight.

Mr. MICHEL. In choosing these areas where attention will be given, is this determined by those of you responsible here in this country for running the show?

Dr. LEAVITT. Yes, sir, with the assistance of an advisory committee.

Mr. MICHEL. We are going to have the names of these advisory committee people placed in the record.

What is this National Advisory Health Council? Is that the same thing?

Dr. LEAVITT. No, sir, it is not.

INTERNATIONAL POST-DOCTORAL FELLOWSHIPS

Mr. MICHEL. Which is the group that would have to do with screening the fellowship applicants?

Dr. LEAVITT. For the International Post-doctoral program?

Mr. MICHEL. Yes.

Dr. LEAVITT. There is a separate committee, the International Post-doctoral Fellowship Review Committee which screens each of the applicants for that program.

Mr. MICHEL. Those persons are selected by whom?

Dr. LEAVITT. They are selected by the National Institutes of Health and they come from U.S. universities and medical centers.

Dr. MARSTON. Mr. Michel, I think part of the question that you are asking—relates to the postdoctoral fellowship selection process which involves local nominating committees in 33 countries. They are nominating now, I think, about twice as many scholars as we are able to support.

This is developed as a truly cooperative effort in which the senior scientists in a given country choose their very best young men, who after correspondence with U.S. scientists, come to this country and become involved in biomedical research problems.

This brings to this country some of the top talent from other countries in the world and has really been a very effective program.

Mr. MICHEL. You mentioned these representatives of 33 countries. Of course, there are obviously three times or more that many countries,

and obviously some of them would not have anyone with the kind of expertise you are looking for to participate here. I am aware of that. How are these 33 countries conscious of the fact that there is such a thing and that they can nominate people to come and participate?

Dr. MARSTON. I have a special interest in this program. I used to be chairman of the committee at one time. These were set up initially through meeting with the most responsible scientific organizations on a country-by-country basis to assure that they would exert a major effort to choose their best people to come to this country. I suppose you are still doing that, Dr. Leavitt?

Dr. LEAVITT. Yes, sir; we are.

Dr. MARSTON. They advertise locally and the universities know of the program. Then they follow the careers of the young men after they return, as their preceptors do here.

Mr. MICHEL. They come to this country on a visitor's visa?

Dr. LEAVITT. Yes, a limited visa.

Mr. MICHEL. Do any of these people eventually stay in this country?

Dr. LEAVITT. No, sir; they must leave.

To answer your question further, they do not always return home, but they must leave the United States.

Many do go to the United Kingdom and Canada, but they must leave the United States.

Mr. MICHEL. We mentioned before the problem of the exchange students particularly in the medical professions, and we hope that they will get the advantage of our training and go back and utilize the training in their country, where there is a need.

But liking our country, they want to stay and we are rather torn at this side of the table when we are caught short with those people in short supply and we would like to keep them.

We do have an obligation in this whole area of international understanding and cooperation to foreclose our being contributors to a brain drain of another country.

Dr. LEAVITT. Yes, sir.

Dr. MARSTON. If I could add one more thing on this one: This has always been an important part of this program. Two things have contributed to a greater success here. First, the applicant has to have a commitment of a position when he returns to his own country. The second thing is that the program operators take every precaution to assure that everything is done to get the applicant to return to his country at the end of his visit.

I think this matter of stimulating senior scientists to develop an interest in the young investigator and assuring him of facilities in which to work and use his experience upon his return, is probably the more important factor.

FUTURE BUDGET PLANS

Mr. MICHEL. The Fogarty Center is a division of the National Institutes of Health; is it not?

Dr. LEAVITT. Yes, sir.

Mr. CARDWELL. We promise not to make it an institute.

Mr. MICHEL. We have the figure of $3,460,000 for fiscal 1970. What do you envision, Doctor, a year from now that figure will be, and then maybe 5 or 10 years from now?

Dr. LEAVITT. I have not made specific projections, Mr. Michel, at this point. I would certainly wish to expand the international post-doctoral fellowship program. I would like to bring that program up to a total of $2 million.

I would like to increase the number of fellowships by 25. We will have increasing needs for the Fogarty scholars-in-residence program and the conference program. At this point, since the program is new, we have been operating just 9 months, I think it would be unwise for me to project too far in advance.

I certainly have every hope, to answer your question of 10 years from now, that the program will have expanded greatly or I would not be fulfilling the expectations of this committee.

Mr. MICHEL. Thank you, that is all, Mr. Chairman.

Mr. FLOOD. Mr. Natcher.

Mr. NATCHER. I have no questions, Mr. Chairman.

Mr. FLOOD. Mr. Shriver?

CONFERENCES SPONSORED BY PRIVATE FOUNDATIONS

Mr. SHRIVER. Thank you, Mr. Chairman.

Relative to these conferences that you conduct, are there any foundations doing similar things and spending their funds for similar activities?

Dr. LEAVITT. Yes, sir, The Kellogg Foundation through a number of university centers has a comparable activity. This center does provide at NIH a facility and opportunity that has never been possible before.

Mr. SHRIVER. My next question was, what advantage is this to the Government of the United States over and above private foundations doing the same kind of thing? Why are we doing the conference bit when foundations are offering funds for the same purpose?

Dr. LEAVITT. We have unusual talent and resources at NIH which I think should be more fully utilized than they are at present. I think it will also provide an opportunity for us to behave perhaps like a medical Brookings Institution, so when problems of concern to the executive and legislative branch come up we can consider them.

Mr. SHRIVER. That is private, that is not Government. You are part of Government.

Dr. LEAVITT. There are problems that confront us which perhaps could be most effectively dealt with through our own facility at NIH.

Mr. SHRIVER. Like what?

Dr. LEAVITT. Problems of immunology of single organ transplantation. We have a wealth of talent at NIH that could be more fully utilized in concert with counterparts from U.S. universities and foreign institutions.

Mr. CARDWELL. Mr. Shriver, as you learned I am not a scientist, but I have been privy to some of the discussions of what the center should

be and why. This question that you have raised I have heard discussed several times. I think one explanation in answer to your question is that whereas the efforts of private foundations are very significant in this field, they tend to link the scholar and the scientist to the American University. True, this accounts for a large share of the medical research effort in this country. But there is a focus of national leadership in the Federal Government in the field of medical research. One distinction that you would have with this program is that it tends to link these people with the U.S. Federal Government. They identify with this center the leadership of health research. It comes together in one place. This is one—it is not the only answer—facet of this particular question.

Mr. SHRIVER. If you want to add to that, as I said before, please feel free to.

(Addition to remarks follow:)

Universities have long held conferences and seminars on a myriad of subjects. Despite this university activity, a number of specialized institutions exist outside the universities for the conduct of conferences, seminars and workshops on broad topics which cross disciplinary or university departmental barriers. For example, the World Affairs Council, with its many regional branches all over America, has long pursued an adult educational program of conferences and seminars. Experience indicates that the institutional setting in the average university does not necessarily provide the kind of enviornment needed for a successful cross disciplinary conference program. Because of the unique nature of the National Institutes of Health, combining as it does research with administration of research support, consideration of public policy regarding modern biological discoveries can best be done at NIH. The Washington area is rich in scientific talent and scientific resources. In addition to the laboratories and scientists of the NIH, the facilities of the Library of Medicine, and laboratories of other Federal agencies are available. In no other city could one find the background in research, knowledge of research administration, and legislative and executive responsibility for national science policy.

COORDINATION WITH U.N. AND AID

Mr. SHRIVER. How are your programs coordinated with the health activities of the United Nations and the health activities of the Agency for International Development?

Dr. LEAVITT. We are not involved in the direct support of research or in the direct support of services such as we would find in the Agency for International Development. We would make contributions to WHO and the United Nations only through the Office of International Health which is at the departmental level, and would provide that office with necessary documentation and other assistance upon request.

We would have no direct relationship.

Mr. SHRIVER. You have direct relationship in supervising the funds under Public Law 480 accumulated in other countries through the sale of surplus commodities.

Dr. LEAVITT. Yes, sir.

Mr. SHRIVER. How much a year does that amount to?

Dr. LEAVITT. About $5 million.

Mr. SHRIVER. So you or your office administers, in addition to that which is requested here, about $5 million that represents funds accumulated in other countries through the sale of our surplus commodities, is that right?

Dr. LEAVITT. The Public Health Service appropriation request for Public Law 480 funds, which is presented to this subcommittee by the Office of International Health, if I recall, is $15 million, of which the NIH portion is $5 million.

Mr. SHRIVER. That is what I wanted to clear up. I notice on page 204 of the justifications it is stated that although the appropriation for Public Law 480 scientific activities is expressed in terms of dollars, it is not spent as dollars. Those excess foreign currencies were obtained as the result of dollar expenditures by our Government.

Dr. LEAVITT. Yes, sir.

Mr. SHRIVER. They represent dollars that we have paid at some time.

Dr. LEAVITT. Yes, sir.

Mr. SHRIVER. Will the entire $225,000 allocated for the Fogarty scholarships in 1969 actually be used before July first?

Dr. LEAVITT. I am extremely hopeful that they will be. Hence my committee meeting on March 31, 1969, to select candidates for the program.

We wish to obligate the funds before the termination of the fiscal year.

RESULTS OF INTERNATIONAL PROGRAMS

Mr. SHRIVER. The description in the justifications of the positive, concrete results of this program, include such terms as vigorous ideas and inspiration. Would you describe some of the activities of the past recipients now in their home countries to illustrate what you are talking about?

You can do this for the record. It goes back to what results can we cite on the floor of the House of the expenditure of money for foreign students in this country or through programs that you administer.

Dr. LEAVITT. Yes, sir, we have recently compiled a bibliography.

Mr. SHRIVER. We do not need that, but some examples of the results of the expenditures.

Dr. LEAVITT. Yes, sir.

(The information follows:)

EXAMPLES OF SCIENTIFIC ACTIVITIES OF INTERNATIONAL POSTDOCTORAL FELLOWS

Dr. J. E. Dumont of Belgium

Dr. Dumont's studies have contributed to our understanding of thyroid disease. In particular, testing of thyroid function and diagnosis of thyroid disease. He is now the Director of the Institute of Nuclear Medicine, University of Brussels.

Dr. Carlos Basilio of Chile

Dr. Basilio has made significant contributions to the elucidation of the genetic code, which have been published in the Proceedings of the National Academy of Sciences.

Dr. H. H. Kleeberg of South Africa

Dr. Kleeberg has made significant contributions to species specificity in tuberculosis vaccine.

Dr. Flavio M. De Freitas of Brazil

Dr. De Freitas has published extensively and has made considerable contributions in the field of pulmonary and circulatory physiology. He has also done important studies in comparative physiology.

Dr. Jorge Soni of Mexico

Dr. Soni has returned to his home country and has made significant contributions in circulation physiology, particularly on the pulmonary system.

Dr. Stevan Milkovic of Yugoslavia

Dr. Milkovic has been very active and has made contributions in endocrinology of the pituitary and the adrenal glands.

Dr. Ulf A. Friberg of Sweden

Dr. Friberg has been an active worker and made contributions towards the knowledge of the structure of calcified tissues, including bones and teeth.

Dr. Kazutoshi Hirota of Japan

Dr. Hirota has made contributions in experimental surgery, studying the transplantation of gastric pouches in dogs in order to learn more about organ transplantation.

Dr. Chuan Chiung Chang of Taiwan

Dr. Chang has been engaged in pharmacological research studying the effect of various chemicals and drugs on nerve stimulation. His research is highly regarded by many workers in neuropharmacology.

Dr. Albert W. Liley of New Zealand

Dr. Liley is one of the leading obstetricians in New Zealand and he is also widely recognized for research on intrauterine transfusion prior to birth of an infant. This research has had great impact on the survival of infants with erythroblastosis fetalis, which is associated with Rh blood factor.

Dr. Jaime Villablanca of Chile

Dr. Villablanca from Chile trained with Dr. John Schlag. During his fellowship he has published at least two papers on the cortical control of brain stimulation. He has returned to Chile to join a very active group of neurophysiologists at the University of Chile and continues to collaborate with Dr. Schlag. The Chilean neurophysiologists are also cooperating with their counterparts at the University of Wisconsin and Washington University in St. Louis.

Mr. SHRIVER. Thank you, Doctor.
Thank you, Mr. Chairman.
Mr. FLOOD. Thank you, Dr. Leavitt.
Dr. LEAVITT. Thank you, Mr. Chairman.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for
Advanced Study in the Health Sciences

Amounts Available for Obligation

	1969 Estimate	1970 Estimate
Appropriation	$ 600,000	$3,460,000
Unobligated balance brought forward	500,000	....
Comparative transfers from: "General Research and Services, NIH"	2,811,000	....
Comparative transfers to: "Salaries and Expenses, Office of the Director"	-37,000	....
Total obligations	3,874,000	3,460,000

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
	Operations:						
	(a) Grants:						
198	(1) Research	...	$ 150,000	...	$ 150,000	...	$ .....
199	(2) Fellowships	...	1,636,000	...	1,570,000	...	- 66,000
202	(b) International center	52	1,588,000	58	1,740,000	+6	+152,000
205	Facility planning and construction	...	500,000	...	.....	...	-500,000
	Total	52	3,874,000	58	3,460,000	+6	-414,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions.	52	58	+6
Full-time equivalent of all other positions.....	3	3	..
Average number of all employees.....	52	57	+5
Personnel compensation:			
Permanent positions.....	$ 630,000	$ 680,000	+$ 50,000
Positions other than permanent....	25,000	25,000	...
Other personnel compensation.....	2,000	2,000	...
Total, personnel compensation...	657,000	707,000	+ 50,000
Personnel benefits.....	80,000	84,000	+ 4,000
Travel and transportation of persons.....	219,000	228,000	+ 9,000
Transportation of things.....	41,000	41,000	...
Rent, communications and utilities..	88,000	93,000	+ 5,000
Printing and reproduction.....	62,000	68,000	+ 6,000
Other services.....	748,000	309,000	- 439,000
Supplies and materials.....	65,000	74,000	+ 9,000
Equipment.....	128,000	136,000	+ 8,000
Grants, subsidies, and contributions.....	1,786,000	1,720,000	- 66,000
Total obligations by object..	3,874,000	3,460,000	- 414,000

Summary of Changes

1969 estimated obligations	$3,874,000
1970 estimated obligations	3,460,000
Net change	$ -414,000

	Base Pos.	Base Amt.	Change From Base Pos.	Change From Base Amt.
Increases:				
A. Program:				
International center	52	$1,555,000	+6	+$100,000
B. Centrally furnished services from the "National Institutes of Health Management Fund"	...	33,000	...	+ 52,000
Total increases	...	....	+6	+152,000
Decreases:				
A. Program:				
1. Fellowships	...	1,636,000	...	-66,000
2. Facility planning and construction	...	500,000	...	-500,000
Total decreases	...	....	...	-566,000
Total net change requested	...	....	+6	-414,000

Explanation of Changes

1. Fellowships - In 1970 183 awards will be funded, a program decrease of 5 awards and $66,000.

2. International Center - The program increase of $100,000 and 6 positions is required to accomplish the aims and objectives and strengthening of several basic programs that have been developed and initiated on a modest scale, such as the scientific administration of the Scholars-in-Residence Program and the Fogarty International Center Conference Program.

3. Facility Planning and Construction - The $500,000 decrease is a non-recurring item appropriated in 1968 for planning the new John E. Fogarty International Center building.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Title II - Administration	
Section 207 (g)	
Service Fellowships.....	Indefinite
Title III - General Powers and Duties of Public Health Service	
Part A - Research and Investigation In General	
Section 301.....	Indefinite
International Cooperation	
Section 308.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Title II -- Administration

Public Health Service

"Section 207.(g) In accordance with regulations, individual scientists, other than commissioned officers of the Service, may be designated by the Surgeon General to receive fellowships, appointed for duty with the Service without regard to the civil-service laws and compensated without regard to the Classification Act of 1923, as amended, may hold their fellowships under conditions prescribed therein, and may be assigned for studies or investigations either in this country or abroad during the terms of their fellowships."

Title III -- General Powers and Duties of Public Health Service

PART A -- RESEARCH AND INVESTIGATION

In General

"Section 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man, including water purification, sewage treatment, and pollution of lakes and streams. In carrying out the foregoing the Surgeon General is authorized to--.....

(c) Establish and maintain research fellowships in the Service with such stipends and allowances, including traveling and subsistence expenses, as he may deem necessary to procure the assistance of the most brilliant and promising research fellows from the United States and abroad;

(d) Make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for such research or research training projects as are recommended by the National Advisory Health Council....."

International Cooperation

"Section 308. (b) In carrying out his responsibilities under this section the Surgeon General may --

(1) establish and maintain fellowships in the United States and in participating foreign countries;

(2) make grants to public institutions or agencies and to non-profit private institutions or agencies in the United States and in participating foreign countries for the purpose of establishing and maintaining fellowships;

(5) facilitate the interchange between the United States and participating foreign countries, and among participating foreign countries, of research scientists and experts who are engaged in experiments and programs of research or research training, and in carrying out such purpose may pay per diem compensation, subsistence, and travel for such scientists and experts when away from their places of residence at rates not to exceed those provided in section 5 of the Administrative Expenses Act of 1946 (5 U. S. C. 73b-2) for persons in the Government service employed intermittently."

The President in his message to Congress in February 1967, announced his intention to seek funds to establish, at the National Institutes of Health in Bethesda, Maryland, an International Center for Advanced Study in the Health Sciences. On May 10, 1967, he submitted an amendment to the 1968 budget, requesting funds to finance planning studies for the Center's facilities. Both the House and Senate reports on the 1968 appropriation requests commended the proposal to establish an International Center for Advanced Studies in the Health Sciences and in the 1968 and 1969 Appropriation Acts, Public Laws 90-132 and 90-557, funds were appropriated for the John E. Fogarty International Center for Advanced Studies in the Health Sciences. This Center was established as a Division of the NIH by the Secretary of the Department of Health, Education, and Welfare on February 26, 1968.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer from:			
"General Research and Services, NIH"	$2,811,000	....	For the programs and functions of the Office of International Research transferred to the Fogarty International Center.
Comparative transfer to:			
"Salaries and Expenses, Office of the Director".....	-37,000	....	To provide funds covering expenses for the Office of the Director which were previously funded through the NIH Management Fund.

John E. Fogarty International Center for Advanced Study in the Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$ 500,000	$500,000	$725,000	$500,000
1969	600,000	600,000	600,000	600,000
1970 1/	3,460,000			

1/ Includes activities previously funded in the appropriation "General Research and Services, NIH".

John E. Fogarty International Center for
Advanced Study in the Health Sciences

Year	Estimate to Bureau of Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$ 500,000	$ 500,000	$500,000	$725,000	$500,000
1969	600,000	600,000	600,000	600,000	600,000
1970 1/	3,667,000	3,460,000			

1/ Includes activities previously funded in the appropriation "General Research and Services, NIH".

Justification

John E. Fogarty International Center for
Advanced Study in the Health Sciences

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	52	$ 737,000	58	$ 791,000	+6	+$ 54,000
Other expenses.....	--	3,137,000	--	2,669,000	--	- 468,000
Total	52	3,874,000	58	3,460,000	+6	- 414,000

General Statement

The dream of the late Congressman John E. Fogarty of "a great international center for research in biology and medicine dedicated to international cooperation and collaboration in the interests of mankind" is being fulfilled by the creation of the John E. Fogarty International Center for Advanced Study in the Health Sciences at the National Institutes of Health.

The National Institutes of Health is a world-wide symbol of research. It has the capacity to exercise leadership on an international basis for the advancement of medical and biological sciences. The establishment of the John E. Fogarty International Center is the beginning of a new dimension in the attack on the problems of disease and ill health and is dedicated to the use of science for peaceful purposes and the good of mankind.

The Center will provide an opportunity and a facility for scholars, scientists and leaders in the biomedical sciences to assemble for discussion, study and research, and a locus for the international activities of the National Institutes of Health.

Research Grants

	1969 estimate	1970 estimate	Increase or Decrease
Research projects.....	$130,000	$130,000	....
Special programs.....	20,000	20,000	....
Total research grants...	150,000	150,000	....

	1969 estimate	1970 estimate	Increase or Decrease
Research Project Grants to Former International Postdoctoral Fellows.....	$130,000	$130,000	....

Introduction

This program has been designed to make optimum use of research training received in the United States by promising young foreign biomedical investigators previously supported by NIH International Postdoctoral Fellowships. The program provides some of the resources needed by these talented and carefully selected individuals to begin independent research careers in their home countries. Applications for these grants receive careful review by the International Fellowship Review Committee. The grants are limited to $2,500 for each of three years, are not renewable, and provide funds for equipment and supplies which must be purchased in the United States.

The productive relationships of the Fellow and his American preceptor provide a diversified attack on problems of immediate concern to the health of the American people.

Increasing costs of conducting research are expected to result in a decrease in the number of grants that can be supported in 1970. Therefore, we plan to support 52 grants in 1970 compared to 56 in 1969.

Distribution of Research Grants

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
1. Non-Competing Continuations.....	56	$130,000	52	$130,000	-4	....
2. Scientific evaluation.....	..	20,000	..	20,000	..	....
Total, research grants..	56	150,000	52	150,000	-4	....

Fellowships

	1969 estimate	1970 estimate	Increase or Decrease
Total fellowships.....	$1,636,000	$1,570,000	-$66,000

	1969 estimate	1970 estimate	Increase or Decrease
International Postdoctoral Fellowships.....	$1,411,000	$1,400,000	-$11,000

Introduction

The International Postdoctoral Fellowships Program offers a unique opportunity for the sharing of scientific information on an international basis by permitting foreign investigators to work for a period of a year or two in collaboration with, and in the laboratories of, American colleagues in the United States. This program provides U. S. scientists access to the ideas of vigorous young investigators with stimulating and different viewpoints. In addition, since Fellows return to do independent research in their home countries, a basis is provided for the future collaboration between investigators here and those in different environmental settings.

Program Plans in 1969 and 1970

This program will be continued in 40 countries during 1970. Each country, through a nominating committee composed of prominent scientists of that country, submits its recommendations for fellowships. These nominations are competitively reviewed by the International Fellowship Review Committee at the NIH.

Funds requested for 1970 will provide for 167 awards compared to 168 in 1969, a decrease of one. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

	1969 Estimate	1970 Estimate	Increase or Decrease
Fogarty Scholarships.....	$225,000	$170,000	-$55,000

Introduction

The primary objective of this new program is to provide an environment conducive to the discussion, expansion and evolution of ideas. Within this environment the program will promote fruitful exchange of ideas between distinguished leaders in science, scholars in other disciplines and other creative individuals. The ultimate objective is the elucidation of current

problems confronting society as a result of modern biomedical research, the delineation of problems to come and the synthesis of new approaches for the solution of these problems.

The program proposes to select outstanding scientists and other scholars who will focus their attention on broad aspects of important issues raised by the findings of modern biomedical research. While in residence at the Center the scholars will be encouraged by group interaction to attack broad problems, the solutions to which require an interdisciplinary approach or whose solution lies beyond the knowledge of a single individual. The program will draw the scholars from the international biomedical community, and from among those people who possess special qualifications in science administration, those whose scholarly attainments suggest that they can contribute to the interactions of the group. The scope of this program will include a continuing series of comparative studies and assessments of the trends of international science policy and the organizational structure and management of research and development on an international scale.

The unique environment at the NIH offers an unusual opportunity for scholars to interact with large numbers of intramural staff scientists in discussion--focusing attention on important health problems, holding small conferences, workshops and, on a group basis, assessing the state-of-the-art in many disease areas. It is expected that scholars will provide inspiration to others and delineate important areas of research.

Program Plans in 1969 and 1970

The Program is new and much of the effort in 1969 will be devoted to the development of the Program, its goals and management. It is expected, however, that by the end of 1969 we shall have completed our plans and awarded Fogarty Scholarships to a number of outstanding individuals.

By 1970, interest in the Fogarty Scholarships is expected to create a supply of applicants for the opportunity to participate in this new and unique Program. Through an advisory committee, high selectivity will assure the most effective contribution to this Program.

Funds requested for 1970 will provide for 16 awards, compared to 20 in 1969, a decrease of 4. This decrease reflects the priorities in the 1970 President's Budget related to national health programs.

Distribution of Fellowships

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Continuations						
Noncompeting.....	63	$ 407,000	63	$ 407,000		...
Supplementals.....	(6)	6,000	(6)	6,000		...
New awards.....	125	1,223,000	120	1,157,000	-5	-$66,000
Total fellowships..	188	1,636,000	183	1,570,000	-5	- 66,000

Fellowships (By type of program)

	1969 estimate		1970 estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
International Post-doctoral.....	168	$1,411,000	167	$1,400,000	-1	-$11,000
Fogarty Scholarships	20	225,000	16	170,000	-4	- 55,000
Total fellowships	188	1,636,000	183	1,570,000	-5	- 66,000

International Center

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	52	$ 737,000	58	$ 791,000	+6	+$ 54,000
Other expenses.....	..	851,000	..	949,000	..	+ 98,000
Total.....	52	1,588,000	58	1,740,000	+6	+ 152,000

Introduction

The John E. Fogarty International Center for Advanced Study in the Health Sciences is designed to facilitate and expand the continuing effort of the National Institutes of Health and the United States Government to broaden the knowledge base of the biomedical sciences. The Center serves as the focal point for the international activities of the National Institutes of Health and is responsible for the administration of the International Postdoctoral Fellowships Program, The Scholars-in-Residence Program, The Conference and Seminars Program, International Scientists Reception Center, The Scientific Activities Program (PL 480) and NIH overseas offices located in Rio de Janeiro, Brazil; Paris, France; Tokyo, Japan; and New Delhi, India.

In administering these activities, the Fogarty International Center will focus its efforts on 1) facilitating the useful exchange of distinguished scientists and scholars including promising young scientists; 2) providing an environment, including facilities, which will contribute to the exchange, expansion and evolution of ideas; and 3) promoting international cooperation for the dissemination and sharing of biomedical knowledge both on a bilateral and multilateral basis to supplement and assist that exchange of knowledge by individual scientists and institutions.

Program Plans for 1969 and 1970

Conference and Seminar Program

Objectives of the Conference and Seminar Program are:

> To promote advanced study in the health sciences by conducting international conferences, seminars, workshops and training courses within the scope of the NIH mission, i.e., advancement of knowledge for the nation's health.

To identify the legal, ethical, social and economic problems that may arise from new findings of biomedical research.

To advance our understanding and insight into these problems confronting us by holding cross-disciplinary conferences and seminars.

To stimulate research in particular fields by holding training seminars, workshops and courses, drawing on the international and biomedical research community for participants and faculty.

During 1969 the following colloquia will be held at the Center:

(1) A small symposium on "Reform of Medical Education in Advanced countries."

(2) "Family Planning and the Status of Women."

(3) "Environmental Influence on Genetic Expression - a consideration of Sexual Differentiation."

(4) Biological Control Mechanisms and Neuronal Plasticity.

(5) Integration of Structure and Function in Biological Membranes.

(6) The 6th International Symposium on Pupillography in collaboration with NINDS and NEI.

Follow-up action based on the conclusions of these conferences and seminars will be sought through NIH Institutes, through collaborative arrangements with other countries, with one of the international agencies with health science programs such as the WHO, or with other U. S. government agencies.

The Fogarty International Center is unique. It provides the opportunity for scholarly considerations, for informal and unstructured exchange and a facility which will permit and foster daily communication among the professional staff of NIH and the distinguished scientific visitors.

The Conference and Seminar Program provides a means of promoting the intellectual consideration of scientific research; many suggestions for specific conferences are now being considered by an advisory board.

Scientific Activities(PL 480 Program)

The Fogarty International Center has the coordinating and policy formulation function and operating responsibility for the NIH Special Foreign Currency Program supported with an allotment of funds from the appropriation "Scientific Activities Overseas" managed by the Office of International Health, Office of the Secretary, DHEW.

The NIH Special Foreign Currency Program is designed and operated with the objective of extending NIH activities into the international biomedical and health sciences community. The purpose of this activity is to utilize resources indigenous to "excess currency" countries which will contribute to the attainment of the domestic missions of NIH operating units in the areas of biomedical research, health manpower, and medical literature documentation and dissemination. The NIH attempts to achieve this objective through the instrument of collaborative agreements for research and information exchange. Support in "excess currency" countries is provided for projects involving U. S. biomedical scientists, both within NIH intramural laboratories as well as at U. S. academic institutions and foreign research institutions, on problems of mutual interest and importance to both the U. S. and host country and within the responsibility of the NIH.

Biomedical research and the collation and dissemination of scientific information are the major activities in the NIH program. In its program in 1969 and 1970, NIH will support projects in India, Israel, Pakistan, Poland, U.A.R. (Egypt), and Yugoslavia. The program utilizes the unique resources of these countries as represented by trained scientific manpower, multilingual competence, scientific literature of contemporary and historical importance, research institutions and laboratory facilities, anthropological and cultural opportunities, ecology, high incidence of diseases, or clinical materials of interest not found in the U. S. The NIH PL 480 research program is involved in the two major contemporary world problems of nutrition and population, as well as fundamental studies and activities in support of the missions of the several components of the NIH.

The funds used by this program are U. S.-owned foreign currencies, determined to be excess to the needs of the U. S., derived primarily from the sale of surplus agricultural commodities. Although the appropriation is expressed in terms of dollars, it is not dollars. It is, in essence, an authorization for use of a specified dollar-equivalent of U. S.-owned foreign currency acquired without payment of dollars and determined to be excess to the needs of the U. S.

International Scientists Reception Center

The International Scientists Reception Center provides a dignified setting for the reception of visiting American and foreign scientists; affords an opportunity to visitors for discussion of international biomedical problems with professional staff; and for the establishment of appropriate contacts between such visitors and the Fogarty International Center and NIH staff members.

The request this year includes a program increase of six positions and $100,000 for additional staff and conferences to support these activities. There is also an increase of $52,000 for centrally furnished services from the "National Institutes of Health Management Fund."

Facility Planning and Construction

	1969 Estimate	1970 Estimate	Increase or Decrease
Other expenses....	$500,000	....	-$500,000

In 1968, the Fogarty International Center appropriation was $500,000 for planning and design of a building in which to house the John E. Fogarty International Center for Advanced Studies in the Health Sciences. The components of this building will include a complex of conference rooms of varying sizes, lounge and exhibit areas, office space for the Fogarty International Center staff, a cafeteria and dining room and living quarters for Fogarty Scholars-in-Residence.

A contract was signed on December 9, 1969, with the architectural firm of Helmuth, Obata and Kassabaum of St. Louis, Missouri, for complete architectural and mechanical design of the building. Design work started in January 1969, and is planned for completion in one year.

New Positions Requested

Fiscal Year 1970

International Center

	Grade	Annual Salary
Deputy Director.....	GS-15	$19,780
Science Administrator.....	GS-15	19,780
Conference Manager.....	GS-12	12,174
Secretary.....	GS-6	6,321
Secretary.....	GS-5	5,732
Clerk-typist.....	GS-4	5,145
Total new positions.....(6)		68,932

WEDNESDAY, APRIL 2, 1969.

HEALTH MANPOWER

WITNESSES

DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JOSEPH A. GALLAGHER, DEPUTY DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. CHARLES H. BOETTNER, ASSOCIATE DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. FRANK W. McKEE, DIRECTOR, DIVISION OF PHYSICIAN MANPOWER
DR. VIRON L. DIEFENBACH, DIRECTOR, DIVISION OF DENTAL HEALTH
MISS JESSIE SCOTT, DIRECTOR, DIVISION OF NURSING
THOMAS D. HATCH, ASSISTANT DIRECTOR, DIVISION OF ALLIED HEALTH MANPOWER
DR. DANIEL F. WHITESIDE, ACTING DIRECTOR, DIVISION OF HEALTH MANPOWER EDUCATIONAL SERVICES
JOHN W. HAMBLETON, FINANCIAL MANAGEMENT OFFICER, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

HEALTH MANPOWER

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	4,369	5,000	5,124
Positions other than permanent	240	340	344
Other personnel compensation	23	26	26
Total personnel compensation	4,632	5,366	5,494
Personnel benefits: Civilian employees	427	486	498
Travel and transportation of persons	443	581	590
Transportation of things	24	44	44
Rent, communications, and utilities	294	261	270
Printing and reproduction	63	159	160
Other services	2,265	4,386	5,037
Supplies and materials	73	97	102
Equipment	66	67	65
Investments and loans	39,456	41,979	30,500
Grants subsidies and contributions	112,902	153,235	202,704
Total obligations	160,645	206,659	245,464

PERSONNEL SUMMARY

	1968 actual	1969 actual	1970 estimate
Total number of permanent positions	491	449	459
Full-time equivalent of other positions	31	42	42
Average number of all employees	438	472	483
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Institutional support:			
(a) Medical, dental, and related	32,588	66,000	96,400
(b) Nursing	5,657	7,000	7,000
(c) Public health	6,558	9,471	9,471
(d) Allied health professions	8,123	10,975	10,988
2. Student assistance:			
(a) Traineeships	17,135	30,958	25,620
(b) Scholarships and opportunity grants	16,636	24,636	48,800
(c) Loans	38,680	41,979	30,500
3. Manpower requirements and utilization:			
(a) Grants	2,992	4,195	4,425
(b) Direct operations	5,955	10,107	10,870
4. Program direction and management services	1,261	1,339	1,390
Total program costs, funded [1]	135,586	206,659	245,464
Change in selected resources [2]	25,059		
Total obligations	160,645	206,659	245,464
Financing:			
Comparative transfer to other accounts	9,545	90	
Unobligated balance available, start of year		−158	−1,000
Deficiency, start of year	6,382		
Unobligated balance available, end of year	158	1,000	
Unobligated balance lapsing	13,506		
Appropriation available from subsequent year	−27,745	−63,160	−88,800
Appropriation available in prior year	1,985	27,745	63,160
Budget authority	164,477	172,176	218,824
Budget Authority:			
Appropriation	164,663	172,176	218,824
Transferred to other accounts	−186		
Appropriation (adjusted)	164,477	172,176	218,824
Relation of obligations to outlays:			
Obligtions incurred, net	170,190	206,749	245,464
Obligated balance, start of year	8,360	107,047	204,541
Obligated balance, end of year	−107,047	−204,541	−284,098
Outlays	71,504	109,255	165,907

[1] Includes capital outlay as follows: 1968, $62,000; 1969, $67,000; 1970, $65,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $0; 1968, $25,059,000; 1969, $25,059,000; 1970, $25,059,000.

Payment of Sales Insufficiencies and Interest Losses

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Financing: Unobligated balance lapsing	48	32	
Budget authority	48	32	
Budget authority:			
Appropriation (definite)	250	200	957
Transferred to other accounts:			
Health professions education fund	−151	−130	−735
Nurse training fund	−51	−38	−222
Appropriation (adjusted)	48	32	

Health Professions Education Fund

OBJECT CLASSIFICATION (In thousands of dollars)

	1968 actual	1969 estimate	1970 estimate
Other services	26		
Investments and loans	11,540	12,209	1,113
Interest and dividends	403	1,207	2,000
Total obligations	11,969	13,416	3,113

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1968 estimate	1970 estimate
Program by activities:			
1. Loans to health professions schools	11,540	12,209	1,113
2. Federal National Mortgage Association fees for sale of notes	26		
3. Interest accrued on participation certificates	169	734	735
4. Interest to Treasury	234	473	661
5. Interest to health professions schools (differential)			604
Total program costs, funded—obligations	11,969	13,416	3,113
Financing:			
Receipts and reimbursements from:			
Federal funds	−2,100	−780	
Non-Federal sources: Interest on loans outstanding	−493	−1,074	−1,289
Unobligated balance available, start of year	−12,380	−14,655	−3,223
Unobligated balance available, end of year	14,655	3,223	2,134
Budget authority	11,651	130	735
Budget authority: Transferred from other accounts	151	130	735
Appropriation (adjusted)	151	130	735
Authorization to spend agency debt receipts	11,500		
Relation of obligations to outlays:			
Obligations incurred, net	9,376	11,562	1,824
Obligated balance, start of year			17
Receivables in excess of obligations, start of year		−89	
Obligated balance transferred from Participation sales fund		−734	−735
Obligated balance transferred to Participation sales fund		734	735
Obligated balance, end of year		−17	
Receivables in excess of obligations, end of year	89		
Outlays	9,465	11,456	1,841

REVENUE, EXPENSE, AND RETAINED EARNINGS (IN THOUSANDS OF DOLLARS)

	1968 actual	1968 estimate	1970 estimate
Operations:			
Revenue	493	1,074	1,289
Expense	−429	−1,207	−2,000
Net operating gain or loss (−)	64	−133	−711
Analysis of retained earnings:			
Retained earnings or deficit, start of year		215	212
Appropriation to restore insufficiency on participation sales	151	130	131
Grants for interest			604
Retained earnings or deficit, end of year	215	212	236

FINANCIAL CONDITION (IN THOUSANDS OF DOLLARS)

	1967 actual	1968 actual	1969 estimate	1970 estimate
Assets:				
Treasury balance	12,380	14,566	3,223	2,134
Interest receivable		493	1,074	1,862
Loans receivable		11,540	23,749	24,862
Total assets	12,380	26,599	28,046	28,858
Liabilities:				
Interest payable		403	1,207	1,396
Participation certificates outstanding		11,500	11,500	11,500
Total liabilities		11,903	12,707	12,896
Government equity:				
Interest-bearing capital		40	12,249	13,362
Non-interest-bearing capital	12,380	14,441	2,878	1,791
Retained earnings or losses		215	212	236
Total Government equity	12,380	14,696	15,339	15,389

Nurse Training Fund

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Other services	8		
Investments and loans	6,581	7,300	2,671
Interest and dividends	115	471	1,033
Total obligtions	6,704	7,771	3,704

PROGRAM AND FINANCING

Program by activities:			
1. Loans to schools of nursing	6,581	7,300	2,671
2. Federal National Mortgage Association fees for sale of notes	8		
3. Interest accrued on participation certificates	51	222	222
4. Interest to schools of nursing (differential)			184
5. Interest to Treasury	64	249	627
Total program costs, funded—obligations	6,704	7,771	3,704
Financing:			
Receipts and reimbursements from:			
Federal funds	−4,980		
Non-Federal sources:			
Interest on loans outstanding	−274	−626	−831
Loans repaid	−4	−20	−32
Unobligated balance available, start of year	−8,347	−10,448	−3,341
Unobligated balance transferred to other accounts	4	20	32
Unobligated balance available, end of year	10,448	3,341	690
Budget authority	3,551	38	222
Budget authority:			
Transferred from other accounts	51	38	222
Appropriation (adjusted)	51	38	222
Authorization to spend agency debt receipts	3,500		
Relation of obligations to outlays:			
Obligations incurred, net	1,446	7,125	2,841
Obligated balance, start of year			88
Receivables in excess of obligations, start of year		−157	
Obligated balance transferred from Participation sales fund		−222	−222
Obligated balance transferred to Participation sales fund		222	222
Obligated balance, end of year		−88	
Receivables in excess of obligations, end of year	157		
Outlays	1,603	6,880	2,929

REVENUE, EXPENSE, AND RETAINED EARNINGS

Operations:			
Revenue	274	626	831
Expense	−123	−471	−1,033
Net operating gain or loss (−)	151	155	−202
Analysis of retained earnings:			
Retained earnings or deficit, start of year		202	395
Appropriation to restore insufficeincy on particiaption sales	51	38	38
Grants for interest			184
Retained earnings or deficit, end or year	202	395	415

FINANCIAL CONDITION (IN THOUSANDS OF DOLLARS)

	1967 actual	1968 actual	1969 estimate	1970 estimate
Assets:				
Treasury balance	8,347	10,448	3,341	690
Interest receivable		274	626	831
Loans receivable		6,577	13,857	16,496
Total assets	8,347	17,299	17,824	18,017
Liabilities:				
Interest payable		115	471	1,033
Participation certificates outstanding		3,500	3,500	3,500
Principal payments held by or for trustee		−4	−24	−56
Total liabilities		3,611	3,947	4,477
Government equity:				
Interest-bearing capital		3,077	10,357	12,996
Non-interest-bearing capital	8,347	10,409	3,125	129
Retained earnings or losses		202	395	415
Total Government equity	8,347	13,688	13,877	13,540

Mr. FLOOD. Now we have the budget for Health Manpower, and also Health Education Loans.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

We have as our witness Dr. Leonard D. Fenninger, the Director of Bureau of Health Professions Education and Manpower Training. First we will place your biographical sketch in the record.

(The biographical sketch follows:)

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name, Leonard D. Fenninger, M.D.; Position, Director, Bureau of Health Professions Education and Manpower Training; Birthplace and date, Hampton, Va., October 3, 1917; Education, A.B. Princeton, 1938; M.D. University of Rochester, 1943.

Experience—

Present, Director, Bureau of Health Professions Education and Manpower Training, NIH

1961–66, Medical Director, Strong Memorial Hospital, Rochester, N.Y.; Associate Dean, Professor of Medicine, Professor and Chairman, Department of Health Services, University of Rochester, School of Medicine and Dentistry

1958–61, Associate Dean, Associate Professor of Medicine, University of Rochester

1954–58, Assistant Dean, Professor of Medicine, School of Medicine and Dentistry, University of Rochester

1953–54, Research Associate, part time, George Washington University, School of Medicine

1953, Surgeon (R), USPHS

1952–53, Senior, Assistant Surgeon (R), USPHS

1948–52, Fellow, Cancer Research, Rochester

1947–52, Instructor in Medicine, Rochester

1946–47, Assistant Resident Physician, Rochester

1945–46, Assistant, Pathology, Rochester

1945, Assistant, Radiology, Rochester

1944, Assistant, Medicine, School of Medicine and Dentistry, University of Rochester

1944, Intern, Medicine, Strong Memorial Hospital, Rochester

Association memberships—
American Medical Association
American Association for the Advancement of Science
Association of American Medical Colleges (Asst. Sec. 1956–57)
New York State, Monroe County, Medical Society
New York Academy of Sciences
Rochester Academy of Medicine
American Association of Cancer Research
Phi Beta Kappa
Sigma XI
Alpha Omega Alpha
Special awards, citations, publications: Citation, University of Rochester Alumni Federation, 1960; Diplomate, American Board of Internal Medicine; Numerous publications.

Mr. FLOOD. Doctor, in your cast of characters do you have any that we do not know?

Dr. FENNINGER. I think you know Mr. Hambleton and Dr. Gallagher and Dr. McKee, Miss Scott, Dr. Whiteside, Dr. Diefenbach and Mr. Hatch and Dr. Boettner.

Mr. FLOOD. Doctor, I see you have a statement. How do you wish to proceed?

Dr. FENNINGER. I should like to read it.

Mr. FLOOD. Very well, Doctor.

GENERAL STATEMENT

Dr. FENNINGER. Mr. Chairman and Members of the Committee, the need for people prepared to perform nearly all kinds of health services is urgent. It is a need that is both quantitative and qualitative. Many believe that the needs will shortly present us with insurmountable problems if more is not done to develop additional health manpower than has been done in the past. Our present efforts are not sufficient.

The health problems of many who dwell in our cities, the differences in incidence and prevalence of illness among the poor as compared with those who are more fortunate, long waits in hospital emergency rooms whose staffs are overworked, delays in appointments with physicians and dentists—all attest to the lack of availability of skilled health workers.

At no other time have the disparities between the expectation of and needs for health services and the capability of supplying these services been more obvious. The current capacity of the schools of the health professions and occupations is not great enough to prepare the health personnel to provide the services needed. Production must be increased as rapidly as the capability of these educational and training institutions will permit. New schools must also be created. The shortages are of such magnitude that every school, every institution capable of increasing its productivity, while maintaining the quality of its educational programs, must make the greatest effort to keep up with the growing demand for health services which can best be rendered by well prepared and dedicated people. These institutions can make the necessary effort only if they receive strong support and major resources from all segments of our society, public and private, individuals and groups.

The Bureau of Health Professions Education and Manpower Training serves as a focus for health manpower activities. Under specific statutory authorities, the Bureau assists institutions to expand their capabilities for producing able physicians, dentists, nurses, and other health professionals to meet the needs and demands for health services—demands which have been stimulated by health care programs sponsored by the Federal Government. These responsibilities are carried out primarily through assisting the development and construction of new institutions and new programs and the expansion, rehabilitation and maintenance of existing institutions engaged in the education and training of health personnel; by providing assistance to students who are attending these schools; by encouraging and assisting schools to develop new curricula, new methods of teaching and curricula for new types of health personnel.

The schools and programs which receive assistance under these authorities are the fundamental resources for the production of the practitioners who will provide health services of many types, of the teachers and administrators who are essential for the additional people needed to provide these health services and of the investigators who develop the new knowledge so essential in the improvement of people's health in the future. These schools and programs, considerably in excess of 1,000, are of many types. They exist in many different communities and although they are all concerned with education and training, their responsibilities vary widely; some are new schools just developing their educational programs; some are parts of complex universities; others are community colleges; some are in hospitals that provide significant education and training. There are schools in transition from one type of educational program to another or are developing an affiliation with another institution; some are having particularly difficult financial problems because of the educational and other responsibilities which they have recently assumed in fields of health and in a society undergoing rapid and ever-increasing change. There are schools with financial problems of long standing that threaten their existence and the quality of education and training which they offer. Among them are schools with the potential to make significant changes in their educational programs and others that have the potential for significant expansion of their enrollments and their productivity. All of these many institutions, no matter where they are, whether they award associate degrees, diplomas, baccalaureate or advanced degrees, are free standing, or schools of universities, are engaged in producing the health manpower on which all health services depend. These institutions are essential to improving the availability and quality of health services if those who need these services are to have access to them.

I should like to emphasize at this point that with the growth of knowledge and technology and with the growing demand for health services, many types of people prepared in many different settings are essential to make health services of high quality available to all who need them. The physician, the dentist and the nurse are familiar to almost everyone. Less familiar are those in the health-related or as it is sometimes called the "allied" health professions and occupations. These professions have arisen relatively recently and have assumed increasing importance in the provision of health services. This im-

portance will continue to increase in the future as different patterns of patient care emerge and as we devise better means of preventing illness. All of the people in the health and health-related professions must work in concert, in a combined effort, if individuals are to have better health.

INSTITUTIONAL SUPPORT

Support of the Schools of the Health Professions: Schools of the health professions find it extremely difficult, and some almost impossible, to continue to respond to ever-increasing demands that science and social change are placing on them. They are under severe stresses to increase their enrollments, to provide educational opportunities for more students from low-income families, to improve and revise their educational programs, to provide more health services in their communities, to create and develop new knowledge and to perform their unique function of educating and training students and developing competent faculty members. The cumulative effort of these burdens has profoundly affected the financial status of these schools which, as I have already pointed out, are our national resources for the education of essential health personnel.

The Health Manpower Act of 1968 increased the eligibility and broadened the authority for stimulating and assisting schools of the health professions in their efforts to meet the Nation's needs for health professionals. In fiscal year 1970, for the first time, schools of pharmacy and veterinary medicine become eligible for institutional (formula) and for special project grants which heretofore have been limited to schools of medicine, osteopathy, dentistry, optometry, and podiatry.

The purposes of the special project grants have been broadened specifically to authorize projects to plan, develop, or establish new programs or to modify present programs of education in the respective health professions; to develop training for new levels or types of health professions personnel. The authority for special project grants now provides a most essential flexibility for the simultaneous support of a variety of efforts directed toward maintaining and increasing the Nation's supply of trained health professionals as well as special but interrelated programs that will enhance the education of their students.

The act continues the authority for special project grants to assist schools in serious financial straits and those which have special need for financial assistance to meet accreditation requirements. A number of schools are making desperate efforts to maintain enrollments and we know that some will require substantial assistance. Some schools say that with help they can undertake significant expansion of their first-year classes in the fall of 1970. It will be particularly important to have the funds to assist them in this endeavor and to encourage other schools to expand in future years. (Schools undertaking substantial expansion will, of course, seek not only special project funds, but also funds to assist them in necessary construction and remodeling and financial aid for students commensurate with the enrollment increases and the opportunity they afford to students from low-income families.) The budget justification for construction will be treated at greater length in a separate statement.

Nursing—Diploma, Associate Degree and Baccalaureate: The schools of nursing that prepare the nurses so vital to the care and cure of those who are ill and to the maintenance of health, are finding it increasingly difficult to operate their expensive programs in nursing education and often find it impossible to expand their enrollments. Faculty who are well prepared to teach are already in very short supply. Expansion of enrollment and maintenance and improvement of nursing educational programs, so necessary at a time of increasing complexity of health services and of serious shortages of nurses in many communities and in many fields of nursing, require substantially more teachers and administrators than are now prepared to fulfill these functions.

New programs of nursing education are being started, particularly in community and 4-year colleges. They require faculty, facilities, equipment, and student support if they are to succeed. Existing programs of nursing education require financial assistance to continue their present levels of enrollment. This assistance is needed for the same purposes as in the new schools. It is essential that their production be maintained and that their capabilities be increased.

The Health Manpower Act of 1968 provides important expanded authority through special project grants to enable institutions and agencies which do not have programs of nurse education, to plan and to develop and establish much-needed programs and to contribute to the improvement of all aspects of nursing education. The act also provides, in this period of transition in nursing education, grants to junior colleges and colleges which are planning and developing arrangements with diploma programs. Assistance can be provided to the hospital schools to plan and phase their educational programs so that this transition in nursing education will be orderly and the production of nurses will be maintained while the transition occurs.

Maintenance of present enrollments in existing schools is an essential step in providing the nurses necessary for health services. Establishment of new schools and expansion of those schools that have the potential to expand must occur if shortages of nursing personnel are to be alleviated.

CHANGE IN NURSE TRAINING PROGRAMS

Mr. FLOOD. I am not so sure how you use that word, "transition."

Dr. FENNINGER. A number of schools that started out as hospital schools of nursing are working out an affiliation agreement with either community colleges or 4-year colleges where the clinical program—clinical experience—will be given in the hospital and the basic education will be given in the community or 4-year college. I think there are a number of reasons for this. One is that the students in the United States are more and more selecting educational institutions—that is, community colleges and liberal art colleges and universities—for their education rather than going into vocational or apprentice types of programs as they have in the past.

Mr. FLOOD. Do you believe that?

Dr. FENNINGER. I believe there is a good deal of evidence to this effect, Mr. Flood, yes.

Mr. FLOOD. We have had the impression to the contrary.

We have been getting the impression that we are finally getting around to the thoughts of the Germans and the Russians and instead of university degrees that many, many students do not want; that we are now belatedly catching up with Western Europe and making a point out of creating 2-year certificate schools; of course permitting and encouraging those who wish to go on to get degrees, to do so.

We have been told that there is now being ushered into the educational scheme in this country a whole new spectrum, belatedly, of the 2-year scientific and technical diploma schools.

Dr. FENNINGER. I think this is quite true, Mr. Flood.

Mr. FLOOD. Isn't that quite different from what you have just said?

Dr. FENNINGER. I think in the field of nursing education the people who are going into schools of nursing and the major development in nursing education has recently been in the community college itself which is, of course, a 2-year school and gives an associate degree in nursing.

I think both these paths are being followed simultaneously.

Mr. FLOOD. The "transition" gives me pause. Transition, as I read your mind, means that you are on the way to something new and abandoning everything else behind you. You are transiting; you are going some place else.

Dr. FENNINGER. I believe the diploma schools are going in the direction of forming affiliations with the junior colleges and the 4-year colleges.

Mr. FLOOD. Must they?

Dr. FENNINGER. I don't know whether or not they must. We are simply observing that this is in fact taking place, and I think there are a number of reasons for it. There are resources within a community college, for example, for the general education of nurses that are often greater because they supply education for a much larger number of students than a diploma program within a hospital would.

Mr. FLOOD. But this is not necessarily so in every case?

Dr. FENNINGER. No, it is not necessarily so in every case.

Mr. FLOOD. In the case where it is not so, what do you have in mind?

Dr. FENNINGER. We intend to continue to support the diploma schools, which currently are the major source of registered nurses as well as associate degree and baccalaureate programs, and to assist the diploma schools that are undergoing transitions, to make the transition at the same time they maintain their productivity of nurses.

Mr. FLOOD. Then the word "transition" doesn't alarm me quite as much as it did.

Dr. FENNINGER. Student Assistance: Among the important measures to attract able students into the health professions and occupations is the availability of financial assistance. When young people are in high school, or even before that, they often become interested in health careers but may feel they cannot undertake the necessary education because of the expense involved. Knowledge that financial aid may be available to them if they undertake study in one of the health professions or nursing frequently encourages them to enter one of these schools with the expectation that financial need will not keep them from completing their education.

The cost of education is rising. This increase in cost is reflected in the expense to the students who are in the schools of the health professions and nursing. Student assistance is therefore of increasing importance to enable students to complete their course of study. Scholarship assistance is particularly important if we are to enable increasing numbers of young people from low income families to enter nursing or the other health professions of medicine, osteopathy, dentistry, optometry, pharmacy, podiatry, and veterinary medicine.

The health professions and nursing loan and scholarship funds requested for fiscal year 1970 will aid more than 50,000 students.

Summary of Budget Request: Mr. Chairman, we are requesting $218,824,000, which together with carryover funds is an increase of $48,580,000 over the fiscal year 1969 operating level.

Mr. FLOOD. Nearly a quarter of a billion dollars.

Dr. FENNINGER. Yes, it is, sir.

The principal increase in the appropriation requested will provide an additional $30,400,000 for institutional (formula) and special project educational improvement grants to schools of medicine, osteopathy, dentistry, and other eligible schools of the health professions. The balance of the increase requested is primarily for health professions scholarships and loans and for nursing scholarships.

1. The increase for educational improvement grants will—

(*a*) Assist schools in serious financial straits to move toward a sound educational and financial base.

(*b*) Provide financial resources and incentives to schools with the potential in the immediate future for significant and substantial increases in their enrollments and other schools to plan for and ultimately achieve increases in enrollment so that we may have more physicians, dentists, and other health professionals.

2. Increases in the funds for loans and scholarships will enable highly motivated students to pursue a career in the health professions and nursing who, for economic reasons, might otherwise be unable to enroll.

Mr. Chairman, we are facing great difficulties in the provision of adequate health services for our people. The most critical limitation lies in the increasing disparity between the availability of qualified health manpower and the increasing demand on our health manpower for more health services. We are grateful to the Congress for enacting the Health Manpower Act of 1968 and the legislation which preceded it. This Act will certainly assist in alleviating these critical problems. I will be happy to answer any questions you may have.

Mr. FLOOD. We know you very well, of course, Doctor, and we have a very high opinion of you.

Dr. FENNINGER. Thank you.

BUDGET PRIORITIES FOR ASSISTANCE TO MEDICAL EDUCATION

Mr. FLOOD. My personal interest in the subject is not entirely academic or professional, as I suppose you know.

I want you to pay some attention to this first question and don't answer it casually because we are getting tons of mail—every member of the House certainly—on this kind of question. I have been spoken to by nearly every member, I think, of the House at some time

or other on the Floor, in the corridors, in the dining room and what-not, about the contents of this first question. In effect it is, how do you cut the pie. There are special pleaders for this element and that element, but it has reached a tempo in recent weeks that I have never seen before. In one sense it is good because I have never seen so many Members of the Congress interested in the subject before. Of course, the word is coming from back home. I am sure after we return after the Easter recess there will be much, much more of this— which is a good sign too, because it indicates the people back home now are knowledgeable.

In this appropriation you are requesting funds for institutional support and for student assistance. Those two things.

Now, in another appropriation you are requesting funds to assist schools in the construction of facilities.

Which of these three types of assistance—institutional support, student aid, construction of facilities—do you think has the greatest urgency and should have the highest priority in what is a fierce competition for Federal dollars at the present time? You are requesting increases for all three. Let the blood be upon your own head.

Dr. FENNINGER. Yes, sir. I think you have raised probably the most important question that every institution faces; that every hospital faces; that every health care center faces—the problem as to how to balance among the urgent needs in a variety of demands, not only in health, but in all the other aspects of our society.

I think the truth of the matter is the whole concern about the development of able people in the general aspects of health and health service, which includes teachers, supervisors and administrators, and also includes investigators and practitioners—a matter we have sort of set aside as a Nation for a fairly long perod of time. It has only been in quite recent years that interest has arisen in having a relationship between public and private resources, the institution's State resources and the Federal government, to support education and training in the health professions and occupations. So, in a sense we are behind the times already and we are in a catch-up situation, not only in terms of the institutions' capacities to turn out more people, but also in terms of attracting young people in, and then getting their skills distributed and used well, to provide an increased range of services in the prevention of illness, in the maintenance of health, in the cure and care of people who have had the misfortune to lose their capacity to adapt and become ill.

One of the problems is that all three aspects that we are talking about here—that is a place to teach the students through construction of facilities, renovation and new construction; the people who teach the students who have to be supported through the institution, and the encouragement of students to undertake the career which means the support of the student himself through loan and scholarship programs, all three of these are, in my judgment, essential to accomplish the task.

Mr. FLOOD. When I was at Harvard Law School, Dean Pound would ask me a question—this was a hundred years ago, of course—and I would answer. Perhaps I would talk a half an hour to answer him. I would tell him all the law that I knew. He would listen patiently and then tell me, "Mr. Flood, you have restated the question, now what is the answer?"

Which of these three is No. 1? We know what you said is so and you said it very well. Which is No. 1?

Dr. FENNINGER. I don't see that any of these actually can be deferred at this time, Mr. Flood. That is why I went into the background. I think we have deferred for a long time the maintenance, renovation and improvement of the facilities——

Mr. FLOOD. Now, we want you to help us pick the priorities—if you don't we will. We need your counsel, advice, and experience.

CONSTRUCTION OF TEACHING FACILITIES

Dr. FENNINGER. Well, I would say, assuming these priorities are absolutely demanded and that there cannot be a balanced resource going not only into maintaining the schools, but to increasing their productivity, obviously one cannot turn out more students in any given year, or maintain enrollment without the funds that are used annually, we can once more defer the capital costs of new facilities as we have in the past and hope that this will at some time take care of itself and that eventually we can catch up with it, as long as we can keep the daily operation going today. On the other hand, if enrollments are going to increase——

Mr. FLOOD. Now, that takes care of one. Now, there are two more left.

STUDENT ASSISTANCE

Dr. FENNINGER. I was just getting around to student aid because the students in school now dependent on loans and scholarships which are derived from our programs as part of the total loan and scholarship resources, their continuation in school and their successful completion of the course in many instances will be determined by the availability of money which they can borrow, or which they receive as grants-in-aid from Federal sources. If one wishes not to have students suddenly have to leave school and get a job in order to live, or to earn money for the next year and therefore defer their time of graduation, then I think it is essential to maintain the level proposed for scholarships and loans in the budget for fiscal year 1970.

Mr. FLOOD. I am still not clear. You have made construction the low man on the totem pole. I expected that. Everybody always does. That is the easiest thing to do. As between institutional support and student aid, where are you? Which is your prize pigeon?

Dr. FENNINGER. Both are really my prize pigeons because they are so closely interlocked.

Mr. FLOOD. Yes, but that doesn't help me. You have got to pick one.

Mr. MICHEL. If I might interject, Mr. Chairman, on the students, are there not more applicants willing to pay their own way today than we have slots for?

Dr. FENNINGER. It depends on which school and which category and which discipline one speaks of, Mr. Michel. There are applicants to certain types of professional schools—medical schools, for example—where there are twice as many applicants as there are places, although eventually about 60 percent of the people who apply to the schools are ultimately admitted, but in any given year there are about twice as many applications as there are admissions.

A number of these applicants have resources behind them which will enable them to borrow money or get money from home so that they can continue their education. This is not true of students who are going into nursing and it is much less true of students who are going into the other health professions which are covered under the Health Manpower Act.

I also think one might question the advisability of encouraging the selection of students on an economic basis rather than on the basis of interest, motive, ability and desire.

Mr. FLOOD. I am still waiting for you to answer my question.

Dr. FENNINGER. I think you recognize my dilemma.

Mr. FLOOD. Well, I recognize my own.

Dr. FENNINGER. I suppose in terms of immediate recource on a 1-year basis, and assuming that this is a critical situation and one we are going to have to deal with this year—

Mr. FLOOD. You have stated the question again.

INSTITUTIONAL SUPPORT

Dr. FENNINGER. It would perhaps be more possible to generate additional student aid from sources other than the Federal Government on a short-term basis in the time remaining before the school year starts than it would be to generate the operating funds. So, given that extremity of choice, I think my first priority would have to go to the continuing support of the operations and functions of the school.

Mr. FLOOD. Now, that that is over, you can breath deeply and we will go on.

Dr. FENNINGER. It is a very difficult question.

Dr. MARSTON. Mr. Chairman, I think that it is clear that one does different things for different institutions because the needs are different among the thousand institutions that Dr. Fenninger is talking about. It is not possible to see clearly what the impact of any one choice would be on a specific institution. This is part of the worry that Dr. Stewart and then I and then Dr. Fenninger have had in this problem, which is a very real one that you have raised.

GRANTS TO SCHOOLS OF PHARMACY AND VETERINARY MEDICINE

Mr. FLOOD. Now, we have been talking all through these hearings about the shortage of physicians, nurses, and dentists in the country, and about the steps that should be taken to overcome it. Yet when we examine your budget, we find a very, very substantial part of it is actually going for the education of optometrists, podiatrists, pharmacists, veterinarians. For example, of the total increase of $12,784,000 which you are requesting for 1970 for institutional grants, $12,500,000 is for schools of pharmacy and veterinary medicine.

How do you explain that one? Put those two together.

Dr. FENNINGER. These schools as you know, Mr. Flood, were added in the legislation that was passed last year in the Health Manpower Act as far as eligibility for basic improvements grants, or formula institutional grants, were concerned. This is based on a formula with a fixed sum per school plus 75 percent of the remaining sum to be divided on the basis of enrollment and increases in enrollment and 25 percent on the basis of the number of graduates.

In making the calculations as to the number of students that were enrolled in these more than 90 schools that have been added to the ones that are already eligible for institutional grants under the Health Manpower Act our estimate of the cost for these basic grants would be that figure—$12,500,000.

Mr. FLOOD. Out of $12,784,000?

Dr. FENNINGER. Yes. The remainder of the increase is based on the projected increases in enrollments of the currently eligible schools and the fact that the Health Manpower Act also states that no school which received funds during the fiscal yeear 1969 will receive less in fiscal year 1970.

Mr. FLOOD. You are asking for an increase of $17,616,000 for special project grants. Now, how much of this will go for schools of pharmacy and veterinary medicine?

Dr. FENNINGER. As you know, Mr. Flood, these were awarded on a competitive basis on application. At this particular point I don't think we could predict how the judgments would be made by the review committees and councils in their establishment of priority based on quality of application.

We do have information about our experience in 1968 in the distribution among schools I believe. Mr. Hambleton can probably give it to you or submit it in the record.

(The information follows:)

AWARDS IN FISCAL YEAR 1968 FOR HEALTH PROFESSIONS SPECIAL EDUCATIONAL IMPROVEMENT GRANTS

Type of school	Fiscal year 1968 awards		
	Number	Amount	Percent
Medicine	23	$5,476,610	54
Dentistry	11	2,689,059	27
Optometry	7	637,610	6
Osteopathy	2	410,299	4
Podiatry	5	918,127	9
Total	48	10,131,705	100

Mr. FLOOD. That brings me back to a restatement of the question again. Aren't we spreading ourselves a little bit too thin when there is danger, as you and your colleagues have told us now for 4 years, of medical and dental schools closing.

Dr. FENNINGER. Again, Mr. Flood, all of the schools eligible under the law are contributors, as you know, to various aspects of health care and the maintenance of health and the prevention of illness. They also contribute to some degree—some of them do—to the development of new medical knowledge and new health knowledge. So that again, in raising the question about priorities, which is the basic question that I understand you to be raising, I think that those that require the longest term of education, where the greatest investment is made and where they will make the largest returns—that is of those schools eligible under the health professions section of the Health Manpower Act—where they will make the greatest return in terms of human health is where priorities should be put.

Mr. FLOOD. Do you want to close the dental school and open a school of pharmacy some place?

Dr. FENNINGER. I do not anticipate this problem would arise, no.

DEPENDENCE OF MEDICAL SCHOOLS ON FEDERAL ASSISTANCE

Mr. FLOOD. Your budget justifications contain the statement that medical schools "are increasingly dependent on Federal financial support for their survival."

Now we are back to a very fundamental problem. A very serious, very, very important problem that has been discussed in the Congress for many, many years, and is today, in regard to other subjects as well as this. Do you think this is good? Why shouldn't medical education continue to be the responsibility of the private sector and of the State, or the local government, just as it has been in the past? Why not?

This is a very fundamental, philosophical, political problem.

Dr. FENNINGER. It is indeed, Mr. Flood, and I suppose it applies across the board not only in medical education and health education, but in other kinds of education, and in other kinds of social services, with an increasing participation on the part of the Federal Government at the request of the citizens of the country—

Mr. FLOOD. I have stated the question. There is nothing new about the question, but we have got to hear from you about it.

Dr. FENNINGER. Of course, personally I believe the broader the base of support and the greater the variety of support flowing into any social institution or essential educational institution, the more opportunity there is for good education to take place and good training to take place.

I think one of the great advantages of American education and almost all of our social activities has been that in the past we have had public and private interests; we have had local, State and Federal resources being made available to provide a variety of services that are deemed essential.

On the other hand, the schools of the health professions have become increasingly, in a sense, looked on as national resources and regional or national rather than local institutions which, I suppose, then leads to a decision to have national resources flowing to them to a greater extent, especially as their costs rise and as there has not been a concomitant rise in support, particularly in the private sector, and as resources in other sectors are now hard pressed for the use of funds as well.

BLOC GRANT FOR MEDICAL SCHOOLS

Mr. FLOOD. In view of what you have said, if the Federal Government is going to take over the responsibility in the future, why shouldn't there be just a flat formula grant to each medical school as we do with land grant colleges?

Dr. FENNINGER. I think there are many different ways in which one might have resources flow to institutions and there are different purposes for having resources go to them.

Mr. FLOOD. All right, but why shouldn't we do just what I said? Why shouldn't we do exactly what we do with land grant colleges, and make a flat formula grant to each medical school?

Dr. FENNINGER. This would certainly be a possible mechanism for the supply of resources.

Mr. FLOOD. I know it would be "a mechanism", but is it the best one? Should we do the same as we do with land grant schools? If not, why not?

Dr. FENNINGER. I think particularly at a time when there is a very rapid change in the whole area of medical knowledge, and the whole field of education, and where one would like to have the opportunity to encourage change and increase the rate of change, a single mechanism of supplying funds, which is on the basis of a formula, or a capitation, is likely not to give opportunities for variation among schools; not likely to give encouragement to schools to try quite different ways of doing their jobs of educating.

It is not likely to stimulate schools to undertake the production of new knowledge at the same time that they are experimenting with ways of giving service and at the same time they are training a variety of people within the institutions for a variety of new and changing social roles.

Mr. FLOOD. That is what you were shooting at, wasn't it, Dr. Marston?

Dr. MARSTON. Yes, sir.

TYPES OF NURSING SCHOOLS

Mr. FLOOD. Now, you are discontinuing the formula grants to the diploma schools of nursing. You are substituting a program of project grants to three types of nursing schools: diploma, associate degree, and collegiate.

Now, suppose you describe the differences among these three types of nursing schools.

Dr. FENNINGER. I would be glad to start, but I think Miss Scott, who really knows these schools better than I do, could speak better to them.

Miss SCOTT. There are three types of schools of nursing which prepare the nurse to take state board examinations and become a registered nurse. The first one is the diploma program which is the oldest type of nursing program. It is hospital-based, located in our service institutions.

Mr. FLOOD. Like the one we have at the Mercy Hospital.

Miss SCOTT. That is right.

Mr. FLOOD. And I am on the board at the Mercy Hospital.

Miss SCOTT. And I lived one block from Mercy Hospital all my life, as you know.

These schools of nursing have been in existence in this country since the early 1800's. Basically the nursing program is divided between classroom work and nursing practice on the wards in the hospital. These programs have been 36 months in length. Interestingly enough, in the last 10 years some of them have been reduced in length from 36 months down to 24 months, which closely approximates the length of the second type of nursing program. That is the associate degree program which is located in the junior or community college.

These associate degree programs are 2 years in length. One year is liberal arts education, general education, and the second year is nursing practice in hospitals and in some public health agencies. The students who come from these programs receive an associate degree from the junior or community college.

The third type of nursing program is based in universities or colleges. These programs are 4 years in length. The first 2 years are liberal arts and basic sciences and the last 2 years are nursing courses and clinical nursing practice in various settings.

Mr. FLOOD. They get a B.S. degree in what, nursing?

Miss SCOTT. Some schools offer a B.S. degree in science, some offer a B.S. degree in nursing, depending upon the institution.

We find that the diploma schools are decreasing in numbers in the country, while the associate arts programs are growing markedly. I think in 1960 we had something like 50 junior college nursing programs in the country and this year we have 330. We are having a decreasing number of diploma programs which points up the shift between the two types of nursing programs that Dr. Fenninger was talking about.

Mr. FLOOD. Can you tell us how many nurses are being presently turned out by each type of school?

If you don't know off the top of your head, you can put that in the record.

Miss SCOTT. I can supply it for the record.

(The information follows:)

Graduations 1968:

Associate degree	6,213
Baccalaureate degree	7,415
Diploma schools	28,197
Total	41,825

PHASING OUT OF DIPLOMA SCHOOLS

Mr. FLOOD. Are you people deliberately trying to phase out, get rid of, the diploma schools?

Miss SCOTT. I don't think so, Mr. Flood. I think the students coming out of our high schools are making this decision. We are seeing in nursing the crystallization of a trend that has been occurring over a period of time in education. To the contrary, we are not trying to close diploma programs; we are trying to keep a number of them open so we will have the nurses produced for this Nation that we need.

We do know the students are selecting to go to the junior college programs. It is less expensive for them.

Mr. FLOOD. I think you have given me the answer. The answer to my question is "No."

Miss SCOTT. That is right. We are not.

Mr. FLOOD. What do you say, Dr. Fenninger.

Dr. FENNINGER. No.

Mr. FLOOD. Dr. Marston?

Dr. MARSTON. No.

TRAINING OF NURSES' AIDES

Mr. FLOOD. How are nurses' aides trained? As I say, over the last 10 years I have developed an extraordinary interest in nurses. I don't know exactly how nurses' aides are trained. I see them walking up and down the hall. They come in and out of my room in the hospital and they are very good, very efficient, all the ones I have seen. Is there anything in your budget for the training of nurses' aides?

We have the Labor Department budget. Does the Labor Department support such nurses' aide training?

Dr. FENNINGER. There is nothing in our budget directly for the support of nurses' aide training.

Mr. FLOOD. Who trains them? How do they get trained?

Miss SCOTT. Nursing aide training programs for the most part are managed by the individual institutions. You will find, I think, in most hospitals, as they have in Wilkes-Barre a nurse on the staff who sets up a training program for the aides they hire. The aides are trained for the individual institutions for the wards or patient units on which they are going to work.

Mr. FLOOD. How do you recruit them?

Miss SCOTT. Do you mean to become nurses' aides?

Mr. FLOOD. Yes.

Miss SCOTT. I think there are people coming to work in our service institutions because they have a kind of commitment that they want to work and take care of people. They may want to try their wings in this direction to find out whether or not they want to go into nursing. Some of them move from being nursing aides into the practical nurse program or the registered nurse program.

Mr. FLOOD. How are they trained? What happens?

I walk in, and I want to be a nurses' aide. Now, what happens? What will I do?

Miss SCOTT. I think what would happen probably would be that you would enroll in a class established by that institution. Let's take the Mercy Hospital. They want to hire a number of people to work on their service wards and on their private floors. Depending upon the kind of service Mercy Hospital wants to provide for its patients, it will set up a program to teach the nurses' aides how to make beds, how to take temperatures, how to give baths. The procedures which are so essential to patient care——

Mr. FLOOD. Are these basic techniques pretty much standardized?

Miss SCOTT. Yes, they are. I think there is a common core in nursing relating to direct patient services.

Mr. FLOOD. How long does it take to train a nurse's aide?

Miss SCOTT. The training varies from 3 to 6 weeks usually.

Mr. FLOOD. Is that all?

Miss SCOTT. Yes. With ongoing training as they become more proficient on their jobs.

ALLIED HEALTH EDUCATIONAL IMPROVEMENT GRANTS

Mr. FLOOD. Now, you are asking $9,750,000 in 1970 for allied health educational improvement grants. That is the same dollar amount you had for 1968 and 1969. Who gets this and what are they doing with it?

Dr. FENNINGER. This goes to a variety of institutions starting with the junior colleges. It also goes to 4-year schools and the schools of allied health and health-related professions that are now evolving in the university setting. It goes for specified disciplines, specified in regulations, and it is awarded on a formula basis, through the basic improvement grants. This is for 2-year programs leading to the associate degree and programs leading to the baccalaureate degree or above baccalaureate degree.

Mr. FLOOD. You say this is distributed on a formula basis. You say more and more institutions are becoming eligible year after year. That means that the amount one institution gets is lower and lower, is that right?

Dr. FENNINGER. Yes, sir. The amount per institution fluctuates.

Mr. FLOOD. Do you think the money is being used effectively under those circumstances?

Dr. FENNINGER. I would say in most instances the money is being used effectively in the support of programs into which students come to prepare themselves in the allied health professions.

Mr. FLOOD. Despite the fact that it is going down and down as the number increases and increases? It is just as effective?

Dr. FENNINGER. I understood you to ask the question whether it was being used effectively.

Mr. FLOOD. Yes.

Dr. FENNINGER. It is obviously not as effective when funds fluctuate greatly. There are however variations in the resources flowing into any institution.

Mr. FLOOD. In view of the resource, it is being used effectively?

Dr. FENNINGER. It is being used effectively.

HEALTH PROFESSIONS AND NURSING STUDENT LOANS

Mr. FLOOD. You are requesting an increase in appropriations, but the amount actually available for health professions and nursing student loans is going down; isn't it? How do you explain that?

Dr. FENNINGER. Yes, sir; it is actually going down and perhaps Mr. Hambleton has the figures to explain it.

Mr. FLOOD. You are asking for an increase in appropriations?

Mr. HAMBLETON. That is right. We are asking for a $5 million increase in appropriation.

Mr. FLOOD. But the amount actually available is going down. How do you put those two together?

Mr. HAMBLETON. We have two methods of financing loans. One is from this appropriation, through a grant to the schools, and the other is through the revolving fund. For instance, the total from both funds for health professions loans in 1969 is $26,429,000. In 1970, it is $21,113,000, an overall reduction of $5,316,000. That is because we have about $10 million less in the revolving fund in 1970 than we had in 1969. So we are increasing the appropriation by $5 million to help offset that deficiency. It is a different method of financing.

Mr. FLOOD. Why is the amount in the revolving fund lower?

Mr. HAMBLETON. The amount in the revolving fund is lower because we haven't been authorized to sell the notes which we have received from schools in 1969, and so we don't have that cash to loan in 1970.

Mr. FLOOD. I will tell you what you do for the record. Set up a table for 1968, 1969, and 1970, showing: (1) The amounts appropriated; (2) the total amounts available; and (3) the number of students receiving loans.

This is for both the health professions and the nurse student loan program. Put that in the record.

Mr. HAMBLETON. Yes, sir.

(The information follows:)

HEALTH PROFESSIONS STUDENT LOANS

	1968	1969	1970
Amounts appropriated	$15,000,000	$15,000,000	$20,000,000
Amounts allocated for loans from appropriated and revolving funds	26,659,476	26,429,000	21,113,000
Numbers of students receiving loans	23,255	23,053	18,416

NURSING STUDENT LOANS

Amounts appropriated	$16,000,000	$9,610,000	$9,610,000
Amounts allocated for loans from appropriated and revolving funds	16,389,885	16,910,000	12,281,000
Numbers of students receiving loans	24,532	27,000	29,000

USE OF OFFICE OF EDUCATION GUARANTEED STUDENT LOAN PROGRAM

Mr. FLOOD. The budget says although the health professions and the nurses' loans will be decreased, there will be an offsetting increase in the health professions and nursing students receiving loans under the Office of Education's guaranteed loan program.

Now, will you tell us how the Office of Education's guaranteed loan program compares with the health professions and the nurse student loans? Who is eligible?

Dr. FENNINGER. The students who are enrolled in a university or college which is participating in the guaranteed loan program under the Office of Education would be eligible to make application.

Mr. FLOOD. To save a little time, suppose you get this: Who is eligible? What interest is paid by the student? Is there a requirement as to family income? Under what terms and conditions are these loans available to health professions students? Put that in the record.

(The information follows:)

COMPARISON OF PROVISIONS OF THE GUARANTEED LOAN PROGRAM, OFFICE OF EDUCATION, WITH THE HEALTH PROFESSIONS STUDENT LOAN AND NURSING STUDENT LOAN PROGRAMS, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING

Provisions	Guaranteed loan	Health professions student loan	Nursing student loan
Student eligibility	Full-time Half-time	Full-time	Full-time.
Amount of loan per year.	Up to $1,500	Up to $2,500	Up to $1,500.
Aggregate amount	$7,500		$6,000.
Interest	7 percent	3 percent	3 percent.
Grace period	9 to 12 months (option of lender).	1 year	9 months.
Repayment period	Not less than 5 years nor more than 10 years.	10 years	10 years.
Minimum monthly repayment.	$30 per month	$15 per month	$15 per month.
Deferment	Up to 3 years for active duty in uniformed service, Peace Corps, VISTA, or for return to school on full-time basis.	Up to 3 years for active duty in uniformed service or Peace Corps; up to 5 years for advanced professional training; reenters same or another such school within grace period as a full-time student.	Up to 3 years for active duty in uniformed service or Peace Corps; up to 5 years for advanced professional training; reenters same or another such school within grace period as a full-time student.
Cancellation	Death	Death	Death.
	Permanent and total disability.	Permanent and total disability	Permanent and total disability.
Up to 50 percent at rate of 10 percent per year.		Practice in medicine, dentistry, osteopathy, optometry in designated shortage areas.	Full-time employment as professional nurse.
Up to 100 percent at rate of 15 percent per year.		Practice as above in designated rural shortage areas.	Practice as above in designated shortage area hospitals.

PROPOSED INCREASE FOR SCHOLARSHIPS

Mr. FLOOD. While the loans are going down, you are here proposing an increase of about $12 million for scholarships.

Dr. FENNINGER. Yes, sir.

Mr. FLOOD. This is reversing the trend. The trend in the Congress and, I thought, in the executive branch is to shift from grants to loans.

Now, are you in fact substituting scholarships for loans?

Dr. FENNINGER. Nearly $5 million of that increase is for the health professions scholarships now in the fourth year of the program. You will recall that when the program was started only students in the first year were eligible each year a class has been added. This year, students in all years, in schools of medicine, dentistry, and the health professions, will be eligible to apply for loans.

The appropriation request for scholarships is based on the formula in the law for all classes in the eligible schools of the health professions. You see, the program started 3 years ago and we are now going into our fourth year. So nearly $5 million of that is simply to give scholarships to the first-year students entering in these schools while the scholarships that have been awarded in the second, third and fourth years continue.

Mr. FLOOD. Were you going to add something?

Dr. FENNINGER. I was going to say the remainder has to do with the new nurse scholarship program provided for under the nursing section of the Health Manpower Act which is a program differing from the one we have had before and greatly expands both the eligibility of institutions—the students in the different kinds of institutions—as well as emphasizing the opportunities for students from lower income families to enter nursing. It replaces the nurse educational opportunity grants program, which expires on the 30th of June. These are the two elements.

Mr. FLOOD. What are the requirements for these scholarships and who is eligible? Are they people who can't get a loan? What are the requirements?

Dr. FENNINGER. These are students from extremely severe economic circumstances.

Mr. FLOOD. What is the eligibility requirement?

Dr. FENNINGER. They must be students of exceptional financial need who need such financial assistance to pursue a course of study.

EXPANDED USE OF NURSES TO PROVIDE MEDICAL CARE

Mr. FLOOD. Look at page 49. Here you describe a project which certainly intrigues me.

A recently completed project demonstrated that the professional nurse could serve as the primary source of care for large numbers of adult ambulatory patients, a role heretofore performed exclusively by physicians. Wider use of such nurse clinics could substantially improve the efficiency and effectiveness of the health service system, and it is particularly good for the organization and delivery of health services to certain hard-to-reach populations, such as those within the inner city and in rural areas.

I have known this all along. Didn't we already know this? What is the difference between this and the visiting nurse program we have had for many years?

Dr. FENNINGER. I think perhaps Miss Scott could descirbe this project in some detail.

Miss SCOTT. This project was carried out at the University of Kansas.

Mr. FLOOD. How does it differ from the visiting nurse program?

Miss SCOTT. It differs in that it has to do with an ambulatory clinic setup in the institution. It was developed around chronically ill persons, women mostly, and the care was provided by a nurse. The visiting nurse goes out in the home and gives care; in this case, under the general direction of physicians, the patients come to this ambulatory clinic, are seen by the nurse, cared for by the nurse and, depending on the patient's needs, the nurse may request the physician to see them. It was found that through this method the patients were seen faster and the kind of care provided for them had more continuity than the care provided in the usual clinic setting. We find this kind of care is providing better assistance to patients on a more prolonged basis and with more continuity.

Mr. FLOOD. Where did you say this was tried?

Miss SCOTT. At the University of Kansas.

Mr. FLOOD. Are you going to try it other places?

Miss SCOTT. Yes. We have had a project in the Bronx, and one in Colorado.

Mr. FLOOD. What do you think about it?

Miss SCOTT. I think this extends the therapeutic role of the nurse. It will enable us to provide better care and have a different relationship between nurses and physicians.

Mr. FLOOD. What do the nurses think of it?

Miss SCOTT. For the most part nurses support it. It is not so different from some of the public health nurse activities in clinics.

CONTINUING EDUCATION OF PHYSICIANS

Mr. FLOOD. Take a look at page 52. You say you are supporting "a feasibility study in the determination of individual practice profiles as a basis for correlation between continuing education needs and efforts."

You never wrote that, but say something about it.

Dr. FENNINGER. This is a project Dr. McKee has been concerned with in his division.

Mr. FLOOD. Go ahead, Dr. McKee. I know what a feasibility study is, but in connection with what in this case? You say "as a basis for correlation between continuing education needs and efforts."

Dr. MCKEE. This is a project we have underway in Wisconsin under the aegis of members of the faculty of the university, in which we have a study of some individual practitioners.

The purpose of this project is to determine what the individual in the practice of medicine would need in the way of continuing education to make him a better practitioner.

Mr. FLOOD. That makes sense.

Dr. MCKEE. Our programs in continuing education are feasiblity studies. We go out and look at various situations and encourange new methods that might be applied in other parts of the country.

Mr. FLOOD. It might not be bad to have a requirement that physicians go back to school from time to time.

Dr. McKee. The Oregon Medical Society is advocating regular participation in continuing education as one of their requirements for membership.

Mr. Flood. Good. Of course some physicians do it on their own regularly.

Dr. McKee. Yes, sir.

Mr. Flood. Mr. Michel.

Mr. Michel. I might just make the observation that what we are really talking about here is an elementary thing like taking a Pap smear to detect cancer in women, but we have some practitioners who cannot even do that.

Mr. Flood. I have heard that. That certainly points it up. That is a thing the average layman, beginning with me, was sure that any practicing doctor could do, take a Pap test, but this is not true.

UNOBLIGATED BALANCE FOR NURSE SCHOLARSHIPS

What would be the result if we dropped the language in the bill to permit the nurse scholarship program to utilize in 1970 any of the 2-year funds appropriated for 1969 for nurse opportunity grants that might be available? What would be the result of that?

Mr. Hambleton. About 1,000 students with serious financial needs could not get scholarships and probably could not therefore pursue a nursing career.

Mr. Flood. Carryovers will be scrutinized very carefully this year, believe me.

Dr. Fenninger. This is 1,000 student nurses.

Mr. Flood. We are doing this in all subcommittees, not just here. You had better explain the carryover.

Mr. Hambleton. This was a part of the Department's program to defer obligations this year and as a result reduce the cash outlay.

ADVANCE OBLIGATIONAL AUTHORITY

Mr. Flood. Carryovers are under the gun this year. Let us do this for the record. Look at page 7. You have some adjustments there relating to appropriations available in the prior year and appropriations available from the subsequent year. I want you to explain that in general, but support it with some details, and give us the reason for this considerable difference in the figures for 1969 and 1970.

Mr. Hambleton. Yes, sir.

(The information follows:)

Advance Obligational Authority

There are several student assistance programs within this appropriation, under which advance obligational authority is provided to the schools so they may arrange with the students for traineeships, loans or scholarships several months prior to the school year. This authority, as included in the appropriation language, applies to the following programs: Nurse, Public Health, and Allied Health traineeships; Health Professions and Nursing student loans; and Health Professions and Nurse scholarships.

The adjustments and differences in 1969 and 1970, as reflected on page 7 of the budget (Volume VI), between appropriated funds (NOA available) and obligated amounts, are the result of implementing this advance obligational authority. Specifically, under this authority, in addition to commitments made from the

current year's appropriation for the current year's activity, we may also make commitments (obligations) during the last quarter of the current year for students entering school in the next year. To this end we commit up to 50 percent of the next year's authorization for traineeships and loans and up to 100 percent of the next year's authorization for scholarships. These advance commitments, made in fiscal year 1969 for example, will be subtracted from the fiscal year 1970 appropriated funds, but 50 percent (or 100 percent as appropriate) of the following year's authorization (fiscal year 1971) will be added.

Since the authorizations for these several programs, as included in the "Health Manpower Act of 1968," increase from year to year, the obligational authority which may be advanced increases also and is reflected in the increased obligations for 1970 over 1969. In addition, we are requesting that the Nurse scholarship program, which this year has 50 percent advance obligational authority, be given 100 percent authority like that of the Health Professions scholarship program.

PERCENTAGE OF STUDENTS RECEIVING ASSISTANCE

Mr. MICHEL. Doctor, I noted somewhere here in your justifications a plan to help 1,000 veterinary students with scholarships in 1970. Do we have a figure of the total graduates from veterinary schools that we will have in 1970?

Mr. HAMBLETON. Yes, sir. We will have 1,170 graduates in 1970.

Mr. MICHEL. What percent of total enrollment will be the recipients of scholarships?

Mr. HAMBLETON. Scholarships in 1970, will be given to 988 students of veterinary medicine, about 20 percent of enrollment.

Mr. MICHEL. How many scholarships will be given to ordinary medical students?

Dr. FENNINGER. About 8,000.

Mr. MICHEL. And what is our total number of medical students?

Dr. FENNINGER. About 38,000 including students of osteopathic medicine.

Mr. HAMBLETON. 22 percent of medical students will receive scholarships.

Mr. MICHEL. And how does that figure compare in the field of dentistry?

Mr. HAMBLETON. Dentistry is 24 percent.

Mr. MICHEL. And what about nursing?

Mr. HAMBLETON. Nursing would be much lower. We will give 13,000 scholarships with this estimate and there are about 140,000 nursing students. The scholarships would be about 9 percent.

Mr. FLOOD. How many?

Mr. HAMBLETON. 140,000.

Mr. MICHEL. Going back to the Chairman's original line of questioning in these three critical areas and trying to smoke out any priorities you might have, I can understand that it is an interrelated kind of thing that would be pretty hard to separate and sift out one from the other with the exception of new construction, but we do know that there are considerably more applicants to enter medical schools than can be accepted. I think you said there are probably twice as many applicants as there are slots and that 60 percent of the applicants to medical schools are accepted. Is it not true that those who do apply in that category in the main are willing and able to foot the bill for themselves, or is their application dependent upon receiving the assist of scholarship aid, whether it comes from the university or from Federal sources or State sources?

Dr. FENNINGER. It is my impression that 40 percent of the students in medical schools are receiving some assistance, either from public or private funds, and either a scholarship, a loan, or a combination thereof.

I think one thing that is often forgotten is that many students in graduate schools are considered by their families as on their own and many of them are married, and so what might have been true 15 or 20 years ago so far as the student and his sources of funds from his family is no longer true because of earlier marriage and the feeling of many families is if they get a student through college the responsibility to go beyond that level should be the student's own or provided by some other mechanism.

Also, as the number of students graduating from college increases and as the opportunity for college education for students from less privileged families increases, and as the schools assume more responsibility in providing education, the mixture of students is changing.

REQUIREMENTS FOR ADMISSION TO MEDICAL SCHOOL

Mr. FLOOD. Do medical schools put a quota on females?

Dr. FENNINGER. Not to my knowledge.

Mr. FLOOD. Are you sure?

Dr. FENNINGER. I recall a question similar to this asked of Dr. Marston. As far as I know the percentage of women being admitted to medical colleges is the same as the percentage of women applying for admission.

Mr. SHRIVER. What about the other health-related schools such as veterinary schools?

Dr. FENNINGER. I do not know the percentage of females entering veterinary schools.

Mr. FLOOD. What about Catholics and Jews? Are there quotas for them? They used to have quotas.

Dr. FENNINGER. I do not know if there was ever a quota system, but to my knowledge there is not a quota system at the present time.

Mr. FLOOD. At the present time there is not?

Dr. FENNINGER. No, sir; not to my knowledge.

Mr. MICHEL. Mr. Chairman, your earlier exchange with Dr. Marston was beneficial to me in connection with a letter I received from a girl applicant to the Illinois Medical School where she had been rejected. I suspect it had something to do with her grade level, because as I understand you have to be almost a straight A student. They are only taking the cream of the crop and if you are a B student you do not have a shot at it. This prompts me to ask the question of how we could best utilize this group of students who are not at the top but who have the motivation and the inclination to get in the medical field, not to be specialists but to go as far as they can with their ability and perhaps go in the paramedical field. It seems to me we should provide a means for those who want to get in the medical field but who are short of being straight A students to have the opportunity to move into it. This presents a problem of logistics. There are only a certain number of medical facilities in existence now and I think your testimony suggests that those existing schools should be given some assist to take on this additional burden of students that we want to thrust upon them. Is that correct?

WILLINGNESS OF MEDICAL SCHOOLS TO EXPAND ENROLLMENTS

Dr. FENNINGER. I think it is more than our wanting to thrust them upon the schools. I think there has been a change in the past 2 or 3 years on the part of the universities—and what is most notable in the medical schools also applies to other schools—a recognition that they will have to increase their productivity in view of a clearly demonstrated social need. So I think, although they may have become increasingly aware because of the publicity and the public demand, I think there is also generating within the schools themselves a desire to increase their enrollments and increase the productivity of the plant and of the faculty. The rate at which these increases can take place will depend on the rate at which resources flow in to the schools. This is particularly true in some of the older schools with problems of renovation and of space to take care of more students.

Mr. MICHEL. The other day I received in the mail a communication from the university which my oldest boy is attending making the usual pitch for a contribution to the university, and it indicated that notwithstanding tuition and board, which will run probably $3,600 this year, that the cost actually to the university of educating that boy is three times that, obviously coming from other sources. What figures do we have available showing the actual cost to a university of educating a medical student?

Dr. FENNINGER. The best information is the material published in the education number of the Journal American Medical Association each fall, generally in November, in which expenditures of medical schools are indicated. As Dr. Marston pointed out in discussing some of the problems in setting up priorities, the schools themselves are very different in their history, in their resources, and in their educational programs.

Mr. FLOOD. Do we have any class B schools?

Dr. FENNINGER. No, sir. The last of those was closed before World War II.

Mr. MICHEL. And we do not want to go back to those days, do we?

Dr. FENNINGER. I think most people in the United States would find this difficult to accept. By and large we are a nation that likes the best of everything and we see very little reason why we should have second best or third best and condone that by having second- and third-class schools.

CAREER OPPORTUNITIES IN HEALTH-RELATED PROFESSIONS

May I go back to the question of individuals who cannot get in the medical schools? We have encouraged students to prepare themselves for medicine and often their sights have been so limited in that direction that they are not prepared for the disappointment of not being permitted to enter medical school and they do not shift over to other opportunities, which include careers in administration or other professions allied to health for which they might be well prepared indeed. A part of the reason for this is our failure to let them and their families know of the various fields in which opportunities are available, such as investigative or administrative or other fields that can make use of the skills of people who may not be prepared for the

specific discipline of medicine. We have been increasingly interested in encouraging all kinds of agencies to let counselors know and the families know and the children themselves know what the range of opportunity is.

Mr. SHRIVER. I thought they were doing that, providing that kind of information. In other words, the student who really wants to become a doctor, does he not know of those possibilities? I remember when I was going to school there was a young fellow who wanted to be a doctor but he could not get in the medical school, so he went into dentistry and he is serving a great need and probably making more money than a medical doctor.

Dr. FENNINGER. It is my impression from talking to counselors and others in schools of medicine that many candidates are unaware of what other routes might be taken. And certainly the person who may be trying early in his college career to see whether he or she is capable of going to medical school and finds himself not likely to be accepted by a medical school is pretty likely to shift entirely away from a health discipline. I think we should try to attract them in a health career.

Mr. MICHEL. The attraction is not only for those with a high professional level but a subprofessional level in the field of medical care.

Dr. FENNINGER. Or in one of the professions that is not so strictly looked upon as being a health-related profession. Management, for example, is a very important and complex phenomenon which people from a variety of backgrounds can do very well.

Mr. FLOOD. I have not seen many things as heartwrenching as these boys who from the time they were 10 years old wanted to be a doctor, and all through school they had that goal in mind, and they cannot get in a medical school. I have talked to so many of them and they are desolate. It is a terrible thing.

Mr. CARDWELL. The irony of it is we need doctors.

Mr. FLOOD. I have never seen such dedication as in young men who want to be doctors.

EXPANDING MEDICAL SCHOOL ENROLLMENTS

Dr. MARSTON. I called attention to the joint statement of the two medical organizations that we should make a serious effort to permit all qualified applicants to be admitted to a medical school. Both of these organizations have come out in the last year with a statement that they believe this should be the goal.

Mr. MICHEL. Didn't we during World War II have an accelerated program to get doctors?

Dr. MARSTON. Yes, and I think in the last 6 months I have heard people talk of the same urgency as we had in World War II.

Mr. MICHEL. How was this accomplished?

Dr. MARSTON. First, the payment problem was eliminated because people were accepted on the basis of their capability. Second, the schools went on a year-round basis with a couple weeks off in the summer and about 3 days off around Easter, and the faculty taught the year round. Then the internships were shortened from a year to 9 months to save time. So altogether they compressed the schedule and made a greater use of the same facilities by acceleration of the activities. Every effort was made to have as many students as possible. I

believe this is what Dr. Fenninger was talking about when he said there has been a change in attitude in the last year or so. Schools are talking about an urgency similar to the urgency in World War II.

Dr. FENNINGER. Some people shifted over before the speedup. Of course physicians were being removed from the community and clinical teachers were assuming additional care because the doctors were being drained off from the community. But there were other kinds of activities that were held in abeyance. In other words, the long-term investment was cut back for the crucial short-term investment. But obviously this cannot be sustained.

CRITERIA FOR SELECTION OF MEDICAL STUDENTS

Mr. FLOOD. Also, Mr. Michel raised the point you have to be straight A or you are not in the ball park. This annoys me for some reason. It used to be the scuttlebutt around Cambridge that the Harvard Law School was the graveyard for Phi Beta Kappas. I don't know how that fits in the medical schools, but that was the scuttlebutt around Cambridge and I can assure you as far as lawyers are concerned, the best lawyers I have ever seen were certainly not straight A's in law school by a darn sight.

Dr. FENNINGER. First of all let me say that different schools have different criteria for selecting students and they also have different applicant pools from which they draw. Frequently the statement is made that you have to be a straight A student or you cannot get in a medical school, but I know this is not the fact. There are a number of students who do indeed get into medical school who do not have straight A averages. There are straight A students who do not get into medical school because they may be perceived to lack something necessary for a good physician.

Mr. FLOOD. They have to have personal interviews before they are admitted?

Dr. FENNINGER. Some schools require personal interviews.

Mr. FLOOD. Are they bona fide, these interviews?

Dr. FENNINGER. I can only speak for the three schools with which I have had direct experience to say they are and the applicants gain a great deal of understanding of what medical schools are like by interviews just as the faculty gains additional information about the students. But there are a lot of students who are not straight "A" students who are successful in medical school and successful interns and very successful practitioners.

INSTITUTIONAL GRANTS TO SCHOOLS OF NURSING

Mr. MICHEL. Would you address yourself as to why there are no funds for institutional grants for nursing schools?

Dr. FENNINGER. I cannot.

Mr. MICHEL. Why?

Dr. FENNINGER. As a matter of fact, I do not know.

Mr. MICHEL. Can we get some answer for the record?

Dr. FENNINGER. One factor is that the nurse training section in the Health Manpower Act of 1968 provides that $15 million shall be available for special project grants.

Mr. HAMBLETON. The language in the Health Manpower Act of 1968 specifies that of the funds appropriated for institutional support, $15 million shall be for project grants and as the budget request is $7 million, the entire amount must be for special projects rather than basic institutional grants.

REDUCTION IN FUNDS FOR CONSTRUCTION OF NURSING SCHOOLS

Mr. FLOOD. I believe in another budget item there is a cutback of about $10 million. Did you cut construction of nursing schools from $18 million to $8 million?

Mr. HAMBLETON. The present construction budget for nurses is for $8 million.

Mr. FLOOD. A $10 million cut from 1969.

Mr. MICHEL. Why?

Dr. MARSTON. The answer is the fiscal constraint on the budget this year.

Mr. MICHEL. Give me some answer for the record.

(The information follows:)

NURSING INSTITUTIONAL FORMULA GRANTS

The Health Manpower Act of 1968 authorizes appropriation of funds for formula grants to all three types of schools of nursing: diploma, associate degree, and baccalaureate for the first time in fiscal year 1970. The statutory formula provides for: a basic grant to each school of $15,000 and of the remainder, 75 percent distributed on the basis of enrollment and 25 percent on the basis of the relative number of graduates.

Section 808 provides a combined authorization for the two separate programs under institutional grants (i.e., projects for the improvement of nurse training and formula grants). It also specifies that of the sums appropriated the first $15 million shall be available for projects for the improvement of nurse training.

There are over 1,300 schools eligible for the formula grants. A request of $20 million for 1970 would have been required for each school to receive the basic grant of $15,000 authorized in this legislation without any provision for funds for incentive payments to the schools based on numbers of students and numbers of graduates. This would be in addition to the specified $15 million for project grants for a total of $35 million. Fiscal restraints were such that only $7 million was allowed for Nursing; therefore, there are no funds for formula grants.

Mr. MICHEL. Is there not a $1 million carryover from 1969 for nurse scholarships?

Mr. HAMBLETON. Yes, sir. This was part of the Department's program for deferring obligations this year to reduce cash outlay.

Mr. MICHEL. And again on the funding of nursing school construction; it is what figure?

Mr. HAMBLETON. $8 million.

Mr. MICHEL. And how many schools will be aided out of that $8 million?

Dr. FENNINGER. This is in construction?

Dr. MICHEL. Yes.

Dr. GALLAGHER. That is a difficult question to answer because there are different types of schools educating and training nurses, the baccalaureate, associate degree schools, and diploma schools.

Mr. MICHEL. Can you give us an idea?

Dr. GALLAGHER. I would prefer to submit that for the record after looking at what is ahead of us by specific types of schools.

(The information follows:)

Projects approved and unfunded in fiscal year 1969 (approximately $25 million) will be carried forward for consideration with those to be approved in fiscal year 1970. In the awarding of funds for construction of nursing facilities the priority assigned to the project by the reviewers, the school's readiness to go to construction, availability of land, matching funds and other administrative considerations are all taken into account. Because a project may require as little as $250,000 or as much as $3 million it is impossible to say how many schools would receive grants from the $8 million.

Mr. MICHEL. Since it has been cut drastically, would priority be given to the pending applications and would that freeze out new applications?

Dr. GALLAGHER. Not necessarily because we make grant awards by depending in part upon the priority of the applications assigned by review process of prior groups and depends upon the quality of the application. We try not to freeze out late arrivals. Some schools have a large staff and get their applications in earlier than others that do not have a large staff.

RESEARCH ON UTILIZATION OF HEALTH MANPOWER

Mr. MICHEL. I know that research is needed to develop methods to improve the quality and utilization of health manpower. How much will you be spending on that kind of research?

Dr. FENNINGER. Would you like a description of the kind of projects?

Mr. MICHEL. In the interest of time why don't you supply that for the record?

Dr. FENNINGER. A few examples?

Mr. MICHEL. Yes.

(The information follows:)

HEALTH MANPOWER RESEARCH

Following are examples of the kinds of research projects being undertaken to improve the quality and utilization of health manpower.

PHYSICIAN UTILIZATION

Investigators at the University of Utah in Salt Lake City are obtaining information by questionnaire from a group of about 800 local cooperating physicians in an attempt to measure overall patient care performance. Investigations thus far indicate that the college and medical school grades of these 800 physicians generally do not correlate significantly with their on-the-job performance, nor do their medical college admissions test scores. A main objective of the study, therefore, is to secure more valid prediction of physician performance to be used as aids in the selection of more appropriate medical school applicants.

PHYSICIAN EDUCATION

Investigations at the Ohio State University College of Medicine in Columbus will attempt to identify means for improving the training of physicians by using computer-assisted independent study in the medical school program. The investigators intend to divide the incoming freshman class into two groups. Approximately one-third of the entering class, the experimental group, will study the medical curriculum in an independent fashion using suitably programed computer instruction. The remaining two-thirds of the class, the control group, will proceed with the medical curriculum by means of standard didactic lectures and laboratory sessions as currently practiced. A major objective is to identify the strengths and weaknesses of this kind of independent study and to develop concepts, techniques, and materials which will be released for use by other medical schools.

NURSE TRAINING

A training program for in-service educators, consisting of a series of six 5-day conferences held at 3-month intervals, is being sponsored by the San Francisco State College through funds provided through the short-term traineeship program. The purpose of these conferences is to improve the effectiveness and the ability of nurse in-service educators and so, in turn, help them to improve the quality of on-the-job continuing education for all nursing personnel in a number of hospitals throughout the State of California. Since this conference method, with interim faculty consultation to the in-service educators in their own hospitals is innovative in nature, an evaluation of the effectiveness of this method is being supported by means of a research project grant.

New ways to improve the quality and utilization of health manpower are under study in a number of Division of Nursing-sponsored projects. For example; the Rancho Los Amigos Hospital, one of the largest rehabilitation centers in the world, is exploring ways in which a clinical nursing specialist can best and most realistically be utilized in institutional settings. This project is based on the down-to-earth notion that there will never be enough clinical nursing specialists to provide expert nursing care to individual patients. Rather they propose to develop ways in which the expertise of the specialists can be shared. Serving as consultant, coordinator, teacher, the clinical nurse specialist works through others to improve nursing care of all patients.

Equally important is the application of facts and principles learned through research; practicing nurses and nursing students must learn and know how to apply the nursing knowledge in all care settings. They must also understand the implications of medical and other scientific advances on their practice. Developments in physiology and pharmacology and other scientific medical disciplines can affect nursing care substantially and require application through nursing practice and services. Research projects underway are studying the potential of biological research in nursing and more specifically, studies of peripheral circulation as they relate to nursing care. Many of these projects are interdisciplinary with the nurse, the physician, and the technologist working together to develop better methods of education and training and prevention and cure of illness.

The total of research effort of this sort is $3,495,000 in 1969 and $3,627,000 in 1970.

TRAINING COURSES FOR NURSES

Mr. MICHEL. Then I note on page 40 of the justifications you are planning to support 2,000 nurses for long-term training and 5,000 for short-term training courses. Will you supply for the record what you mean by short-term and long-term training courses?

Dr. FENNINGER. Yes.

(The information follows:)

The purpose of the professional nurse traineeship program is to improve the quality of patient care by increasing the number of graduate nurses with preparation for positions as administrators, supervisors, teachers, and clinical specialists in hospitals and related institutions, public health agencies, and schools of nursing. The program provides long-term traineeships for full-time academic study in universities and colleges and traineeships for short-term intensive training courses sponsored by certain public and nonprofit institutions.

The short-term program is to assist nurses to update management and teaching skills most needed to improve the quality of patient care in the institutions or agencies in which they are employed. It offers short-term training courses to nurses in administrative, supervisory, and teaching positions who may be unable to undertake longer periods of full-time academic study. Such courses provide a means by which nurses are enabled to meet new developments in patient care and in community health practice.

The professional nurse traineeship program was established in 1956 and since that time has had a significant impact in improving nursing education and nursing services. In the 11 fiscal years from 1957 to 1968, 20,000 nurses have received traineeships for full-time study, and since 1960 when short-term training was initiated, another 36,000 have received traineeships for short-term intensive courses.

COST OF NURSING EDUCATION

Mr. MICHEL. Do we have any figures on what the average cost of a diploma in a nursing school is?

Miss SCOTT. It ranges from no cost at all to about $2,000.

Mr. FLOOD. I do not understand that.

Mr. CARDWELL. You are talking about tuition?

Miss SCOTT. Tuition and fees.

Dr. FENNINGER. This is the expense to the student.

Mr. MICHEL. I cannot help making reference to a letter I have just received from the acting director of the School of Nursing at the Methodist Hospital of Central Illinois at Peoria in which she says:

Our hospital carries a large financial responsibility in maintaining a 3-year diploma nursing program. The increasing costs to the students only make a small dent in the total budget of the school. This school is one of the largest in the central Illinois area and has been graduating nurses since 1902. The idea of closing the school has been discussed and dismissed. If there is to be an discontinuation of this program, it will be due to a gradual transition to one of the academic programs growing up in the area.

I should add at this point we have just recently built a new junior college under our new Junior College Act, and I know as a matter of fact that in this area there is a definite training program. The writer of this letter goes on to say:

To accomplish this transition without drastic changes in the fees and expenses of the students, financial assistance is needed from outside sources. The above mentioned act (the Health Manpower Act of 1968) has been and is one of these sources.

Then she says:

On January 31, 1969, an application for nursing student loan and scholarship program participation was sent to the Department of Health, Education, and Welfare.

The request was for something like $35,000-plus. She says:

We are waiting for the proper forms on which to apply for an institutional grant which would be $15,000-plus and a project grant for the improvement of our curriculum so that we may gain accreditation and thereby increase our enrollments.

There is just one other sentence in here that I think is kind of appropriate:

We do not feel that the education of nurses should be the sole responsibility of the ill.

That is a pretty telling point, I believe. Of course they are obviously asking for any assistance we can give.

That is all, Mr. Chairman.

Mr. FLOOD. Mr. Shriver.

ORGANIZATIONAL LOCATION OF HEALTH MANPOWER PROGRAMS

Mr. SHRIVER. Doctor, on page 15 of the justifications it is pointed out that this committee has questioned the logic of divorcing health manpower training that is directly and explicitly service oriented from the service-oriented health programs in your Bureau and gives an explanation of what has happened. Will you explain why the functions should be shared by the two agencies?

Dr. FENNINGER. First of all, everything that is supported for education in the health professions and occupations is for service. There is no reason to prepare a physician, or a nurse, or a technician, unless he is going to serve. All these people are essential to service and the person working in basic research is preparing the way for the person who will take this knowledge and apply it in serving the needs of others.

Second, within any institution that provides service there is also education and training going on. I know of no hospital of any size in the United States that is not training a number of different kinds of people.

Third, as institutions of higher education are becoming increasingly engaged in the community, they are increasingly recognizing the continuity in the spectrum of education which starts early and continues, and more and more medical schools are forming affiliations with junior colleges and hospitals where a variety of people are receiving their education and training in the same location. In a hospital I was once associated with we had a very broad spectrum of education and training ranging from a wide variety of health aides and technicians through postdoctoral training in the specialties of medicine and dentistry. All these people will be serving together in giving health care. I think it is quite logical, and in fact this development is taking place rapidly right now, to keep the educational and training spectrum together administratively since they are so interrelated, rather than to separate one traditional group from another, such as the physician and the technician on whom he depends in giving care to patients.

I think one of the problems in the delivery of care and in the organization of services for care is that we have tended to put in compartments the people engaged in rendering the service. One of the crucial things we need to do is to have people understand the component parts involved in providing health services and to respect the person for the work he does rather than the title he holds.

SUPPLEMENTAL FUNDS FOR HEALTH PROFESSIONS SCHOOLS IN SERIOUS FINANCIAL NEED

Mr. SHRIVER. Have the supplemental requests for medical and dental schools mentioned on page 14 been granted?

Dr. FENNINGER. They have not been approved, Mr. Shriver; no.

Mr. FLOOD. What is the magnitude of those, Mr. Shriver?

Mr. SHRIVER. $12 million.

Mr. FLOOD. How many schools?

Mr. SHRIVER. Forty-eight.

Dr. FENNINGER. The council to review these applications is meeting today and tomorrow.

Mr. SHRIVER. That will be taken care of, then, before the end of this fiscal year?

RECRUITMENT OF STUDENTS

Dr. FENNINGER. Yes.

Mr. SHRIVER. You mentioned on pages 27 and 57 the effort to recruit students in the health field. How is that done and how successful has it been?

Dr. FENNINGER. I think this varies a good deal from one discipline to another and from one school to another.

Mr. SHRIVER. Why don't you put something in the record on that.

(The information follows:)

RECRUITMENT

Educational programs to prepare people for the health occupations depend on attracting able young people to careers in health. Young people should be made aware of the opportunities in the respective fields of health early in their school experience, as well as when they complete high school or college. The opportunities to recruit older people are also substantial, as shown by the increasing number of older women returning to the labor market.

Successful recruitment requires a combination of:

(a) accurate information about the requirements for employment in specific occupations.

(b) informed counseling services,

(c) availability of education and training opportunities, and

(d) the availability of employment opportunities and incentives.

There is considerable evidence that adequate and accurate information is not reaching enough of the potential recruits. Guidance counselors and school officials are often unaware of many opportunities in the health fields.

Recruitment has been considered primarily the responsibility of the professions and of voluntary agencies and community groups. However, it is clear that the efforts of these groups need stimulation and coordination.

Changes in society and in education are profoundly influencing the recruitment into the health occupations. To recruit successfully from minority groups and the disadvantaged, schools must develop training programs flexible enough to adapt to the particular needs of the students. It is important to identify potential candidates from these groups and to find more effective ways to assist these students to meet their cultural, educational, and financial needs.

Success in recruiting is related to the availability of places in educational institutions, employment opportunities, and the interest and capabilities of the individual.

The Bureau of Health Professions Education and Manpower Training is supporting a number of different kinds of recruitment activities. The Bureau has a contract with the National Health Council to develop a health careers program within the Council, to serve as a central focal point for information and technical assistance on health careers. The health careers program will attempt to identify National, State, and local needs for health careers information. It is developing a nationwide system for responding to inquiries about health careers. It will provide information and technical assistance on the organization, financing, and operations of Health Careers Councils. It is stimulating and encouraging the growth of Health Careers Clubs in high schools and organizations in the communities. It has established a joint committee with the National Vocational Guidance Association, to develop and carry out programs to stimulate and aid counselors and teachers in recruiting and counseling for the health careers.

The Division of Nursing has underway two contracts to encourage recruitment of the disadvantaged into nursing. One is with a group in Boston, Open Doors Wider in Nursing (ODWIN), to extend its work in identifying qualified youth of exceptional financial need and encouraging them to complete secondary school and undertake post-secondary educational training in the field of nursing. The other contract is with the American Nurses' Association to work with community action groups, school personnel, and nurse volunteers in the District of Columbia area to develop recruiting material that will appeal to disadvantaged young people with a potential for nursing.

The Division of Dental Health develops and evaluates methods and techniques for recruitment of students to careers in dentistry. It also develops brochures directed toward attracting high school graduates for careers as dental assistants and dental hygienists. Brochures are also developed for use by high school guidance counselors and directors of schools providing training in the field of allied dental manpower to provide information concerning occupational opportunities in dental hygiene and dental assisting.

Research is being conducted in the recruitment of women and minority groups for careers in dentistry. This effort is under continuing evaluation to improve and strengthen the techniques developed to date. Not enough information is now available regarding those factors which affect dental recruitment so that research will be continued in this important area.

Mr. SHRIVER. On page 29 I notice you describe the success of one case in the institutional grant program. In that one case has the school required continuing assistance?

Dr. FENNINGER. It would continue to be eligible for the basic improvement grant. It is an example of the possible successes that can be had in these programs.

Mr. SHRIVER. And you will continue aiding the schools with similar types of grants in the future?

Dr. FENNINGER. Yes.

Mr. SHRIVER. Under the allied health educational improvement grants on page 36 it looks as if the dollar amount remains about the same, but the funding level for each grantee has gone down from 95 percent to 55 percent. Is the level of assistance in these very important fields adequate?

Dr. FENNINGER. As you know, there are many sources that are going in the allied health programs and this is only one of the Federal programs.

Mr. SHRIVER. What other Federal programs are there?

Dr. FENNINGER. The junior colleges, for example, which is where the big development is taking place in this field, are eligible under the Office of Education for funds to support facilities and educational programs. Our programs under allied Health Act really support the health-differentiated part of the student's educational experience.

PERCENTAGE OF STUDENTS RECEIVING FEDERAL ASSISTANCE

Mr. SHRIVER. The tables on pages 44 and 45 show that the health professions scholarship and student loans programs are each providing 23 percent of the enrollment of participating schools. Does that mean the Federal Government is supporting 46 percent of the students in those institutions?

Mr. HAMBLETON. No, sir; a great many students who get loans also get scholarships.

Mr. SHRIVER. What would be the percentage, would you say?

Dr. FENNINGER. The total percentage of students in medical schools, for example, receiving Federal assistance?

Mr. SHRIVER. Yes.

Dr. FENNINGER. I do not know exactly what the figure is. Would you like that for the record?

Mr. SHRIVER. Yes. I wonder how good a job we are doing with the student loans. This is relatively new but is extremely important. I am getting a great deal of mail from these colleges in my State and apparently we did not fully fund it last year. This is not related entirely to the health field.

(The information requested follows:)

HEALTH PROFESSIONS STUDENTS RECEIVING LOANS AND/OR SCHOLARSHIPS AS A PERCENTAGE OF TOTAL ENROLLMENT

	Fiscal year 1968 recipients	Total enrollment	Percentage
Medical	13,010	34,538	37.6
Osteopathy	1,015	1,823	55.6
Dental	6,189	14,955	41.3
Optometry	832	1,994	41.7
Podiatry	298	933	31.9
Pharmacy	3,491	14,122	24.7
Veterinary medicine	797	4,623	17.2
Total	25,632	72,988	35.1

Dr. FENNINGER. The schools themselves have requested more moneys than we have been able to let them have for loan programs. I assume they have had to turn to other sources to augment what they have gotten from our Bureau.

HEALTH EDUCATION LOANS

Mr. FLOOD. Dr. Fenninger, your next appropriation is for "Health education loans." Since the request is for interest payments and is a technical item, we'll insert your statement in the record.

Thank you, gentlemen, 10 o'clock tomorrow morning.

(The statement follows:)

Mr. Chairman, and members of the committee, the Allied Health Professions Personnel Training Act of 1966 established two revolving funds, the Health Professions Education Fund and the Nurse Training Fund to provide loans to students of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine, and nursing.

An institution which borrows funds from the Health Professions Education Fund or the Nurse Training Fund to provide loans to its students executes a note payable to the Secretary, Department of Health, Education, and Welfare, for the amount of the loan. The note bears an interest rate determined by the Secretary to be adequate to cover the cost of the funds to the Treasury and estimated losses from defaults. The Secretary in turn agrees to pay to the borrowing institution: (1) 90 percent of its losses from defaults, (2) the amount by which interest payable by the school on such sum exceeds the interest received by the institutions on student loans made from such sums, (3) collection costs, and (4) amount of loans canceled.

In 1968, student loans were awarded from the revolving funds for the first time. In that year, 21,100 health professions students, including nursing students received loans totaling $18,120,000. In 1969, the estimates are that 25,000 students will borrow $19,509,000, and in 1970, some 8,330 students will borrow $3,784,000.

In fiscal year 1968, $15 million in notes received from participating institutions were placed in a trust fund against which certificates of participation were issued and sold by the Government National Mortgage Association to private interests. Funds derived from the proceeds of these certificates were deposited in the revolving funds and loaned to schools in fiscal year 1969. Principal and interest collected by the institutions on student loans made from borrowed capital will be given to the Secretary for deposit in the revolving funds or for payment to the Government National Mortgage Association.

In addition to authority to make loans from these funds in 1970, the budget includes an appropriation request of $957,000 necessary to meet the obligation of these revolving funds for interest payments to holders of the Government National Mortgage Association participation certificates (6.38 percent of $15 million in certificates sold).

Thank you, I shall be happy to answer any questions.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Health Manpower

Amounts Available for Obligation

	1969	1970
Appropriation	$172,176,000	$218,824,000
Comparative transfer to: "Office of the Secretary, salaries and expenses".	-90,000	---
Unobligated balance brought forward	157,737	1,000,000
Cutback required by P.L. 90-364	-1,201,000	
Total currently authorized for obligation	171,042,737	219,824,000
Plus: Proposed release of reserve for increased pay costs	201,000	---
Total available for obligation 1/	171,243,737	219,824,000

Disposition of cutback:	
To be used for pay costs in this account	201,000
To be carried forward for obligation in 1970	1,000,000
Total cutback	1,201,000

1/ Excludes estimated obligations due to advance obligational authority, the details of which are on page 7.

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
28	Institutional support:						
	(a) Medical, dental, and related	---	$66,000,000	---	$96,400,000	---	+$30,400,000
	(b) Nursing	---	7,000,000	---	7,000,000	---	---
	(c) Public health	---	9,471,000	---	9,471,000	---	---
	(d) Allied health professions	---	10,975,000	---	10,988,000	---	+13,000
38	Student assistance:						
	(a) Traineeships	---	20,670,000	---	20,670,000	---	---
	(b) Scholarships and opportunity grants	---	16,876,737	---	29,000,000	---	+12,123,263
	(c) Loans	---	24,610,000	---	29,610,000	---	+5,000,000
47	Manpower requirements and utilization:						
	(a) Grants	---	4,195,000	---	4,425,000	---	+230,000
	(b) Direct operations	364	10,107,000	374	10,870,000	+10	+763,000
61	Program direction and management services	85	1,339,000	85	1,390,000	---	+51,000
	Total NOA available	449	171,243,737	459	219,824,000	+10	+48,580,263

ADVANCE OBLIGATIONAL AUTHORITY

	1969 Estimate Amount	1970 Estimate Amount
NOA available	$171,243,737	$219,824,000
Appropriation available from subsequent year	63,160,000	88,800,000
Appropriation available in prior year	-27,744,530	-63,160,000
Total obligations	206,659,207	245,464,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	449	459	+10
Full-time equivalent of all other positions	42	43	+1
Average number of all employees	472	482	+10
Personnel compensation:			
Permanent positions	$4,999,900	$5,124,200	+$124,300
Positions other than permanent	339,900	343,900	+4,000
Other personnel compensation	26,000	26,000	---
Total personnel compensation	5,365,800	5,494,100	+128,300
Personnel benefits	486,000	497,600	+11,600
Travel and transportation of persons	580,900	590,800	+9,900
Transportation of things	43,500	43,500	---
Rent, communications, and utilities	261,000	270,100	+9,100
Printing and reproduction	158,700	159,700	+1,000
Other services	4,385,800	5,036,800	+651,000
Supplies and materials	97,200	102,300	+5,100
Equipment	67,100	65,100	-2,000
Investments and loans	41,978,600	30,500,000	-11,478,600
Grants, subsidies, and contributions	153,234,607	202,704,000	+49,469,393
Total obligations by object	206,659,207	245,464,000	+38,804,793

Summary of Changes

1969 NOA available	$171,243,737
1970 NOA available	219,824,000
Net change 1/	+48,580,263

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay raise	---	---	---	$13,000
B. Program				
Institutional support				
1. Health professions educational improvement grants	---	$66,000,000	---	30,400,000
2. Project grants for improvement of nurse training	---	4,000,000	---	3,000,000
3. Allied health new methods grants	---	1,225,000	---	13,000
Student assistance				
4. Health professions scholarships	---	11,219,000	---	4,781,000
5. Nurse scholarships	---	5,657,737	---	7,342,263
6. Health professions student loans	---	15,000,000	---	5,000,000
Manpower requirements and utilization				
7. Research grants:				
Physician manpower	---	902,000	---	100,000
Nursing	---	2,593,000	---	32,000
8. Research training grants:				
Nursing	---	700,000	---	98,000
9. Direct operations:				
Physician manpower	90	2,795,400	---	273,000
Nursing	148	4,142,000	---	20,000
Allied health manpower	53	1,336,600	---	108,000
Health manpower educational services	73	1,806,000	10	211,000
Total, program increases	---	---	10	51,378,263

	Base		Change from Base	
	Positions	Amount	Positions	Amount
C. Payment to "National Institutes of Health management fund" for centrally furnished services..	---	$27,000	---	$199,000
Decreases				
A. Built-in				
1. Non-recurring program costs.....	---	---	---	-10,000
B. Program				
1. Payments to diploma schools of nursing.....	---	3,000,000	---	-3,000,000
Total net change requested.....	---	---	+10	+48,580,263

1/ Excludes advance obligational authority.

Explanation of Changes

Institutional support

Health professions educational improvement grants

The requested increase of $30,400,000 will provide $12,784,000 for institutional grants of which $12,500,000 will support an estimated 92 newly eligible schools of pharmacy and veterinary medicine. The balance of the increase of $17,616,000 will provide $6,498,000 for increased continuation costs on special improvement grants and $11,118,000 for new grants with priority being given to schools in severe financial straits to correct educational deficiencies which might jeopardize accreditation. Practically all health professions schools have serious financial needs. However, about 50 schools are in serious academic and fiscal straits, among them some 20 medical and 15 dental schools.

Project grants for improvement of nurse training

The requested increase of $3,000,000 for a total of $7,000,000 in 1970 will provide all three categories of nursing schools, diploma, associate degree, and collegiate, with project grants to improve the quality of nursing education programs and to increase the numbers of nurses trained. This replaces the present $3,000,000 level of support for payments to diploma schools which has been discontinued at the close of fiscal year 1969.

Allied health new methods grants

The requested increase of $13,000 together with $1,225,000 in 1969 will support 16 projects to increase the efficiency of personnel training of health technologists for additional or more effective health services.

Student assistance

Health professions scholarships

The request for $16,000,000, an increase of $4,781,000, will provide scholarships to students of exceptional financial need to pursue a course of study in schools of medicine, dentistry, osteopathy, podiatry, pharmacy, optometry, and veterinary medicine.

These funds will support approximately 4,500 first-year students and will provide continued support for approximately 13,650 second, third, and fourth-year students. Students of veterinary medicine will become eligible for scholarships for the first time in 1970, and approximately 1,000 students enrolled in these schools will be supported.

Nurse scholarships

The requested increase of $7,342,263 will provide a total program of $13,000,000 (including $1,000,000 carryover from 1969) and will provide financial assistance to an estimated 13,000 students of exceptional financial need to enable them to pursue a course of study in nursing. In 1969, approximately 10,000 scholarships were granted under the Nurse Educational Opportunity Grant Program recently expanded by the Health Manpower Act of 1968.

Health professions student loans

The requested increase of $5,000,000 together with $15,000,000 appropriation in 1969 will provide a Federal Capital Contribution of $20,000,000. This, together with an estimated balance of $1,113,000 for loans in the Revolving Fund, will support a program level of approximately $21,113,000 for loans to more than 18,000 students in health professions schools, a reduction of about 5,000 under the previous year. The program level in 1969 of $26,429,000 includes a balance of $11,429,000 for loans in the Revolving Fund and supports 23,000 student loans. However, it is expected that the total number of health professions students receiving loans under this program and the Office of Education Guaranteed Loan Program will be greater than the total recipients in 1969.

Manpower requirements and utilization

Research grants--Physician manpower

The $1,002,000 estimate for 1970, an increase of $100,000 over 1969, will support 15 grants compared to 12 in 1969. The increase is for non-competing continuations of grants funded in prior years.

Research grants--Nursing

The $2,625,000 estimate for 1970, an increase of $32,000 over 1969, will support 47 grants compared to 53 in 1969. The increase is for non-competing continuations of grants funded in prior years.

Research training grants--Nursing

The $798,000 estimate for 1970, an increase of $98,000 over 1969, will support eight grants compared to seven in 1969. The increase is for non-competing continuations of grants funded in prior years.

Direct operations--Physician manpower

The increase of $273,000 is for continuation costs of contracts in such areas as the role of a liberal arts college in continuing education of the physician practicing in an isolated community, physician utilization in a teaching hospital in its attempts to care for urban ghetto needs, and the use of audiovisuals in medical education.

Direct operations--Nursing

The increase of $20,000 is for continuation costs of contracts for nursing student recruitment.

Direct operations--Allied health manpower

The increase of $108,000 is for continuation costs of contracts in the areas of manpower supply and distribution, improved utilization of professionals, and manpower recruitment.

Direct operations--Health manpower educational services

The increase of $211,000 includes eight positions and $128,000 to carry out administrative duties related to increases in educational improvement and scholarship grants programs and two positions and $83,000 to continue development of a National Health Manpower Intelligence System, including $51,000 for continuation costs of contracts related to the Intelligence System and information clearinghouse needs for data on health occupation training such as availability of training facilities, numbers of students accommodable, curriculum content, and availability of scholarships and stipends.

Decreases

Payments to diploma schools of nursing

Authorization for this program expires June 30, 1969. The Health Manpower Act of 1968 (PL 90-490) replaced it with broader authority for institutional grants to all three categories of nursing schools: diploma, associate degree, and collegiate.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1969 House Report	
Health manpower education and utilization	
1. Committee expectation that medical and dental schools in serious financial straits receive special consideration in the awarding of educational improvement grants (page 14 of House Report).	1. In 1969, the 48 health professions schools having the greatest financial need will receive $13,700,000 to continue projects approved in 1968; 91 percent of these funds will go to medical and dental schools. In addition, supplemental requests by the same economically depressed schools are being reviewed by peer groups at the present time and total $12,000,000; 89 percent of these funds are for medical and dental schools.
2. Committee suggestion that at least three grants should be made looking toward alleviating the serious shortage of general practitioners for family services (page 14 of House Report).	2. At least five special project grants have been awarded in 1968 and recommended for continuing support in 1969 under the Health Professions Educational Improvement Grants Program. A large share of each of these grants will be used to develop new or to expand existing programs designed to help reduce the shortage of general practitioners for family services.

3. The Committee does not see the logic of divorcing health manpower training that is directly and explicitly service-oriented from the service-oriented health programs for which the newly-created Health Services and Mental Health Administration will be responsible. The Committee therefore hopes that very serious consideration will be given to the most effective point of responsibility for manpower education and utilization programs that are not an integral part of the university-based professional education and research complex. It would seem that many of the programs for the training of nurses and allied health professionals, for student assistance, for continuing education, and for the development of service technology could be more effectively administered as part of the programs that are focused on comprehensive health planning and on the organization of the delivery of health services. The Committee hopes that these questions will be given early consideration and that they can soon be resolved (pages 14 and 15 of House Report).

3. On December 26, 1968, a reorganization within NIH established a new Bureau of Health Professions Education and Manpower Training (BHPEMT) combining the Bureau of Health Manpower with certain other elements of NIH. During the discussions of the proposed reorganization, the interrelationships between the professional health practitioner and allied health personnel and between institutions and organizations which provide health services and those which train health personnel were thoroughly considered. Because the skills of many health workers, including physicians, dentists, nurses, and other professional and technical health personnel must be brought together to provide health care and services of high quality and because institutions and organizations which render health services are essential to the education and training of all health personnel, there should be coordination within the Federal government as well as within educational institutions in the planning of programs of education and training and in the development and support of curricula and facilities for education and training of students in the health and allied health professions. The decision was therefore made to provide the focus for the education and training of health professions, allied health professions and nursing personnel in the newly created BHPEMT.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301 - Research Grants, Research Training Grants and Research Fellowships	Indefinite
Section 306 - Traineeships for Professional Public Health Personnel	$10,000,000
Section 309 - Project Grants for Graduate Training in Public Health and Grants to Schools of Public Health	15,500,000
Section 742 - Health Professions Student Loans	35,000,000
Section 744 - Payments to Schools to Cover Certain Costs Incurred in making Student Loans from Borrowed Funds	Indefinite
Section 770 - Grants to Improve the Quality of Schools of Medicine, Dentistry, Osteopathy, Optometry, and Podiatry	117,000,000
Section 780 - Scholarship Grants to Schools of Medicine, Osteopathy, Dentistry, Optometry, Podiatry, Pharmacy, or Veterinary Medicine	Indefinite
Section 792 - Grants to Improve the Quality of Training Centers for Allied Health Professions	20,000,000
Section 793 - Traineeships for Advanced Training of Allied Health Professions Personnel	5,000,000
Section 794 - Grants for Development of New Methods	4,500,000
Section 808 - Special Project and Institutional Grants to Schools of Nursing	35,000,000
Section 821 - Traineeships for Advanced Training of Professional Nurses	15,000,000
Section 824 - Nursing Student Loans	20,000,000
Section 827 - Payment to Schools to Cover Certain Costs Incurred in Making Student Loans from Borrowed Funds	Indefinite
Section 860 - Scholarship Grants to Schools of Nursing	Indefinite

Title III - Part A - Research and Investigation

Research Grants, Research
Training Grants and Research Fellowships

Section 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific insitutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man, including water purification, sewage treatment, and pollution of lakes and streams. In carrying out the foregoing the Surgeon General is authorized to--...

(c) Establish and maintain research fellowships in the Service with such stipends and allowances, including traveling and subsistence expenses, as he may deem necessary to procure the assistance of the most brilliant and promising research fellows from the United States and abroad;

(d) Make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for such research or research training projects as are recommended by the National Advisory Health Council, or, with respect to cancer, recommended by the National Advisory Cancer Council, or, with respect to mental health, recommended by the National Advisory Mental Health Council, or, with respect to heart diseases, recommended by the National Advisory Heart Council, or, with respect to dental diseases and conditions, recommended by the National Advisory Dental Research Council, and include in the grants for any such project grants of penicillin and other antibiotic compounds for use in such project; and make, upon recommendation of the National Advisory Health Council, grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs: PROVIDED, That such uniform percentage, not to exceed 15 per centum, as the Surgeon General may determine, of the amounts provided for grants for research or research training projects for any fiscal year through the appropriations for the National Institutes of Health may be transferred from such appropriations to a separate account to be available for such research and research training program grants-in-aid for such fiscal year;....

Traineeships for Professional Public Health Personnel

Appropriation

Section 306. (a) There are hereby authorized to be appropriated for the fiscal year ending June 30, 1957, and for each of the next twelve fiscal years, such sums as the Congress may determine, but not to exceed $4,500,000 for the fiscal year ending June 30, 1965, $7,000,000 for the fiscal year ending June 30, 1966, $8,000,000 for the fiscal year ending June 30, 1967, $10,000,000 each for the fiscal year ending June 30, 1968, and the two succeeding fiscal years and $14,000,000 for the fiscal year ending June 30, 1971, to cover the cost of traineeships for graduate or specialized training in public health for physicians, engineers, nurses, sanitarians, and other professional health personnel.

Project Grants for Graduate Training in Public Health

Appropriation

Section 309. (a) In order to enable the Surgeon General to make project grants to schools of public health and to other public or nonprofit institutions providing graduate or specialized training in public health, for the purpose of strengthening or expanding graduate or specialized public health training in such institutions, there are hereby authorized to be appropriated not to exceed $2,000,000 for each fiscal year in the period beginning July 1, 1960, and ending June 30, 1964, $2,500,000 for the fiscal year ending June 30, 1965, $4,000,000 for the fiscal year ending June 30, 1966, $5,000,000 for the fiscal year ending June 30, 1967, $7,000,000 for the fiscal year ending June 30, 1968, $9,000,000 for the fiscal year ending June 30, 1969, $8,500,000 for the fiscal year ending June 30, 1970, and $12,000,000 for the fiscal year ending June 30, 1971.

Grants to Schools of Public Health

Appropriation

Section 309. (c) There are also authorized to be appropriated $5,000,000 for the fiscal year ending June 30, 1968, $6,000,000 for the fiscal year ending June 30, 1969, and $7,000,000 for the fiscal year ending June 30, 1970, to enable the Surgeon General to make grants, under such terms and conditions as may be prescribed by regulations, for provision, in public or nonprofit private schools of public health accredited by a body or bodies recognized by the Surgeon General, of comprehensive professional training, specialized consultive services, and technical assistance in the fields of public health and in the administration of State or local public health programs, except that (1) in allocating funds made available under this subsection among such schools of public health, the Surgeon General shall give primary consideration to the number of federally sponsored students attending each such school, and (2) for any fiscal year ending after June 30, 1968, such portions of the funds made available under this subsection as the Secretary may determine, but not exceeding one per centum thereof, shall be available to the Secretary for evaluation (directly or by grants or contracts) of the program authorized by this subsection.

Title VII - Health Research and Teaching
Facilities and Training of Professional
Health Personnel

Part C - Student Loans

Health Professions Student Loans

Appropriation

Section 742. (a) There are hereby authorized to be appropriated to the Secretary of Health, Education, and Welfare to carry out this part (other than section 744) $5,100,000 for the fiscal year ending June 30, 1964, $10,200,000 for the fiscal year ending June 30, 1965, $15,400,000 for the fiscal year ending June 30, 1966, $25,000,000 each for the fiscal year ending June 30, 1967, and the two succeeding fiscal years, and $35,000,000 each for the fiscal year ending June 30, 1970, and the next fiscal year.

In addition to the sums authorized to be appropriated by the preceding sentence, there are authorized to be appropriated $500,000 for the fiscal year ending June 30, 1967, $1,000,000 for the fiscal year ending June 30, 1968, and $1,500,000 for the fiscal year ending June 30, 1969, which sums shall be available for carrying out this part (other than section 744) solely with respect to students of veterinary medicine.

There are further authorized to be appropriated to the Secretary such sums for the fiscal year ending June 30, 1972, and each of the two succeeding fiscal years as may be necessary to enable students who have received a loan under this part for any academic year ending before July 1, 1971, to continue or complete their education. Sums appropriated pursuant to this subsection shall be allotted among loan funds at schools which have established loan funds under this part.

Payments to Schools to Cover Certain Costs Incurred
in Making Student Loans from Borrowed Funds

Appropriation

Section 744. (b) If a school borrows any sums under this section, the Secretary shall agree to pay to the school (1) an amount equal to 90 per centum of the loss to the school from defaults on student loans made from such sums, (2) the amount by which the interest payable by the school on such sums exceeds the interest received by it on student loans made from such sums, (3) an amount equal to the collection expenses authorized by section 740(b) (3) to be paid out of a student loan fund with respect to such sums, and (4) the amount of principal which is canceled pursuant to section 741(d) or (f) with respect to student loans made from such funds. There are authorized to be appropriated without fiscal year limitation such sums as may be necessary to carry out the purposes of this subsection.

Part E - Grants to Improve the Quality
of Schools of Medicine, Dentistry, Osteopathy,
Optometry and Podiatry

Section 770. (a) There are authorized to be appropriated $117,000,000 for the fiscal year ending June 30, 1970, and $168,000,000 for the fiscal year ending June 30, 1971, for institutional grants under section 771 and special project grants under section 772.

(b) The portion of the sums so appropriated for each fiscal year which shall be available for grants under each such section shall be determined by the Secretary unless otherwise provided in the Act or Acts appropriating such sums for such year.

Part F - Scholarship Grants to Schools
of Medicine, Osteopathy, Dentistry, Optometry,
Podiatry, Pharmacy, or Veterinary Medicine

Appropriation

Section 780. (a) The Surgeon General shall make grants as provided in this part to each public or other nonprofit school of medicine, osteopathy, dentistry, optometry, podiatry, pharmacy, or veterinary medicine which is accredited as provided in section 721(b) (1) (B) or section 773 (b) (2), for scholarships to be awarded annually by such school to students thereof.

(b) The amount of the grant under subsection (a) to each such school shall be equal to $2,000 multiplied (1) for the fiscal year ending June 30, 1966, by one-tenth of the number of full-time first-year students of such school; (2) for the fiscal year ending June 30, 1967, by one-tenth of the number of full-time first-year students and second-year students of such school; (3) for the fiscal year ending June 30, 1968, by one-tenth of the number of full-time first-year students, second-year students, and third-year students of such school; and (4) for the fiscal year ending June 30, 1969, and each of the next two fiscal years, by one-tenth of the number of full-time students of such school. For the fiscal year

ending June 30, 1972, and for each of the two succeeding fiscal years, the grant under subsection (a) shall be such amount as may be necessary to enable such school to continue making payments under scholarship awards to students who initially received such awards out of grants made to the schools for fiscal years ending prior to July 1, 1971.

Part G - Training in the Allied Health Professions

Grants to Improve the Quality of Training
Centers for Allied Health Professions

Appropriation

Section 792. (a) There are authorized to be appropriated $9,000,000 for the fiscal year ending June 30, 1967, $13,000,000 for the fiscal year ending June 30, 1968, $17,000,000 for the fiscal year ending June 30, 1969, and $20,000,000 for the fiscal year ending June 30, 1970; for the grants under this section to assist training centers for allied health professions to develop new or improved curriculums for training allied health professions personnel and otherwise improve the quality of their educational programs.

Traineeships for Advanced Training
of
Allied Health Professions Personnel

Appropriation

Section 793. (a) There are authorized to be appropriated $1,500,000 for the fiscal year ending June 30, 1967, $2,500,000 for the fiscal year ending June 30, 1968; $3,500,000 for the fiscal year ending June 30, 1969, and $5,000,000 for the fiscal year ending June 30, 1970; to cover the cost of traineeships for the training of allied health professions personnel to teach health services technicians or in any of the allied health professions, to serve in any of such professions in administrative or supervisory capacities, or to serve in allied health professions specialities determined by the Surgeon General to require advanced training.

Grants for Development of New Methods

Appropriation

Section 794. There are authorized to be appropriated $750,000 for the fiscal year ending June 30, 1967; $2,250,000 for the fiscal year ending June 30, 1968, $3,000,000 for the fiscal year ending June 30, 1969, and $4,500,000 for the fiscal year ending June 30, 1970; for grants to public or nonprofit private agencies, institutions, and organizations for projects to develop, demonstrate, or evaluate curriculums and methods for the training of health technologists.

Title VIII - Nurse Training

Part A - Grants for Expansion and Improvement of Nurse Training

Special Project and Institutional Grants

Appropriation

Section 808. (a) There are authorized to be appropriated $35,000,000 for the fiscal year ending June 30, 1970, and $40,000,000 for the fiscal year ending June 30, 1971, for improvement grants under section 805 and institutional grants under section 806.

(b) Of the sums appropriated under subsection (a) of this section $15,000,000 shall be available for each of the fiscal years ending June 30, 1970, and June 30, 1971, for grants under section 805.

Part B - Assistance to Nursing Students

Traineeships for Advanced Training of Professional Nurses

Appropriation

Section 821. (a) There are authorized to be appropriated $8,000,000 for the fiscal year ending June 30, 1965, $9,000,000 for the fiscal year ending June 30, 1966, $10,000,000 for the fiscal year ending June 30, 1967, $11,000,000 for the fiscal year ending June 30, 1968, $12,000,000 for the fiscal year ending June 30, 1969, $15,000,000 for the fiscal year ending June 30, 1970, and $19,000,000 for the fiscal year ending June 30, 1971, to cover the cost of traineeships for the training of professional nurses to teach in the various fields of nurse training (including practical nurse training), to serve in administrative or supervisory capacities, or to serve in other professional nursing specialties determined by the Surgeon General to require advanced training.

Nursing Student Loans

Appropriation

Section 824. There are authorized to be appropriated to the Secretary of Health, Education, and Welfare for Federal capital contributions to student loan funds pursuant to section 822(b) (2) (A) $3,100,000 for the fiscal year ending June 30, 1965, $8,900,000 for the fiscal year ending June 30, 1966, $16,800,000 for the fiscal year ending June 30, 1967, $25,300,000 for the fiscal year ending June 30, 1968, $30,900,000 for the fiscal year ending June 30, 1969, $20,000,000 for the fiscal year ending June 30, 1970, and $21,000,000 for the fiscal year ending June 30, 1971, and such sums for the fiscal year ending June 30, 1972, and each of the two succeeding fiscal years as may be necessary to enable students who received a loan for any academic year ending before July 1, 1971, to continue or complete their education. Sums appropriated pursuant to this section for any fiscal year shall be available, in accordance with agreements under this part, for Federal capital contributions to schools with which such agreements have been made, to be used, together with deposits in such fund pursuant to section 822(b) (2) (B), for establishment and maintenance of student loan funds and (3) for transfers pursuant to section 829.

Payments to Schools to Cover Certain Costs Incurred in Making Student Loans from Borrowed Funds

Appropriation

Section 827. (b) If a school of nursing borrows any sums under this section, the Secretary shall agree to pay to the school (1) an amount equal to 90 per centum of the loss to the school from defaults on student loans made from such sums, (2) the amount by which the interest payable by the school on such sums exceeds the interest received by it on student loans made from such sums, (3) an amount equal to the amount of collection expenses authorized by section 822(b) (3) to be paid out of a student loan fund with respect to such sums and (4) the amount of principal which is canceled pursuant to section 823(b) (3) or (4) with respect to student loans made from such sums. There are authorized to be appropriated without fiscal-year limitation such sums as may be necessary to carry out the purposes of this subsection.

Part D - Scholarship Grants to Schools of Nursing

Section 860. (a) The Secretary shall make grants as provided in this part to each public or other nonprofit school of nursing for scholarships to be awarded annually by such school to students thereof.

(b) The amount of the grant under subsection (a) for the fiscal year ending June 30, 1970, and the next fiscal year to each such school shall be equal to $2,000 multiplied by one-tenth of the number of full-time students of such school. For the fiscal year ending June 30, 1972, and for each of the three succeeding fiscal years, the grant under subsection (a) shall be such amount as may be necessary to enable such school to continue making payments under scholarship awards to students who initially received such awards out of grants made to the school for fiscal years ending prior to July 1, 1971.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to: "Office of the Secretary, salaries and expenses"	$90,000	---	To support seven positions providing program services.

Health Manpower

	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1967	$750,000	$750,000	0	$500,000
1968 1/	160,630,000	154,528,000	$155,278,000	155,028,000
1969	186,227,000	172,176,000	172,176,000	172,176,000
1970	218,824,000			

1/ Excludes amounts for "Dental health" which were carried as a part of this appropriation.

Justification

Health Manpower

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	449	$5,851,800	459	$5,991,700	+10	+$139,900
Other expenses.....	---	165,391,937	---	213,832,300	---	+48,440,363
Total (excludes advance obligational authority).....	449	171,243,737	459	219,824,000	+10	+48,580,263

General Statement

Adequate numbers of skilled health manpower is a principal determining factor in meeting the expanding needs for health services resulting from: (1) The growth in population and changes in the population age distribution; (2) the changes in social attitudes toward health care; (3) the changes in the sources and methods of payment for health services; (4) the changes in scientific knowledge and health technology that have made possible improvement in the quality and range of health services; (5) the particular problems associated with increasing urbanization and the problems of the poor; and (6) the rising level of education of the people and the recognition of the importance of health.

The institutions and organizations which have evolved to provide health services to individuals are no longer adequate to meet the burgeoning needs and expectations of people. Therefore, the existing patterns of organization for the provision of health care and services are being questioned and new patterns are being sought.

While on the one hand the health manpower problems present a complicated challenge, on the other, they present extraordinary opportunities to contribute to improved organization and delivery of services through skilled manpower. Progress continues to be made, but it is painfully slow, as the table following indicates.

	Graduates			
Occupation	1963-64	1964-65	1965-66	1966-67
Dentists	3,213	3,181	3,200	3,360
Nurses	35,259	34,686	35,125	38,237
Physicians	7,690	7,804	7,934	8,148

The following table shows estimates of the magnitude of the problem still confronting us and points out how, in some occupations, the gap between estimated supply and need is widening. Although these estimates are based on existing patterns of health care and of education and will be modified as education and training and the organization for the provision of health services change, they indicate the great effort that must be made to increase the output of health manpower so that health services may be improved.

	Physicians		Dentists		Nurses	
	1968	1975	1968	1975	1968	1975
Estimated Need	363,000	400,000	109,000	137,000	800,000	1,000,000
Estimated Supply	311,000	358,000	100,000	109,000	659,000	795,000
Estimated Shortage	52,000	42,000	9,000	28,000	141,000	205,000

In many of the institutions which produce health manpower there are deficiencies of program, faculty, or facilities which are directly related to inadequate financing. The increasing cost of education in general and education for a health career in particular, the pressures for larger enrollments and the changing curricula have added to the financial difficulties of the educational institutions. If this were not enough, schools are being asked--compelled by social needs--to take on additional responsibilities for the health services for the local community, the states, the regions and of the Nation. While schools have thrived in this environment, all institutions are increasingly dependent on Federal financial support for their survival. A number of schools are threatened with loss of accreditation, others are in danger of closing at the very time that more schools are needed.

A substantial portion of the educational expense for health manpower education and training has traditionally been borne by the students themselves. Many highly motivated and well qualified students are discouraged from pursuing a career in the health field because of lengthy and expensive periods of education. With the need for health manpower in all occupations as great as it is, no qualified student should be excluded from education or training for economic reasons. The goal of the loan and scholarship programs is to reduce financial barriers to health careers.

One of the greatest deterrents to expansion and improvement of education and training for health manpower is the lack of qualified teachers in almost all professional and occupational areas. Institutions must attract many more outstanding individuals who have completed their basic provessional education and are motivated toward further preparation for leadership in teaching, administration and clinical specialization. Traineeships encourage qualified health personnel to undertake advanced education for leadership.

The severe shortage of health manpower and the long lead-time required to increase significantly the numbers of most of the occupations have prompted investigations in search of improvement. Research is needed to develop methods to improve the quality and utilization of health manpower; the distribution of health professionals including geographic and socio-economic factors; to define the expenditures associated with educating health personnel; to improve curriculum, and develop teaching techniques and methods of evaluating health manpower education and training.

This budget has been developed on the basis that resources must be available to meet immediate needs of people requiring health services today and that these needs can best be met through better utilization of existing manpower and better use of existing facilities. The time required to recruit students, to modify and improve curricula, to create new methods of teaching and new curricula in the fields of health, to prepare adequate numbers of teachers, supervisors, administrators and investigators as well as practitioners, to plan and construct new facilities as well as to expand, renovate and modernize those that now exist but are obsolete or run down, to develop new patterns for providing health services and the utilization of personnel, to educate the people to attain better health to provide for better distribution of services both geographically and among different economic groups, is very long. Planning and the operations which result from plans should be carried out in as orderly and coordinated a manner as possible so that the many good aspects of existing health services may be retained,

strengthened and be available to people who need them, while essential modifications expansion and improvement are taking place.

The programs in this budget include:

(1) The coordination of existing information and the development and dissemination of essential information on needs for health personnel, their utilization, distribution and the training and educational programs that are available for students who wish to enter the health fields. This will provide the basis for improvement of health services now and for better planning for the future. Information will also be developed which will be of assistance to educational institutions, organizations and agencies in the creation and development of educational and training programs in health.

(2) Improvement in education and training of health personnel and increasing their numbers through:

(a) The recruitment of increased numbers of able students from all portions of our society into health careers.
(b) Financial assistance to students during their preparation for such careers.
(c) Assistance to those in the health professions and technologies to improve their skills as practitioners, to become teachers, investigators, supervisors, administrators, and clinical specialists, thereby improving the quality of education and training to improve the capability of research in the health sciences and in health education, and increasing the availability and quality of health services. This assistance has both short term and long term implications for improvement in quality as well as quantity of health services.
(d) Grants to educational institutions, organizations and agencies to strengthen existing programs, to expand their enrollments, to develop new curricula, new methods of education and new types of health personnel, and to educate those practicing the health professions in the improved utilization of the skills of other health workers who assist them and can markedly increase the effectiveness of health professionals in providing health services.
(e) Support of programs to return inactive health personnel to active practice and to update their knowledge and skills.
(f) Assistance in the renovation and expansion of the facilities of existing schools and in the planning, development and construction of new schools.

(3) Improvement in the prevention of illness, environmental health and health care through:

(a) Assistance to schools and public and private agencies in the development of essential health manpower programs in public health and in dental public health to provide necessary health care to individuals and to prevent illness and the increasing environmental hazards to health.
(b) Technical assistance in the development of educational and training programs and research in education including continuing education for the health professions and occupations.
(c) Support of research in nursing education, and in nursing practice and nursing technologies, particularly as they apply to changes in nursing education.
(d) Technical assistance and financial assistance to institutions, agencies and organizations in the development of health manpower information, educational programs to improve the health of the public, and in planning for and developing greater health manpower resources throughout the Nation.

INSTITUTIONAL SUPPORT

	1969 Estimate Amount	1970 Estimate Amount	Increase or Decrease Amount
Personnel compensation and benefits	---	---	---
Other expenses	$93,446,000	$123,859,000	+$30,413,000
Total	93,446,000	123,859,000	+30,413,000
Subactivities:			
Medical, dental and related:			
Health professions educational improvement grants	$66,000,000	$96,400,000	+$30,400,000
Nursing:			
Payments to diploma schools of nursing	3,000,000	---	-3,000,000
Project grants for improvement of nurse training	4,000,000	7,000,000	+3,000,000
Public health:			
Grants to schools of public health	4,554,000	4,554,000	---
Project grants for graduate public health training	4,917,000	4,917,000	---
Allied health professions:			
Educational improvement grants	9,750,000	9,750,000	---
New methods grants	1,225,000	1,238,000	+13,000
Total	93,446,000	123,859,000	+30,413,000

HEALTH PROFESSIONS EDUCATIONAL IMPROVEMENT GRANTS	1969 Estimate	1970 Estimate	Change
Institutional grants	$33,716,000	$46,500,000	+$12,784,000
Special project grants			
New	18,579,000	11,118,000	-7,461,000
Non-competing continuations	13,705,000	38,782,000	+25,077,000
Subtotal - special project grants	32,284,000	49,900,000	+17,616,000
Total	66,000,000	96,400,000	+30,400,000

The authority for this program is contained in section 770 of the Public Health Service Act with a 1970 authorization of $117,000,000. The Health Manpower Act of 1968 provided major changes and increased authorization for expanded assistance. Also, schools of veterinary medicine and pharmacy were made eligible for both institutional and project grants.

Practically all health professions schools have serious needs. About 50 schools have annual operating deficits in excess of $1,000,000, of these approximately 20 medical and 15 dental schools are threatened with loss of full accreditation because of lack of sufficient operating funds to maintain the prerequisite quality of their educational programs. At the same time schools need to improve the quality of their educational programs, and to increase the supply of highly trained health manpower. This requires a dramatic increase in their enrollments. In an attempt to attain the results required for more effective teaching and perhaps shorten the time required to produce a health practitioner the funds made available have been of great assistance. Some schools have been helped to correct accreditation problems, others in making improvements in curriculum and still others to remain open however, if all existing schools are to fulfill their mission of producing health manpower, significantly increased support must be supplied. An example of the benefits obtained from the use of these funds follows:

A medical school which was on accreditation probation was awarded both an institutional and special improvement grant, the latter designed to overcome certain of the factors responsible for the probationary status. Through the combined grants this school has been able to augment its faculty by providing more than twenty additional faculty members thus providing more depth and diverse expertise in the faculty. This has resulted in a better training program for the medical students by reducing the class sizes and providing more intimate faculty-student relationships. In addition, the grant permitted modernization and remodeling of existing inadequate laboratories and teaching classrooms and replacement of antiquated teaching equipment. The graduates of this school hold unique positions in the health delivery system of the United States since they contribute to the health and well-being of essentially poor and economically depressed people.

The request for $96,400,000, an increase of $30,400,000 over 1969 will be used to support both institutional and special project grants. The funds will provide $46,500,000 in institutional grants to 264 schools of medicine, dentistry, osteopathy, optometry, podiatry, pharmacy, and veterinary medicine. Project grants in the amount of $49,900,000 will be available to schools of medicine, dentistry, osteopathy, optometry, podiatry, pharmacy, and veterinary medicine.

Health professions educational improvement grant programs are used to:

(1) Improve the quality of health professions education, and

(2) Increase the number of health practitioners.

Institutional Grants

These grants provide basic support for educational programs in the health professions in eligible institutions. They are designed to provide a fixed award of $25,000 to each institution, plus an estimated initial allocation of $340 for each undergraduate student, $540 for each graduate, and an added incentive of $340 for each additional student in excess of the enrollment increase required for eligibility for the grant. The 92 schools of pharmacy and veterinary medicine will participate for the first time as provided by the recently enacted Health Manpower Act of 1968 and will receive an approximate total of $12,500,000. The 172 schools of medicine, osteopathy, dentistry, podiatry, and optometry that have been eligible since the initial authorization of the grants will receive support that is no less than their 1969 levels, requiring an estimated total of $34,000,000. This is in compliance with the Health Manpower Act of 1968 requirement that no school receive less in 1970 under the Health Manpower Act of 1968 than it did in 1969.

Special Project Grants

Project grants were awarded to 48 schools of medicine, dentistry, osteopathy, optometry and podiatry for the first time in 1968 in the amount of $10,132,000. Awards were made to schools which were eligible and had received basic improvement grants. The maximum amount for which a school was eligible, under the statute, in 1968 was $300,000. Fifty-three new grants are expected to be awarded in 1969 at an initial cost of $18,579,000. The continuation of 99 special project grants in 1970 will require an estimated $38,782,000, leaving $11,118,000 for new awards. This gives a total of $49,900,000 for special project grants in 1970, an increase of $17,616,000 over 1969.

In awarding these grants, priority is given to schools in severe financial straits that plan to use the special improvement grant to improve the financial status and to improve those aspects of their educational program whose deficiencies have placed the school's accreditation status in jeopardy. Applications from schools whose accreditation is in jeopardy show a determination to solve specific deficiencies in educational programs which require additional funds to correct them. Applications from schools in serious financial straits have demonstrated careful planning to overcome their most critical weaknesses.

Some schools plan to use the funds from their project grants to add breadth and depth to their curricula by filling in gaps in instructional areas, by the addition of new courses, and by increasing the availability of faculty for students' instruction.

Distribution of basic and special grants by disciplines and by category of expenditure is listed as follows:

HEALTH PROFESSIONS BASIC EDUCATIONAL IMPROVEMENT GRANTS

Type of School	1968		1969		1970	
	No.	Amount	No.	Amount	No.	Amount
Medicine	99	$20,242,500	100	$21,110,500	100	$21,200,000
Dentistry	51	8,859,500	52	9,305,500	52	9,400,000
Optometry	10	1,360,500	10	1,480,500	10	1,600,000
Osteopathy	5	1,063,000	5	1,126,000	5	1,100,000
Podiatry	5	635,000	5	693,500	5	700,000
Veterinary Medicine *	--	--	--	--	18	2,700,000
Pharmacy *	--	--	--	--	74	9,800,000
Total	170	32,160,500	172	33,716,000	264	46,500,000

* Not eligible until 1970.

BUDGETED AMOUNTS BY CATEGORIES OF EXPENDITURES

FOR BASIC GRANTS IN 1968

Category	Grant Amount	Percent
Teaching staff	$20,601,415	64.1
Other staff	3,957,719	12.3
Equipment	3,964,189	12.3
Alteration and renovation	1,825,145	5.7
All other expenses	1,812,032	5.6
Total	32,160,500	100.0

HEALTH PROFESSIONS SPECIAL EDUCATIONAL IMPROVEMENT GRANTS

Type of School	1968 No.	Amount
Medicine	23	$5,476,610
Dentistry	11	2,689,059
Optometry	7	637,610
Osteopathy	2	410,299
Podiatry	5	918,127
	48	10,131,705

BUDGETED AMOUNTS BY CATEGORIES OF EXPENDITURES

FOR SPECIAL GRANTS IN 1968

Category	Grant Amount	Percent
Teaching staff	$5,259,041	51.9
Other staff	1,090,719	10.8
Equipment	2,391,732	23.6
Alteration and renovation	870,177	8.6
All other expenses	520,036	5.1
	10,131,705	100.0

INSTITUTIONAL GRANTS - NURSING	1969 Estimate	1970 Estimate	Change
Formula	$3,000,000	---	-$3,000,000
Project grants	4,000,000	$7,000,000	+3,000,000
Total	7,000,000	7,000,000	----

The authority for this program is contained in sections 805 and 806 of the Public Health Service Act with a 1970 authorization of $35,000,000.

Schools of nursing must maintain and improve the quality of their programs in nursing and increase the numbers of nurses trained if the nurses needed to provide health services to the American people are to be available. Costs for educating nurses have increased steadily in recent years. Schools cannot attract qualified faculties, provide comprehensive and supervised clinical experiences and increase their enrollments without financial assistance. The present authority for partial reimbursement of diploma schools ($3,000,000 in 1969) has been discontinued and replaced by a broader authority for institutional grants to all three categories of nursing schools: diploma, associate degree, and collegiate. The authority included in the Health Manpower Act of 1968 for the years 1970 and 1971 enables schools to make improvements in student-faculty ratios, attract additional qualified faculty members, thereby improving basic curricula. The entire request for these improvements in 1970 is in the form of project grants discussed in the following paragraphs.

Project Grants for the Improvement of Nurse Training

These grants have made possible fundamental changes in nursing programs to accelerate learning, increase the numbers of students that can be taught, and enhance the quality of education in schools with limited faculty and facilities--119 schools of nursing have received project improvement grants. An additional 160 schools have participated in these projects with the 119 schools receiving the grants. A total of nearly 300 schools of nursing are sharing in the benefits of the grants. The ultimate results will have far-reaching effects as the improved quality of students' preparation is reflected in the care they give as practitioners. These grants for improvement of nursing education will be continued and expanded under the Health Manpower Act to include funds for projects in public and private non-profit hospitals, institutions, and agencies that can contribute substantially to improvements in nursing education as well as to programs of nursing education in universities and colleges, junior and community colleges, and hospital schools of nursing in which funds will be used for the improvement, expansion, and extension of their educational programs and services.

Changes in patterns of nursing education continue to occur, requiring modifications, new combinations and other new developments affecting programs--all of which tax the limited financial resources of the schools. Diploma schools, in particular, will require financial assistance to help them with the planning and phasing processes so that preparation of significant numbers of nurses continues during the "orderly transition" of nursing education to academic institutions which will make optimal use of the resources of affiliated hospitals for the clinical experience essential in nursing education.

All settings that provide clinical experience for nursing students must be involved in planning for local health care if the most effective learning is to occur. Education and service must plan and work together to identify and develop those among the variety of health facilities that will continue to provide the most suitable programs. The new legislation, the Health Manpower Act of 1968, makes hospitals and other agencies engaged in teaching and in contributing to the development of nursing education eligible to apply for project grants.

Priority for assessment of applications filed under section 805 is based on: (1) the relative need of the applicant (if a school of nursing) for financial assistance to continue in operation or avoid curtailing enrollment or reduction in the quality of training provided; (2) the special need of the applicant for financial assistance in connection with its merger with a school of nursing; (3) the relative need of the applicant for financial assistance to maintain or provide for accreditation as a school of nursing; and (4) the extent to which the project will increase enrollment or full-time students receiving nursing training.

The $7,000,000 requested for 1970 will provide funds to support an estimated 103 grants to hospitals and other agencies as well as schools of nursing to assist in maintaining their enrollment and in improving the quality of their educational programs in accordance with the purposes of the Health Manpower Act of 1968.

FORMULA GRANTS TO SCHOOLS OF PUBLIC HEALTH	1969 Estimate	1970 Estimate	Change
	$4,554,000	$4,554,000	---

The authority for this program is contained in section 390(c) of the Public Health Service Act with a 1970 authorization of $7,000,000.

Schools of public health prepare the majority of the graduate public health specialists for services throught the country. They are a fundamental resource for public health consultation and research to all State and local health agencies as well as Federal agencies. Formula grants to these schools of public health provide basic institutional support so that they may undertake their essential educational efforts.

Schools of public health must continue to improve and expand their programs to meet the tremendous demands of health agencies, academic institutions, and others for health professionals with graduate education in a host of disciplines. People with specialized training in community and environmental health are urgently needed to provide the leadership in program direction, teaching, and the special technical skills so necessary in meeting the changes occurring in society and the environment.

Schools of public health have increased in number from eleven to fifteen since this program's inception in 1959. Three of the four schools most recently established have been accredited in the last three years. Enrollments over the past five years have risen by more than 50 percent, from 1,682 in 1963-64 to 2,637 in 1967-68, and the number of graduates has increased similarly, from 851 to more than 1,200 during the same period. Changes in faculty and modifications in curriculum offerings reflect the national concerns over the need to expand our capabilities to provide adequate health services including medical care administration, improved administration of hospitals, the increasing importance of nutrition and demography, population studies, epidemiology, and public health administration in the maintenance of health, the prevention of illness and the cure of disease.

The schools of public health have used the formula grants primarily to support faculty. For the academic year 1968-69 the schools of public health have budgeted 63 percent of the formula grant monies for salaries of teaching personnel supporting partially or in full more than one-third of the schools' total teaching staff. Twenty-three percent of the funds are allocated for supportive staff and the remaining 14 percent for teaching equipment, travel, and other items.

The 1970 request of $4,554,000 is the same as the 1969 amount. (Distribution to individual schools is shown on the attached table).

GRANTS TO SCHOOLS OF PUBLIC HEALTH

Names of Schools	1968	1969	1970
California, Berkeley	$392,000	$420,600	$420,600
California, Los Angeles	325,400	398,400	398,400
Columbia	203,800	227,500	227,500
Harvard	251,600	270,300	270,300
Hawaii	113,700	165,900	165,900
Johns Hopkins	318,500	390,500	390,500
Loma Linda	92,100	119,400	119,400
Michigan	542,200	638,900	638,900
Minnesota	362,500	379,900	379,900
North Carolina	442,000	488,900	488,900
Oklahoma	168,900	182,200	182,200
Pittsburgh	228,100	257,300	257,300
Puerto Rico	172,100	185,600	185,600
Tulane	184,100	191,100	191,100
Yale	203,000	237,500	237,500
Total	4,000,000	4,554,000	4,554,000

PROJECT GRANTS FOR GRADUATE PUBLIC HEALTH TRAINING	1969 Estimate	1970 Estimate	Change
New and competing	$517,000	$417,000	-$100,000
Non-competing continuations	4,400,000	4,500,000	+100,000
Total	4,917,000	4,917,000	---

The authority for this program is contained in section 309 of the Public Health Service Act with a 1970 authorization of $8,500,000.

Project grants for graduate public health training are awarded in recognition of the national need for special institutional assistance to schools of public health, nursing, engineering, medicine, dentistry, hospital administration, and others to initiate, strengthen, and expand specialized public health courses at the graduate level. Greater support through project grants will assist schools to increase their capacities and to modify existing and develop new academic programs to meet changing social and health needs, to relate to the new health technologies, to make

utilization of scarce manpower more effective, and to plan and develop new patterns of community organization, both urban and rural, and health services administration. Emphasis must also be given to expanding support to a broader base of institutions that provide graduate professional education in the administration, delivery, and evaluation of community and environmental health services.

In 1969 an estimated 117 projects will be funded, including 13 new grants which will alleviate part of the backlog of approved but unfunded applications carried over from 1968.

The 1970 request of $4,917,000, the same as the 1969 amount, will support the same number of projects as in the current year.

ALLIED HEALTH EDUCATIONAL IMPROVEMENT GRANTS	Estimate	Estimate	Change
	$9,750,000	$9,750,000	---

The authority for this program is contained in section 792(a) of the Public Health Service Act with a 1970 authorization of $20,000,000.

Allied health educational improvement grants provide basic support to junior colleges, colleges, and universities for the purpose of improving the quality of academic offerings, strengthening faculty, and helping to meet the costs of increased enrollments of students in the schools offering education and training in allied health professions. Grants to individual schools are based on a statutory entitlement of $5,000 for each of specified allied health curriculums offered by the training institution, plus $500 times the number of full-time students enrolled in these curriculums such as radiologic technology, dental hygiene, occupational therapy, physical therapy, and medical technology.

While the authority for the programs was established in 1966, 1967 was the first year in which funds were made available for these programs. In 1967, 192 grants were awarded, the available funds covering 41 percent of the amounts requested by eligible schools for support of 395 curriculums enrolling more than 11,000 students. In 1968 educational improvement grants in the allied health professions were made to 197 senior colleges and universities and 33 junior colleges, at a funding level of $9,750,000, providing 95 percent of the formula amounts for each grantee. In both years the schools budgeted the largest portion of their improvement awards for teaching and supportive staff and teaching equipment.

The 1969 appropriation, at the same level as 1968, when spread over the base of present grantees plus expansion of educational programs, increased enrollemnts, additional schools meeting eligibility requirements, and the list of eligible curriculums being extended to include sanitarians and sanitary technicians will provide basic support to approximately 65 percent of authorized formula amounts to an estimated 280 institutions.

The 1970 request of $9,750,000 will fund approximately 55 percent of the entitlement provided under the Allied Health Professions Personnel Training Act, in support of about 900 curriculums in which some 26,000 students will be enrolled in more than 300 institutions.

ALLIED HEALTH DEVELOPMENTAL GRANTS--NEW METHODS	1969 Estimate	1970 Estimate	Change
New and competing	---	$715,000	+$715,000
Non-competing continuations	$1,225,000	523,000	-702,000
Total	1,225,000	1,238,000	+13,000

The authority for this program is contained in section 794 of the Public Health Service Act with a 1970 authorization of $4,500,000.

Constantly changing social needs, changing technology in the health and medical sciences, concurrent changes in staffing requirements for the delivery of health services and variations of geographic needs for allied health manpower require continuing study of the education and training of both existing and developing categories of health specialists as well as the stimulation of new educational programs in geographic areas where they do not exist. In this context the Allied Health Professions Personnel Training Act authorizes project grants to develop, demonstrate, or evaluate curriculums and methods for the training of health technologists. The Health Manpower Act of 1968 extends the eligibility to apply for these funds to include public or non-profit "agencies, institutions, and organizations" as well as training centers for the allied health professions. Thus, institutions which do not qualify as training centers but which have the competency to develop, demonstrate or evaluate curricula would be eligible to participate.

In 1968, awards under the developmental program were made for sixteen projects ranging from the creation of new entry-level or sub-baccalaureate jobs, such as the "orthopedic technician," to the creation of new specialties based upon technological innovations in health care, such as biomedical engineering personnel. In the first example, the requirement is for the identification of emerging functions and skills. Other developmental grants have been awarded for projects such as a pilot physical therapy assistant program, a baccalaureate program in toxicology, a diagnostic microbiology technologist program, and an electroencephalography technician training program. These projects have been in existence for just a short time and results are not yet available. However, it is anticipated that they will provide extremely valuable prototypes for the development of training programs for new types of health workers. The 1969 program level provides for continuation of these same projects with further development as outlined in the grant application proposals.

The 1970 request of $1,238,000, an increase of $13,000, will again provide for a total of approximately 16 projects designed to increase the efficiency of training of personnel for additional or more effective health services. These projects will support the study and demonstration of new teaching methods and the development of curriculums and methods for the training of known as well as new types of health technologists.

STUDENT ASSISTANCE

	1969 Estimate Amount	1970 Estimate Amount	Increase or Decrease Amount
Personnel compensation and benefits	---	---	---
Other expenses	$62,156,737	$79,280,000	+$17,123,263
Total	62,156,737	79,280,000	+17,123,263
Subactivities:			
Traineeships:			
Nurse fellowships	$650,000	$650,000	---
Nurse traineeships	10,470,000	10,470,000	---
Public health traineeships	8,000,000	8,000,000	---
Allied health traineeships	1,550,000	1,550,000	---
Scholarships and opportunity grants:			
Nurse scholarships	5,657,737	13,000,000	+$7,342,263
Health professions scholarships	11,219,000	16,000,000	+4,781,000
Loans:			
Health professions student loans	15,000,000	20,000,000	+5,000,000
Nursing student loans	9,610,000	9,610,000	---
Total	62,156,737	79,280,000	+17,123,263

NURSE FELLOWSHIPS	1969 Estimate	1970 Estimate	Change
New and competing.....	$325,000	$110,000	-$215,000
Non-competing continuations.....	325,000	540,000	+215,000
Total.....	650,000	650,000	---

The authority for this program is contained in section 301 of the Public Health Service Act with an indefinite authorization for 1970.

If the practice of nursing is to improve and keep pace with medical and scientific developments, research in nursing care for patients and in nursing services is imperative. Most fields of study have one percent or more of active practitioners with research training. If this proportion were to hold true for nursing, there should be approximately 6,200 nurses with research training. To date, approximately 300-400 nurses have had formal research training.

Consequently, many more nurses must be provided with graduate training in research. Special fellowships in nursing research provide support to nurses for research training at the pre-and post-doctoral levels. This program is an essential adjunct to the research grant program as it prepares nurses to carry on the much needed research for fuller understanding and improvement of nursing care. There is a growing demand for nurse researchers to direct projects, to work as part of medical research teams, and to direct community health research. Approximately 130 fellows will be supported with the requested $650,000 for 1970, the same level of support as in 1969.

	1969 Estimate	1970 Estimate	Change
NURSE TRAINEESHIPS	$10,470,000	$10,470,000	---

The authority for this program is contained in section 821 of the Public Health Service Act with a 1970 authorization of $15,000,000.

The effectiveness of nursing in all areas of practice is influenced by the leadership that is available. Nurses teaching, planning, supervising and/or directing nursing care in hospitals and health agencies, need additional education at the baccalaureate and master's levels for these responsible positions, that is, study in basic sciences, humanities, administration and management beyond their initial nursing programs.

Of the 640,000 registered nurses in 1967, about 83,600 were formally prepared for these leadership jobs. These nurses constituted the best prepared leadership available for over 23,000 health agencies and institutions, 5,400 local boards of education, and 2,300 professional and vocational educational programs, for industry, the military services and other health programs. In patient care settings, leadership includes supervision of registered nurses with less educational preparation, 300,000 practical nurses and 700,000 aides.

Equal distribution of the 83,600 prepared nurses among the 30,700 care institutions and teaching programs would have allowed only two nurses per institution. Since many of these employed considerably more than two prepared nurses, many institutions did not have even one nurse with adequate educational preparation for a leadership position.

Although the Nurse Traineeship Program during the 12 years it has been in existence has increased the number of nurses by more than 20,000 prepared for positions as teachers, administrators, and supervisors, the demand for these specialists continues to grow. The gap between the supply and demand is increasing according to the Program Review Report in the Nurse Training Act of 1964, dated December 1967. The necessity for increasing the number of students in schools of nursing, and the demand for qualified teachers will increase substantially.

Between 1950 and 1967 the estimated number of practicing registered nurses increased from 375,000 to 640,000, a gain of 70 percent. In the same interval both practical nurses and nursing aides increased by more than 150 percent. To utilize the skills of practical nurses and aides most effecitvely in patient care requires planning and supervision by professional nurses.

Increasing medical specialization requires an increasing number of nurse specialists in all areas of nursing. Also present is a continuing shortage and uneven geographic distribution of physicians. This situation, together with the many new technologies resulting from medical research, requires that registered nurses accept responsibility for many activities and functions that were formerly the sole responsibility of physicians. The practice of nursing has become more and more complex and requires an increasingly higher level of nursing skills and educational preparation.

High priority must be given to the optimal utilization of nursing personnel in all settings. Adequate leadership available to plan, supervise, and direct a prepared group of aides and personnel, at a technical level is essential for better utilization of all personnel. This will result in more effective organization and delivery of health services of high quality.

With the $10,470,000 requested for 1970 it is estimated that 2,000 nurses will be supported for long-term training and 5,000 short-term training courses--both programs will be maintained at the same level as in 1969. The short-term traineeship program was designed as a supplement to the long-term traineeship program, to assist graduate nurses who, for a variety of reasons cannot undertake full-time academic study. Short intensive courses focused on specific skills have made it possible for large numbers of nurses already holding key positions to be better prepared to carry out their present responsibilities more adequately. In the three years under the Nurse Training Act, the short-term intensive training program has benefited almost 14,000 trainees through 371 courses offered in 130 sponsoring agencies.

	1969 Estimate	1970 Estimate	Change
PUBLIC HEALTH TRAINEESHIPS	$8,000,000	$8,000,000	---

The authority for this program is contained in section 306 of the Public Health Service Act with a 1970 authorization of $10,000,000.

Public health traineeships provide support to physicians, dentists, engineers, sanitarians, nurses, administrators and other health personnel taking graduate and specialized training in schools providing curricula related to public health. These grants also encourage the development of short-term training to up-grade professional and technical skills of persons already working in public health but who need continuing opportunities to keep pace with rapid progress and changes in the administration and delivery of community and environmental health services.

Public health traineeships are particularly important in light of the increasing demands for professional public health personnel to staff the expanding demand for health services which have been brought about by the provisions of Medicare and Medicaid, comprehensive health planning, regional medical programs, OEO urban and rural health programs.

From 1967 through 1969 appropriations for this program have been at a constant level of $8,000,000, which has provided for approximately 1,300 full-time trainees and approximately 12,000 short-term trainees annually. With increased costs for short-term training, the number of trainees in this program will drop to about 10,800 in 1969.

A table follows showing numbers trained by category in 1968 and 1969:

NUMBERS TRAINED

Category	1968 Estimate	1969 Estimate
Residencies	68	68
Apprenticeships	547	547
Short-term	11,616	10,300
Long-term	1,226	1,213
Total	13,457	12,128

	1969 Estimate	1970 Estimate	Change
ALLIED HEALTH TRAINEESHIPS	$1,550,000	$1,550,000	---

The authority for this program is contained in section 793 of the Public Health Service Act with a 1970 authorization of $5,000,000.

Allied health traineeships provide support of students taking advanced training to prepare them to serve as teachers, administrators, supervisors and specialists in the allied health professions.

Current and foreseeable shortages of physicians, dentists, and other health professionals require a concentrated effort to increase the numbers and improve the utilization of allied health personnel since they require shorter and less costly training and can be drawn from a broad range of the population. It is evident that the capability to accommodate increased enrollments necessary to produce adequate numbers and quality of education of these professional and technical personnel is most heavily dependent on the availability of well-qualified teachers. Thus, the primary emphasis of the traineeship program continues to be on the preparation of teachers for the allied health professions.

The allied health traineeship program was initiated in 1967 with support made available to 64 students in 12 institutions. The program was expanded to reach 257 trainees, in eleven disciplines, in 1968. In 1968 the trainees, most of whom were enrolled in the curriculums of medical technology, dietetics, and occupational and physical therapy, represented 49 educational institutions. In 1969, approximately 400 trainees will receive support through this program.

The 1970 request of $1,550,000 is the same as the 1969 amount.

	1969 Estimate	1970 Estimate	Change
NURSE SCHOLARSHIPS	$5,657,737	$13,000,000	+$7,342,263

The authority for this program is contained in section 860 of the Public Health Service Act with an indefinite authorization for 1970.

Special efforts must be made to reach minority and disadvantaged groups not now entering nursing in sufficient numbers and to identify, encourage and assist qualified young people with serious financial need to undertake education for nursing. Presently 38 percent of the nursing students come from families with incomes of $7,500 or less.

Experience has shown the need for additional financial assistance to students in the form of scholarships as well as loan funds. At least 30 percent of the students enrolled in schools of nursing require financial help in order to attend nursing school.

The present program of opportunity grants for nursing students was made possible by the Allied Health Professions Personnel Training Act of 1966. In 1969, this program provided limited scholarship aid to 10,000 students of exceptional financial need. The Health Manpower Act of 1968 will substitute for this limited authority a more realistic program of scholarship aid for students in schools of nursing awarding the diploma, associate degree or baccalaureate degree. Funds will be allocated to the participating schools using a formula similar to that for the health professions schools. No student can receive more than $1,500 per year. The $13,000,000 reflected for 1970 includes $1,000,000 brought forward from 1969 and will provide financial assistance to approximately 13,000 nursing students or about nine percent of the total number of students attending schools of nursing. The 1969 estimate includes $157,737 brought forward from 1968.

	1969 Estimate	1970 Estimate	Change
HEALTH PROFESSIONS SCHOLARSHIPS	$11,219,000	$16,000,000	+$4,781,000

The authority for this program is contained in section 780 of the Public Health Service Act with an indefinite authorization for 1970.

The request for $16,000,000, an increase of $4,781,000 over 1969, will provide scholarships to students of exceptional financial need who need assistance to pursue a course of study in schools of medicine, dentistry, osteopathy, pharmacy, podiatry, optometry, and veterinary medicine. The annual operating reports for fiscal year 1968 received from all participating schools disclosed that 76 percent of the students receiving scholarships had family incomes or came from families with a combined annual income of $10,000 or less, and 31 percent of the recipients had family income or came from families with income of less than $5,000. These funds will assist approximately 4,500 first-year students and will provide continued support for approximately 13,650 second, third, and fourth-year students which includes students of veterinary medicine who become eligible for scholarships for the first time in 1970. The Health Manpower Act of 1968 also provides for the transfer of funds between scholarships and loans of up to 20 percent as determined by the school. This will enable the schools to provide assistance to students in accordance with the type of assistance that is most in keeping with the student's needs. A distribution of these funds by discipline and other pertinent information follows:

HEALTH PROFESSIONS SCHOLARSHIP PROGRAM
PROGRAM ACCOMPLISHMENTS
by
Fiscal Year and Discipline

Fiscal Year 1967

	Amounts Allocated	Number of Participating Schools	First-year Enrollment in Participating Schools	Number of Students Assisted	Percentage of Students Assisted
Medicine	$1,769,200	88	8,754	1,635	18
Dentistry	808,200	49	3,824	799	20
Osteopathy	97,800	5	469	147	31
Optometry	145,800	10	695	144	23
Pharmacy	1,003,200	70	5,373	1,040	19
Podiatry	51,000	5	288	59	21
Total	$3,875,200	227	19,403	3,824	19

Fiscal Year 1968

	Amounts Allocated	Number of Participating Schools	First-and Second-Year Enrollments in Participating Schools	Number of Students Assisted	Percentage of Students Assisted
Medicine	$3,293,009	95	17,514	3,810	22
Dentistry	1,475,826	50	7,785	1,869	24
Osteopathy	177,049	5	971	316	33
Optometry	248,526	10	1,363	362	27
Pharmacy	1,894,910	73	10,642	2,326	22
Podiatry	108,856	5	597	137	23
Total	$7,198,176	238	38,872	8,820	23

Fiscal Year 1969

	Amounts Allocated	Number of Participating Schools	First-Second- & Third Year Enrollments in Participating Schools 1/	Number of Students Assisted 1/	Percentage of Students Assisted 1/
Medicine	$5,292,984	99	27,604	6,073	22
Dentistry	2,354,245	52	12,023	2,886	24
Osteopathy	287,600	5	1,445	477	33
Optometry	393,400	10	1,970	532	27
Pharmacy	2,730,588	73	15,509	3,412	22
Podiatry	160,000	5	800	184	23
Total	$11,218,817	244	59,351	13,564	23

1/ Estimated.

HEALTH PROFESSIONS SCHOLARSHIP PROGRAM
PROGRAM ACCOMPLISHMENTS
by
Fiscal Year and Discipline
(Continued)

Fiscal Year 1970 2/

	Amounts Allocated	Number of Participating Schools	Total Enrollment of Participating Schools	Number of Students Assisted	Percentage of Students Assisted
Medicine	$7,203,400	100	36,017	7,924	22
Dentistry	3,078,400	52	15,392	3,694	24
Osteopathy	383,000	5	1,915	632	33
Optometry	471,000	10	2,355	636	27
Pharmacy	3,661,800	73	18,309	4,028	22
Podiatry	214,000	5	1,070	246	23
Veterinary Medicine	988,400	20	4,942	988	20
Total	$16,000,000	265	80,000	18,148	23

2/ Projected.

	1969 Estimate	1970 Estimate	Change
HEALTH PROFESSIONS STUDENT LOANS	$15,000,000	$20,000,000	+$5,000,000

The authority for this program is contained in section 742 of the Public Health Service Act with a 1970 authorization of $35,000,000.

The 1970 estimate of $20,000,000, together with an estimated balance of $1,113,000 which will remain on deposit in the Health Professions Education Fund (Revolving Fund) will provide $21,113,000 to support this program. Of this amount an indeterminate (due to lack of experience in this program) sum for loan cancellations, defaults and collection expenses will be paid. The total loan program in 1969 is $26,429,000 made up of $15,000,000 in appropriated funds and $11,429,000 from the revolving fund.

The Health Manpower Act of 1968 provides for the transfer of up to 20 percent of the funds for scholarships and loans from one category to the other according to the needs of students. Highly qualified students who might be unable to pursue a career in the health professions because of economic reasons are able through these programs to enroll in health professions schools. While the number of health professions loans to students of medicine, dentistry and related professions will decline in 1970 to 18,416 from 23,000 in 1969, it is expected that the total number of health professions students receiving loans under this program and the Office of Education's Guaranteed Loan Program will be greater than the total recipients in 1969.

In 1970, the estimated 18,416 students, or 23 percent of the 80,000 students enrolled in schools of medicine, dentistry, osteopathy, optometry, pharmacy, podiatry, and veterinary medicine, which will be participating in this program, will be assisted by Health Professions Student Loans, as identified in the table shown on the following page:

HEALTH PROFESSIONS STUDENT LOAN PROGRAM
PROGRAM SUMMARY
(Funds available from Federal Capital Contributions and Revolving Fund)

Type of School	Number of Participating Schools			Total Enrollment of Participating Schools			Number of Students Assisted			Percent of Students Assisted		
	1968	1969	1970 1/	1968	1969 1/	1970 1/	1968	1969 1/	1970 1/	1968	1969 1/	1970 1/
Medical	93	98	100	33,595	35,117	36,017	12,484	12,375	9,885	37	35	27
Dental	47	50	52	14,075	14,833	15,392	5,944	5,892	4,708	42	40	31
Osteopathy	5	5	5	1,819	1,876	1,915	977	969	774	54	52	40
Optometry	10	10	10	2,031	2,243	2,355	745	739	590	37	33	25
Pharmacy	48	51	73	10,025	10,907	18,309	2,097	2,079	1,661	21	19	9
Podiatry	2	3	5	425	643	1,070	211	209	167	50	33	16
Veterinary Medicine	12	14	18	2,561	3,774	4,942	797	790	631	31	21	13
Total	217	231	263	64,531	69,393	80,000	23,255	23,053	18,416	36	33	23

FISCAL SUMMARY

Type of School	FY 1968 Amounts Allocated	FY 1969 Amounts Allocated	FY 1970 1/ Amounts Allocated
Medical	$14,736,357	$14,240,726	$11,375,684
Dental	6,822,117	6,777,734	5,415,485
Osteopathy	1,044,946	892,880	713,619
Optometry	856,113	883,332	705,174
Pharmacy	1,810,357	2,019,517	1,613,033
Podiatry	234,800	306,034	244,911
Veterinary Medicine	1,154,786	1,308,777	1,045,094
Total	26,659,476	26,429,000	21,113,000
Federal Capital Contribution	(15,000,000)	(15,000,000)	(20,000,000)
Revolving Fund	(11,659,476)	(11,429,000)	(1,113,000)
Average Loan	1,146	1,146	1,146

1/ Estimated

	1969 Estimate	1970 Estimate	Change
NURSING STUDENT LOANS	$9,610,000	$9,610,000	---

The authority for this program is contained in section 824 of the Public Health Service Act with a 1970 authorization of $20,000,000.

The request for $9,610,000, the same as in 1969, together with the estimated balance of $2,671,000 which will remain on deposit in the Nurse Training Fund (Revolving Fund) will provide loans totalling $12,281,000 to students enrolled in nursing schools. The total loan program in 1969 was $16,910,000, made up of $9,610,000 in appropriated funds and $7,300,000 from the Revolving fund. Additional assistance to nursing students will be provided through the nurse scholarship program, authorized by the Health Manpower Act of 1968. Schools receiving loan and scholarship funds may transfer up to 20 percent of amounts received for Federal capital contribution (student loans) and scholarships from one program to the other.

In 1970, the $12,281,000 loan program will assist an estimated 29,000 needy students, over 2,000 more than were supported in 1969. The combined loan and scholarship programs will total $25,281,000, compared to $22,568,000 available in 1969 through the loans and opportunity grants (the forerunner of the scholarship program). The average loan in 1970 is estimated at $423, compared to $626 in 1969 and $664 in 1968. The lower average loan in 1970 is expected to result from many students receiving a combination of loan and scholarship assistance.

NURSING STUDENT LOAN PROGRAM

Totals	1968 Actual	1969 Estimate	1970 Estimate
Number of participating programs of nursing education	690	694	711
Total amount allocated	$16,389,885	$16,910,000	$12,281,000
Total enrollment	101,262	112,655	115,410
Student borrowers			
Number	24,532 1/	27,000	29,000
Percent of enrollment	24% 1/	24%	25%
Average amount of loan	$664 1/	$626	$423

1/ Estimated

MANPOWER REQUIREMENTS AND UTILIZATION

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	364	$14,637,800	374	$14,774,700	+10	+$136,900
Other expenses	---	9,664,200	---	10,520,300	---	+856,100
Total	364	14,302,000	374	15,295,000	+10	+993,000
Subactivities:						
Grants:						
Research grants:						
Physician manpower	---	$902,000	---	$1,002,000	---	+$100,000
Nursing	---	2,593,000	---	2,625,000	---	+32,000
Research training grants:						
Nursing	---	700,000	---	798,000	---	+98,000
Direct operations:						
Physician manpower	90	2,802,400	90	3,113,000	---	+310,600
Nursing	148	4,162,000	148	4,248,000	---	+86,000
Allied health manpower	53	1,336,600	53	1,467,000	---	+130,400
Health manpower educational services	73	1,806,000	83	2,042,000	+10	+236,000
Total	364	14,302,000	374	15,295,000	+10	+993,000

29-867 O—69—pt. 4——66

RESEARCH GRANTS (PHYSICIAN MANPOWER)	1969 Estimate	1970 Estimate	Change
New and competing	$452,000	$452,000	---
Non-competing continuations	450,000	550,000	+$100,000
Total	902,000	1,002,000	+100,000

The authority for this program is contained in section 301 of the Public Health Service Act with an indefinite authorization for 1970.

In fiscal year 1969 the research grant program will support about 12 projects. The studies will be in program areas such as medical and osteopathic curriculum improvement, development of teaching techniques and methods for use in medical and osteopathic schools, continuing physician education techniques and methods, and utilization of skills of physicians with particular reference to the development of curricula and programs of continuing education.

In fiscal year 1970 the requested research grant program will support an estimated 15 studies. Following are examples of the types of projects which will be supported: (1) experimental approaches to the use of computer-assisted and other forms of individualized instruction in medical schools; (2) studies of medical student attitudes and how they may change during the professionalization process; (3) investigations of current admissions policies in the Nation's medical and osteopathic schools; (4) projects to investigate the quality of physician performances and assess the efficiency of physicians in providing services; (5) studies which will focus on innovations in hospitals and their effect on physician performance; (6) the assessment of curriculum changes aimed at the production of physicians specifically oriented toward "family practice" or the practice of community medicine; and (7) studies which will evaluate and assess the techniques and methodologies of various approaches to the problem of continuing physician education.

The potential impact of these research studies on the medical and osteopathic educational community cannot be over estimated. The program has attracted the attention of many highly qualified investigators in schools of medicine, university hospitals, schools of public health, schools of pharmacy, departments of sociology and economics, etc. There has been a 50 percent increase in the number of applications received in Fiscal Year 1969 over Fiscal Year 1968, and indications are that there will be a comparable increase in Fiscal Year 1970. Widespread interest is also indicated by a substantial number of requests for application kits from deans and department heads, as well as from researchers themselves.

RESEARCH GRANTS (NURSING)	1969 Estimate	1970 Estimate	Change
New and competing	$817,000	$817,000	---
Non-competing continuations	1,776,000	1,808,000	+$32,000
Total	2,593,000	2,625,000	+32,000

The authority for this program is contained in section 301 of the Public Health Service Act with an indefinite authorization for 1970.

Research in nursing is an integral part of the larger field of health sciences research. Although its main aim is to improve the practice of nursing, the focus of such research must be directed toward aspects of direct care of patients, on the system for delivery of care, on the settings in which care is given, on education and on the characteristics of the nurse herself. For example, more information is needed on the effects of the nurse as she provides care and health services to patients, the therapeutic significance of the nurse-patient relationship, and the effects with different patterns of nurse staffing and care. Criteria for measuring these are difficult but they are being developed. One nursing research grant is studying nursing care with sensory-deprived patients--those with eyes patched following surgery, another is examining the emotional responses in patients and the effects of nurses and types of nursing care on these responses. Other projects are designed to provide better understanding of the behavior and function of nursing service and utilization of nursing skills.

A recently completed project demonstrated that the professional nurse could serve as the primary source of care for large numbers of adult ambulatory patients, a role heretofore performed exclusively by physicians. Wider use of such nurse clinics could substantially improve the effeciency and effectiveness of the health service system, and has particular significance for the organization and delivery of health services to certain hard-to-reach populations, such as those within the inner city and in rural areas. It should also provide the basis for modifying education of nursing personnel.

Equally important is the application of facts and principles learned through research; practicing nurses and nursing students must learn and know how to apply the nursing knowledge in all care settings. They must also understand the implications of medical and other scientific advances on their practice. Developments in physiology and pharmacology and other scientific medical disciplines can affect nursing care substantially and require application through nursing practice and services. Research projects underway are studying the potential of biological research in nursing and more specifically, studies of peripheral circulation as they relate to nursing care. Many of these projects are interdisciplinary with the nurse, the physician and the technologist working together to develop better methods of education and training and prevention and cure of illness.

The Statutory Program Review Committee emphasized the need for better definition of nursing roles and determination of appropriate patterns of care. The Committee recommended that Federal funds be substantially increased for all mechanisms of support to accelerate and advance research into all aspects of nursing practice. If this research is to be translated into better care in a minimum amount of time, projects must be designed to carry the research to a point where results can be communicated effectively for incorporation into practice. The $2,625,000 for 1970 will support 47 projects, 6 less than in 1969.

RESEARCH TRAINING GRANTS (NURSES)	1969 Estimate	1970 Estimate	Change
New and competing	$120,000	$120,000	---
Non-competing continuations	580,000	678,000	+$98,000
Total	700,000	798,000	98,000

The authority for this program is contained in section 301 of the Public Health Service Act with an indefinite authorization for 1970.

Federal support for research training for nurses is provided in two ways: (1) Special fellowships (described elsewhere) in nursing research are available from the Public Health Service for individual nurses; (2) nurse scientist training grants to institutions provide funds to strengthen the various departments and include stipends for nursing students for preparation in depth in biological, physical and behavioral sciences.

Nurse scientist training grants are now assisting seven universities to provide nurses with graduate education in 28 departments of the universities. These grants make it possible for more nurses to be prepared in fields such as anthropology, microbiology, and sociology; thereby, bringing this knowledge to studies for improving nursing care.

The increase of $98,000 in 1970 will permit the funding of one new grant. Most of the funding requested are required for the continued support of the seven grants begun in prior fiscal years.

DIRECT OPERATIONS (PHYSICIAN MANPOWER)	1969 Estimate	1970 Estimate	Change
	$2,802,400	$3,113,000	+$310,600
The increase is distributed as follows:			
(a) Payment to "NIH Management Fund"		35,000	
(b) Non-competing continuation contracts		273,000	
(c) Annualization of pay raise		2,600	
Total increase		310,600	

In 1967 there were approximately 305,500 active physicians in the United States. Of this number about 294,100 were medical doctors and about 11,400 were osteopathic doctors. This supply of physician manpower is utilized in four major occupational areas: (1) the practice of medicine in the delivery of health services; (2) medical and osteopathic education; (3) biomedical research; and (4) medical administration to provide leadership to national, State, and local health programs.

The demand for health services is expected to rise by 25 percent between 1965 and 1975; but the supply of physicians will increase only about 19 percent. In 1965 there was an estimated shortage of about 50,000 physicians in the United States. Despite existing efforts to increase the number of physicians, a substantial shortage will still exist by 1975. It is apparent that efforts currently underway to increase the quantity of physicians will fall short of the projected need.

The increase in demand for health services is brought about by a number of factors. These factors include general population growth; increase in two high-care groups, i.e., children under 15 and adults over 65 years of age; increase in the general prosperity of the country; implementation of Medicare and Medicaid legislation; a general increase in the national level of education; and changing patterns for the delivery of health services. The urbanization of the Nation's population increases the accessibility of medical services, and also adds to the demand for health care.

The mission of the Division of Physician Manpower is to encourage national programs that increase the quantity, quality, and utilization of physician manpower in the United States. To implement this mission, the Division has formulated realistic objectives for their program of direct operations.

Physician Education

There are long-term programs to encourage and develop new materials and methods aimed at increasing the number of graduating physicians without decreasing the quality of education. Certain aspects require planned, step-wise progressive study. This includes studies of: (1) the attrition rate of medical and oestopathic students (8.2 percent); (2) self-instructional techniques; (3) advanced placement tests; (4) the feasibility of developing two-year schools of basic science to serve as a source of students to fill spaces available from attrition in the last two years of four-year schools; (5) the feasibility of admitting two classes a year to medical and osteopathic schools; (6) utilization of hospitals as teaching centers for medical and osteopathic students; and (7) the retraining of inactive physicians.

The process of change is a gradual and continuous one. Other programs will encourage and support curriculum development, i.e., the delivery of comprehensive community health services as a part of the educational experience of the medical student, and the feasibility of altering the length of physician education without affecting the quality of the educational process.

Other programs will study (1) development of more effective and better trained medical and osteopathic school faculty; (2) more efficient management techniques in medical and osteopathic schools; and(3) fuller utilization of present and future teaching facilities.

Some major work accomplishments through 1969 have been conference support on self-instructional materials in medical education, involvement in studies to design a curriculum in comprehensive and community health care in disadvantaged areas, the retraining of inactive physicians, supporting a national conference on the retraining of inactive physicians which brought together leaders in this area, the development of a model retraining program which will be distributed to all interested, and the professional review and determination on 84 medical school special improvement grant applications. Approximately 115 special improvement grant applications will be processed in fiscal year 1969. The development of studies in advance placement tests for the first year of medical school, the utilization of community hospitals for teaching clinical medicine, the evaluation of admitting classes twice a year and the development of course content in pathology as the first step in the development of a core curricula are major projects for fiscal year 1970.

Project contracts, and studies by the staff will explore and develop various aspects of these objectives. There will also be an increased workload resulting from a professional review and administration of the medical and osteopathic portion of the Health Manpower Act of 1968.

An increase of $107,500 is requested in fiscal year 1970 for this activity for continuation costs of contracts. The contracts for which continuation increases are requested will provide (1) an evaluation of a biannual admissions system at a school of medicine in an effort to determine whether this system would be feasible for use at other medical schools, and (2) a national conference on the use of audio-visuals in medical education to improve the rate of learning

of students, the quality of instruction given and to provide greater flexibility in the curriculum.

Continuing Education

With the constant changes in the theory and practice of medicine, the practicing physician faces increasing difficulty in maintaining the knowledge and skills necessary to provide his patients a consistently high level of up-to-date medical care. The efforts he makes to update his knowledge and skills have been generally classified as continuing education.

Continuing education may include a number of experiences, e.g., reading appropriate journals, attending lectures and seminars in the locality, and attending distant meetings. All of these efforts, however, have limited effect unless the physician can practice in an environment which supports, and indeed, insists on high quality of health services. Our goal is to study the variables involved in providing opportunities for continuing education and to encourage and develop programs at regional, State, and local levels.

Studies which will be supported in fiscal year 1969 and fiscal year 1970, include: (1) a project to evaluate a model for continuing education of practicing physicians based upon a university-directed, combined preceptorship home-study technique; (2) a feasibility study in the determination of individual practice profiles as a basis for correlation between continuing education needs and efforts; (3) a project to develop and study a program of medicine-in-residence for the continuing education of practicing physicians in several communities in central California; (4) a study to evaluate an audio-visual system and its techniques of individual communication for physicians in general practice; (5) development of a comprehensive plan for a regional/local continuing education center for physicians; (6) a study on a short-term trial basis of a program of post-graduate medical education for physicians practicing in impoverished areas surrounding a large urban teaching hospital; (7) a study to compare the effectiveness of four methods of post-graduate education and three methods of case discussion as a method of post-graduate medical education; (8) a three-day conference in the use of computers in medical education; (9) a study of a professional exchange program between a community hospital and a school of medicine and an evaluation of the effects of such a program; and (10) to conduct a study of the development of community hospital programs for the continuing education of physicians.

A significant development in the continuing education of practicing physicians was achieved in fiscal year 1969 by devoting major effort to the following programs: (1) the acceleration and enhancement of the leadership role and activities of the community hospitals in this area; (2) support for the upgrading of the programs of continuing education in medical teaching centers, medical societies, etc.; (3) conducting of conferences on new methodologies, techniques and equipment that may increase the effectiveness of continuing education. The evaluation of these approaches which is built into each pilot project indicates that these programs are most productive.

A major effort will be directed towards identifying and evaluating motivational factors which prompt the busy physician to undertake continuing education. This will be followed by the development and conduct of educational activities to make use of these motives which can lead toward better health care.

An increase of $85,500 is requested for fiscal year 1970 for continuation cost of contracts. The contracts for which continuation increases are requested will provide (1) a conference on evaluation of educational programs related to health, and (2) an evaluation of the role of a liberal arts college in the field of continuing education of physicians.

Physician Supply and Utilization

In order to utilize available physician manpower in the United States more effectively, it is essential to develop and maintain a continuing record of the supply and distribution of physicians by geographic area and specialty. This information will serve as a base for determining the effectiveness of the physician in providing health services. The number of physicians is increasing; however, the need and demand for high quality health services will continue to exceed the supply for some time to come. Improved utilization of the skills of the physician is, therefore, essential to meet the current and anticipated future demand for health services.

It is equally important to study current use of professional skills, to analyze professional responsibilities, and to study the organizational patterns in which the physician functions with others in the delivery of comprehensive health care services.

As a part of the acquisition and dissemination of information by the Bureau, the Division will gather and analyze physician supply data from many sources. In fiscal year 1969 a study was conducted on "How Medical Students Finance Their Education." This study canvassed all the medical and osteopathic students (40,000) in the United States concerning their finances. The results of this study will be published in late fiscal year 1969 or early fiscal year 1970. Another study which has been initiated in fiscal year 1969 through the American Association of Medical Colleges will evaluate the effects on university affiliated teaching hospitals of the Medicare and Medicaid legislation.

In fiscal year 1969 and fiscal year 1970 we will initiate studies on physician practice patterns. Little definitive information exists concerning the relative benefits to be derived from the various types of practice patterns used in the provision of health care. In fiscal year 1969 this program is being implemented with a study in Kentucky of rural practice patterns.

A study to determine those functions of health services which may be delegated by the physician to responsible assistants will be initiated. In this process we will explore new health occupations that could improve physician manpower utilization. This study will be carried out in cooperation with other programs of the Bureau and the Public Health Service.

Through studies in physician utilization during the present and future years, answers will be sought to the optimum mix of physician and auxiliary personnel necessary to provide health services most efficiently. New types of personnel will be developed to extend the capabilities of physicians. Field studies will be designed to determine the effect the physician shortage is having on the consumers of health service to find answers regarding what can be done to make this service more readily available. Special problems will be studied and methods developed to make medical care more accessible through innovations in transportation of the sick and injured and examination by electronic equipment of those persons geographically isolated from health services. These studies will indicate more effective ways of using health manpower as well as indicating needs in certain education experiences for physicians. Studies will also be made of the physician's practice, how he spends his time and what configuration of medical facilities can best improve his daily

output in providing health services through those mechanization and industrial engineering techniques which can be brought to bear to increase output.

Since all of the above studies are related to social, economic, and demographic variables close attention will be paid to physician utilization problems as they relate to the community, to socio-economic status of individuals, and to rural and urban settings.

Some examples of extramural utilization projects continuing through fiscal year 1969 and into fiscal year 1970 include studies to (1) design a rural physician utilization model; (2) ascertain the health service needs of the urban and suburban medically indigent and the design of an efficient physician utilization model relating thereto; and (3) ascertain the health service needs of the urban ghetto as represented by Harlem in New York City. Studying the effects of Public Law 89-97 (Medicare and Medicaid) on teaching hospitals and studies to improve the utilization and efficiency of anesthesiologists are underway and will continue into fiscal year 1970.

Utilization activities to be conducted by Staff in the current and later years include the compilation of State medical licensure law and regulations; maintenance of liaison, cooperation, and dialogue with experts and organizations in the health services field to define and devise new types of personnel to assist the physician in the delivery of health services; development of statistical and administrative methodology standards applicable to usage by the States in order to provide required physician requirement and utilization data; and the preparation of a series of monographs on practices and techniques utilized by practicing physicians which offer potential for an increase of the efficiency of the practicing physician and which will ultimately form the basis for motion picture propagation of these ideas to the physician community in general.

In view of the time lapse in developing resources and facilities to increase the supply of physicians, the major emphasis must be on improving the utilization of the existing physician population to meet current demands for services.

An increase of $80,000 is requested for this activity for continuation cost of contracts. The contracts for which continuation increases are requested will provide (1) a study of the demands for health services in a surburban community, and (2) a study for physician utilization in a teaching hospital in its attempt to meet the needs of an urban ghetto.

Educational Facilities

Expansion and modernization of existing and the construction of new educational facilities is vitally important to the present and future training of health manpower. Currently overloaded and frequently obsolete facilities are unable to fulfill the demand for qualified health manpower needed to serve the Nation. The supply of health manpower in the future depends on the effort made in the next few years. A new medical or dental school requires 10-12 years from its inception until its first class is graduated. Other health manpower schools require a shorter time, but seldom less than six to eight years. Plans for rehabilitating or expanding existing schools also require a long lead time.

In fiscal year 1969 the Educational Facilities program will have a substantially increased workload. This is the result of (1) an accumulating number of approved, funded and on-going projects (148 through fiscal year 1968); and (2) an increased application and pre-application workload (130 pre-application conferences and 60 formal applications for processing through one of 15 review committees and six councils in fiscal year 1969.) In fiscal year 1970, it is anticipated that 160

pre-application conferences will be held, and that 65 additional applications will be processed through one of 17 review committees and six councils. This projection of 1970 program activity reflects the provision from the Health Manpower Act of 1968 which expands the programs' responsibility, allowing funding of research, library, and advanced training facility space.

	1969 Estimate	1970 Estimate	Change
DIRECT OPERATIONS (NURSING)	$4,162,000	$4,248,000	+$86,000

The increase is distributed as follows:

(a) Payment to "NIH Management Fund"	62,000
(b) Non-competing continuation recruitment contracts	20,000
(c) Annualization of 1969 pay raise	4,000
Total increase	86,000

A serious shortage of nurses has persisted for many years, endangering the health of patients and lowering effectiveness in the delivery of health services generally. A basic problem confronting the Nation is how to provide enough nurses to meet the needs of the population, which has been increasing by approximately two million each year since 1960. In addition, the call for nursing service has intensified because of the expanding coverage of our citizens by health and hospitalization insurance, particularly Medicare and Medicaid. Another Federal program, comprehensive health planning, has placed new emphasis on planning to meet the numerous and diverse health needs in the country. The enactment of these health programs requires adequate nursing-manpower to carry them out. Nursing is pivotal to these programs; if nursing manpower is lacking or limited in quantity and quality, the services that patients receive will be correspondingly inadequate.

Research and Technical Assistance

The keystone of nursing is nursing practice. This must be studied and improved if nursing services are to be adequate for the needs of modern health programs. It must also relate to nursing education so that experience of nursing students will be relevant to their professional activities. For many years the extension of health services and facilities and the developments and changes in medical knowledge and practice, without adequate support for appropriate changes in nursing practice have resulted in a dilution in the quality and effectiveness of nursing. Opportunity for professional nurses to use their special knowledge and skill in practicing their own discipline and to collaborate appropriately with physicians in health care for individuals has not kept pace with the health needs of our society and with the prevention of illness.

Sound administrative practices and techniques and automatic equipment have not been widely applied in managing the delivery of nursing services. This results in a myriad of staffing patterns and a widespread inadequate utilization of scarce nursing skills. Poor utilization of professional skills dilutes the quality of health services and the care which patients receive. It is costly.

The gap between supply of nurses and the demand for their services can never be reconciled through numbers alone; the professional competencies of each practitioner must be used to the best possible advantage in all settings. Discriminating utilization of professional talent not only bridges the numerical gap between supply and demand, but also promotes job satisfaction which encourages young people to enter nursing and also encourages nurses to remain active in their profession.

The objective is to improve the quality of nursing education at the same time expanding the capacity of nursing schools by identifying the content of nursing education programs which can be presented by new methods and techniques.

Education and Training

The goals of the Division in this area are: (1) to improve the quality of nursing education to ensure that nursing personnel can meet the demands of modern technological development in the health sciences; (2) to chart the course for a program of continuing education for the nursing profession; (3) to identify the content of nursing education programs which can be presented by new methods and techniques; (4) to ensure the soundness of nursing education development by basic planning; and (5) to increase the supply of qualified applicants to all types of nursing programs. The provisions of the Health Manpower Act of 1968 are the principal means of accomplishment of these goals.

Consultation and technical assistance for nursing education and training to schools of nursing, hospitals and health agencies will be increased in 1970 to ensure the efficient use of grant monies authorized in the new legislation. Evaluation of the Health Manpower Act of 1968 is required under terms of the law. The Division is developing data, evaluative criteria and indices, in order to assess the extent to which the Health Manpower Act of 1968 will meet the objectives.

Manpower Resources

Nursing manpower is a national resource and nursing is a key component of all types of health care programs. Needs for nursing personnel and facilities to educate nurses vary widely from one section of the country to the other; therefore, it is imperative that resources be identified at local, State, and regional levels. The Division is developing tools for the assessment of nursing needs and resources and is furnishing consultation to groups engaged in this kind of planning.

Nursing is a complex subject for manpower analysis because of the sheer numbers involved, the three types of educational programs preparing nurses, the variety of institutions and agencies in which nurses are employed, and the mobility patterns of the predominately female professional group. Through its manpower activities, the Division maintains a perspective on nursing nationwide--the adequacy, quality, distribution, training and utilization of personnel. Studies and surveys conducted by the Division provide the facts and figures which are the basis of this continuing overview as a basis for future projections.

One sizeable group about whom little is known is the estimated 700,000 nursing personnel (nurses' aides, nursing assistants, orderlies, attendants, home health aides, etc.) working with professional and practical nurses. In some settings these individuals give a substantial proportion of direct care to patients yet the extent of their training and their supervision is known to vary widely. It is imperative that information about this amorphous group be collected and analyzed in order to develop guidelines for their training and utilization. This information will also supplement the Division's ongoing inventories of professional and practical nurses

and provide information to assist the profession in its examination of educational preparation for nurse practitioners and assistants to nurses.

Refresher Training

To reduce attrition from the work force, increasing numbers of inactive nurses must be returned to active practice each year. The current new attrition rate is estimated as averaging 2.8 percent annually and reflects both the separation and returns to active status. The Division of Nursing is working with a special staff of State coordinators to reduce the net attrition rate through extensive multi-media promotional and advertising campaigns to promote the return to service of inactive nurses. These Division of Nursing activities with inactive nurses would continue as in the past to be integrated with the inter-agency program of the Department of Health, Education, and Welfare, Department of Labor, American Nurses' Association, and State agencies, for providing refresher training courses utilizing Manpower Development and Training Act funds.

The Division of Nursing fosters the development of other refresher training programs under local sponsorship and encourages the adoption of flexible working schedules and other incentives by hospitals, especially to attract back to active practice, nurses who are married and have families.

In 1969, $1,347,900 is available for Refresher Training activities which are primarily contract programs with the 50 States and the District of Columbia aimed at increasing from 20,000 to 30,000 by 1973 the number of professional nurses who annually return to active practice.

Recruitment

College education is now a realistic goal for groups of people with low and moderate incomes. For these individuals, education is the way to enhance their self-image and raise their socio-economic levels.

The distribution of such groups enrolled in schools of nursing is disproportionate to their distribution in the population. To recruit successfully from this group, schools of nursing must develop programs flexible enough to adapt to students who learn with difficulty because of inadequate elementary and high school education. Numerous methods are presently being used, and more are needed, to provide a bridge for entry into nursing for the educationally disadvantaged. Some of the emphasis schools now place on admission policies and selection must be shifted to assisting students to remain in school and graduate.

Imaginative ways to interest these young people in nursing, early counselling, remedial and tutorial work that begins in high school and continues throughout the nursing curriculum, all will help to increase the numbers of practicing nurses. Despite their high cost in both money and time, such approaches are necessary.

In 1969 program funds of $200,000 will provide for four contracts with institutions of higher learning. The purpose of these contracts is to identify disadvantaged youths of exceptional financial need and encourage them to complete secondary school and undertake educational training in nursing.

An increase of $20,000 is requested in fiscal year 1970 for continuation costs of two contracts which were initiated in 1968.

	1969 Estimate	1970 Estimate	Change
DIRECT OPERATIONS (ALLIED HEALTH)	$1,336,600	$1,467,000	+$130,400

The increase is distributed as follows:

(a) Payment to "NIH Management Fund"	21,000
(b) Non-competing continuation contracts	108,000
(c) Annualization of 1969 pay raise	1,400
Total increase	130,400

Direct operations programs of the Division of Allied Health Manpower are directed toward the development of a comprehensive approach to the expansion and improvement of opportunities and educational programs for a broad range of health professional and technical personnel critically needed to serve in health care, community, and environmental health programs. These activities complement, through experimentation and innovation, the support of ongoing educational programs and students provided under grant authorizations. The scope of concern ranges from the development of new and more effective methods of attracting talented young people from all walks of life into health careers; to providing consultation and technical assistance in the development and evaluation of curriculums for training new types of health workers; to the collection, analysis and dissemination of data on the current supply and future needs for allied health manpower. In addition, the Division has responsibility for program administration of eight major grant support programs.

Important initial steps have been undertaken during 1968 and 1969 to consolidate existing data on the current supply and distribution of allied health manpower and develop capability as well as improved methodology for projecting future requirements. Through support of four pilot projects at the State level, efforts are also being made to develop improved methods of collecting health manpower information and concurrently develop improved competency at the State level for manpower research and planning. In one State, special efforts are being made to determine the numbers and types of personnel serving in environmental health activities.

Concurrent efforts have been initiated to develop better and coordinated programs of recruitment for the allied health occupations, and to undertake efforts to improve utilization of scarce, highly trained health professionals through reassignment of tasks which do not require such advanced training. In this latter area, it may be necessary to create new categories of health occupations specialists. The effort involved requires a functional, operational identification and analysis of the duties, responsibilities and skills required, and the assignment of one or more competency levels for education and training--all before the first instructional materials are prepared and the first trainee enrolled. We are currently engaged cooperatively with the Department of Labor and selected Public Health Service hospitals in developing means by which the already well-accepted techniques utilized in industry can be translated to the health field. Pilot efforts are also being undertaken to develop such techniques in the field of anesthesiology.

Equally important to the development of better allied health manpower data and the experimentation and development described above, is to assure that the greatest possible results are derived through the more immediate impact on supply and quality of allied and public health manpower through the grant programs authorized under the Health Professions Educational Assistance Act (for optometry, podiatry, pharmacy, and veterinary medicine), the Allied Health Professions Personnel Training Act (for twenty-one allied health professions) and the authorities for support of graduate and specialized training in public health. Specialized staff resources are required to assure that services are available to advise and assist institutions regarding the nature and purposes for which support may be sought, providing staff support to the more than a dozen advisory committees and councils engaged in review and approval of grants, and providing professional surveillance of grants, which are currently active in more than 500 institutions and agencies ranging from large medical schools to small community colleges.

An increase of $108,000 is requested for contract continuation costs. The projects for which continuation increases are being requested will provide for extension of efforts to collect and utilize data on allied health manpower supply and distribution, to improve utilization of highly trained professionals, and to develop programs of recruitment for the allied health professions.

	1969 Estimate	1970 Estimate	Change
DIRECT OPERATIONS (EDUCATIONAL SERVICES)	$1,806,000	$2,042,000	+$236,000
The increase is distributed as follows:			
(a) Ten new positions		160,000	
(b) Payment to "NIH Management Fund"		33,000	
(c) Non-competing continuation contracts		51,000	
(d) Annualization of 1969 pay raise offset by non-recurring program costs		-8,000	
Total increase		236,000	

Administration of Grants

A program increase of eight positions and $128,000 will provide staff needed to carry out the administrative duties related to the increases in improvement grant and scholarship programs over 1969 and to carry out major Divisional functions and responsibilities. Six of these positions are needed for the Health Manpower Grants Branch to handle anticipated workload increases resulting from new legislation which expands eligibility of the allied health professions new methods grants to over 3,000 schools and for expansion of health professions improvement grants of over $30,000,000 and to 92 schools of pharmacy and veterinary medicine. Two of the positions will be used by the Student Loan and Scholarship Branch for implementation of the nursing scholarships program with 1,300 potential schools participating and for administering the health professions education fund loan cancellation provisions and nursing forgiveness features as modified by the Health Manpower Act which we anticipate will add appreciably to the workload.

Intelligence System and Clearinghouse

Intelligence System

We will continue the development of a National Health Manpower Intelligence System in order to collect data and produce information on the supply, distribution, and utilization of health manpower. The first phase in the development of a long-range plan to implement the Intelligence System, a systems survey (requirements), initiated in 1969, will be completed in 1970. The program increase requested in 1970 for the Intelligence System of $73,000 and two new positions over 1969, provides for completion of the survey and for the initation of Phase 2 which will involve system design, programming, and testing. In addition, an interim system initiated in 1969 for data gathering, and analysis to meet immediate program informational needs will be continued in 1970.

The program estimate of $638,000 includes $479,000 for contracts, of which $211,000 will be used to contract for initial designing, programming, and testing of the system and $268,000 for the development, analysis, and acquisition of health manpower data. Personnel costs related to the development of the interim and long-range system together with equipment rental costs and other costs will require $159,000. The program increase of $73,000 will permit progress to continue toward the installation and demonstration of the Intelligence System by 1975. The new staff is needed to coordinate and evaluate contract activities.

Clearinghouse

Information produced by the Intelligence System will be distributed through an information clearinghouse on health manpower educational and training activities. The program increase requested in 1970 of $10,000 over 1969, will enable it to provide initial information on health manpower needs, resources and production for national requirements to academic institutions by the end of 1970.

Of the total program increases of $83,000 for both the Intelligence System and Clearinghouse, $51,000 is for continuation costs of contracts. The contracts for which continuation increases are being requested enable the Intelligence System and Clearinghouse to maintain and update the data base of health manpower information. Included will be data obtained on health occupation training such as availability of scholarships and stipends. The clearinghouse will use this data to provide a service to all persons or institutions in need of information on health training as a necessary aid toward meeting the objectives of increasing and improving the supply of health manpower.

PROGRAM DIRECTION AND MANAGEMENT SERVICES

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	85	$1,214,000	85	$1,217,000	---	+$3,000
Other expenses	---	125,000	---	173,000	---	+48,000
Total	85	1,339,000	85	1,390,000	---	+51,000

The increase provides for the following:

(a) Payment to "NIH Management Fund"	48,000
(b) Annualization of pay raise	3,000
Total increase	51,000

The Office of the Bureau Director furnishes leadership and direction to the various programs of the Bureau concerned with the education and utilization of health manpower. It provides administrative management services such as personnel management, financial management and various housekeeping services to insure the efficient operation of the Bureau programs. It provides for consistency throughout the divisions of the Bureau in the quest for maximum operational effectiveness. There are no program increases requested for 1970.

New Positions Requested
Fiscal Year 1970

	Grade	Annual Salary
Health Manpower Educational Services		
(2) Public Health Program Specialist	GS-14	$33,892
(2) Public Health Program Specialist	GS-13	28,818
(2) Public Health Program Specialist	GS-12	24,348
Public Health Program Specialist	GS-11	10,203
Public Health Program Specialist	GS- 9	8,462
(2) Clerical Assistant	GS- 6	12,642
Total new positions	(10)	118,365

PAYMENT OF SALES INSUFFICIENCIES AND INTEREST LOSSES

Program and Financing

	1969 Estimate	1970 Estimate
Appropriation	$200,000	$957,000
Unobligated balance lapsing	-32,000	...
Amounts transferred to other accounts	168,000	957,000
Health Professions Education Fund	(130,000)	(735,000)
Nurse Training Fund	(38,000)	(222,000)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Health Professions Education Fund

Amounts Available for Obligation

	1969	1970
Appropriation (definite)	$130,000	$735,000
Receipts and reimbursements from non-Federal sources	1,074,000	1,289,000
Transferred from other accounts	780,000	...
Unobligated balance brought forward	14,655,000	3,223,000
Other unobligated balances carried forward	-3,223,000	-2,134,000
Total obligations	13,416,000	3,113,000

Obligations by Activity

	1969	1970	Increase or Decrease
Loans to health professions schools	$12,209,000	$1,113,000	-$11,096,000
Interest to health professions schools:			
(Interest losses)	...	604,000	+604,000
Interest accrued on participation certificates	734,000	735,000	+1,000
Interest to Treasury	473,000	661,000	+188,000
Total obligations	13,416,000	3,113,000	-10,303,000

Obligations by Object

	1969	1970	Increase or Decrease
Investments and loans	$12,209,000	$1,113,000	-$11,096,000
Interest and dividends	1,207,000	2,000,000	+793,000
Total obligations by object	13,416,000	3,113,000	-10,303,000

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Nurse Training Fund

Amounts Available for Obligation

	1969	1970
Appropriation (definite)	$38,000	$222,000
Receipts and reimbursements from non-Federal sources	626,000	831,000
Unobligated balance brought forward	10,448,000	3,341,000
Other unobligated balances carried forward	-3,341,000	-690,000
Total obligations	7,771,000	3,704,000

Obligations by Activity

	1969	1970	Increase or Decrease
Loans to schools of nursing	$7,300,000	$2,671,000	-$4,629,000
Interest to schools of nursing (Interest losses)	...	184,000	+184,000
Interest accrued on participation certificates	222,000	222,000	---
Interest to Treasury	249,000	627,000	+378,000
Total obligations	7,771,000	3,704,000	-4,067,000

Obligations by Object

	1969	1970	Increase or Decrease
Investments and loans	$7,300,000	$2,671,000	-$4,629,000
Interests and dividends	471,000	1,033,000	+562,000
Total obligations	7,771,000	3,704,000	-4,067,000

29-867 O—69—pt. 4——67

Justification

Health Education Loans

General Statement

The Allied Health Professions Personnel Training Act of 1966 (P.L. 89-751, dated November 3, 1966) established two revolving funds, the Health Professions Education Fund and the Nurse Training Fund, to provide loans to students of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine, and nursing.

An institution which borrows funds from the health professions education fund or the nurse training fund to provide loans to its students will execute a note payable for the amount of the loan. This note will bear an interest rate determined by the Secretary to be adequate to cover the cost of the funds to the Treasury and estimated losses from defaults.

The Secretary will pay the institution (1) 90 percent of its losses from defaults, (2) the amount by which the interest payable by the school on such sums exceeds the interest received by the institutions on student loans made from such sums, (3) collection costs, and (4) amount of loans cancelled.

Principal and interest collected by the institution on student loans made from borrowed capital will be given to the Secretary for deposit in the revolving funds or for payment to the Government National Mortgage Association.

Health Professions Education Fund

Approximately 1,150 health professions students will receive loans totalling $1,113,000 from the Health Professions Education Fund in 1970. This is a decrease of 12,750 loans from the 1969 level. This revolving fund supplements the existing Federal capital contributions method of capitalizing loan funds in the schools which is budgeted for in the appropriation "Health Manpower." The schools are free to choose either or both methods of obtaining student loan funds. In 1970, the total health professions student loan program will be $21,113,000: $20,000,000 in appropriation for Federal capital contribution and $1,113,000 in revolving fund monies.

From the combined funds, approximately 4,637 fewer students will be provided loans in 1970 than the number in 1969 for a total in 1970 of 18,416 or 23 percent of the 80,000 eligible.

Nurse Training Fund

Approximately 7,180 nursing students will receive loans totalling $2,671,000 from the Nurse Training Fund in 1970. This is a decrease of 4,500 from the 1969 level. This fund supplements the existing Federal capital contributions method of capitalizing loan funds in the schools which is budgeted for in the appropriation "Health Manpower." The schools are free to choose either or both methods of obtaining student loan funds.

In 1970, the total nursing student loan program will be $12,281,000: $9,610,000 in appropriations for Federal capital contributions and $2,671,000 in revolving fund monies. From the combined funds approximately 2,000 additional students will be provided loans in 1970 over the number of 1969, for a total in 1970 of 29,000.

Justification of appropriation request:

$957,000 is requested for fiscal year 1970 as follows:

$788,000 Payment of Interest Differential to Institutions
(604,000) Health Professions Education Fund
(184,000) Nurse Training Fund

$169,000 Payment of Insufficiencies
(131,000) Health Professions Education Fund
(38,000) Nurse Training Fund

INTEREST LOSSES

Health Professions Education Fund

An appropriation of $604,000 for fiscal year 1970 is requested for reimbursement of interest losses of health professions schools, capitalizing student loan funds from the Health Professions Education Fund. Section 744(b) of the Public Health Service Act provides for the reimbursement to the schools for the difference between the interest owed to the government on the loans and the amount (interest) collected from student borrowers. In 1970, it is estimated that $604,000 will be due from schools on the $11,500,000 (at 5.25 percent interest) in notes pledged to the Government National Mortgage Association and that no payments of interest will be received from students during 1970.

Nurse Training Fund

An appropriation of $184,000 for fiscal year 1970 is requested for reimbursement of interest losses of nursing schools, capitalizing student loan funds by loans from the Nurse Training Fund. Section 827(b) of the Public Health Service Act, provides for the reimbursement to the schools for the difference between the interest owed to the government on loans and the amount (interest) collected from student borrowers. In 1970, it is estimated that $184,000 (5.25 percent interest) will be due from schools on the $3,500,000 pledged to the Government National Mortgage Association and that no payments of interest will be received from students in 1970.

INSUFFICIENCIES

Health Professions Education Fund

The 1970 request for insufficiencies is $131,000, a decrease of $23,000 from the amount available in 1969. The estimate is based on the $735,000 interest due the Government National Mortgage Association in 1970 (6.38 percent of $11,500,000 in notes held by private interests), less some $604,000 (5.25 percent of $11,500,000), estimated from interest differential payment to be received through participating health professions schools.

Nurse Training Fund

The 1970 request for insufficiencies is $38,000, a decrease of $8,000 from the amount available in 1969. The estimate is based on the $222,000 interest due the Government National Mortgage Association in 1970 (6.38 percent of $3,500,000 in notes held by private interests), less some $184,000 (5.25 percent of $3,500,000) estimated from interest differential payments to be received through participating nursing schools.

Payments to Schools to Cover Certain Costs Incurred
in Making Student Loans from Borrowed Funds

Appropriation

Section 744. (b) If a school borrows any sums under this section, the Secretary shall agree to pay to the School (1) an amount equal to 90 per centum of the loss to the school from defaults on student loans made from such sums, (2) the amount by which the interest payable by the school on such sums exceeds the interest received by it on student loans made from such sums, (3) an amount equal to the collection expenses authorized by section 740(b) (3) to be paid out of a student loan fund with respect to such sums, and (4) the amount of principal which is canceled pursuant to section 741(d) or (f) with respect to student loans made from such funds. There are authorized to be appropriated without fiscal year limitation such sums as may be necessary to carry out the purposes of this subsection.

Payments to Schools to Cover Certain Costs Incurred in Making
Student Loans From Borrowed Funds

Section 827. (b) If a school of nursing borrows any sums under this section, the Secretary shall agree to pay to the school (1) an amount equal to 90 percentum of the loss to the school from defaults on student loans made from such sums, (2) the amount by which the interest payable by the school on such sums exceeds the interest received by it on student loans made from such sums, (3) an amount equal to the amount of collection expenses authorized by section 822(b) (3) to be paid out of a student loan fund with respect to such sums and (4) the amount of primcipal which is canceled pursuant to section 823(b) (3) or (4) with respect to student loans made from such sums. There are authorized to be appropriated without fiscal-year limitation such sums as may be necessary to carry out the purposes of this subsection.

THURSDAY, APRIL 3, 1969.

DENTAL HEALTH

WITNESSES

DR. VIRON L. DIEFENBACH, DIRECTOR, DIVISION OF DENTAL HEALTH
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. JOHN GREENE, DEPUTY DIRECTOR, DIVISION OF DENTAL HEALTH
MR. EDWARD J. DYER, EXECUTIVE OFFICER, DIVISION OF DENTAL HEALTH
JOHN W. HAMBLETON, FINANCIAL MANAGEMENT OFFICER, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	2,366	2,545	2,570
Positions other than permanent	191	194	194
Other personnel compensation	3	4	4
Total personnel compensation	2,559	2,743	2,768
Personnel benefits: Civilian employees	281	315	317
Travel and transportation of persons	199	200	200
Transportation of things	47	30	30
Rent, communications, and utilities	171	162	163
Printing and reproduction	54	67	67
Other services	1,084	1,245	1,423
Supplies and materials	125	94	94
Equipment	38	70	61
Grants, subsidies, and contributions	4,859	5,259	6,765
Total obligations	9,416	10,185	11,888

PERSONNEL SUMMARY

	1968 actual	1969 estimate	1970 estimate
Total number of permanent positions	260	243	243
Full-time equivalent of other positions	19	20	20
Average number of all employees	245	257	258
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Research	1,121	1,259	1,339
(b) Fellowships	79	150	150
(c) Training	2,598	3,850	5,276
2. Direct operations	4,200	4,926	5,123
Total program costs, funded [1]	7,998	10,185	11,888
Change in selected resources [2]	1,418		
Total obligations	9,416	10,185	11,888
Financing: Comparative transfer to/from other accounts	−9,416	39	
Budget authority (appropriation)		10,224	11,888
Relation of obligations to outlays:			
Obligations incurred, net		10,185	11,888
Obligated balance, start of year			5,806
Obligated balance, end of year		−5,806	−9,019
Outlays		4,379	8,675

[1] Includes capital outlay as follows: 1969, $90,000; 1970, $104,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $0; 1968, $1,418,000; 1969, $1,418,000; 1970, $1,418,000.

Mr. FLOOD. We now have the budget request for dental health. Dr. Viron L. Diefenbach, the Director of the Division of Dental Health will be the principal witness.

We will put your biographical sketch in the record.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name: Viron Leroy Diefenbach, D.D.S.

Position: Assistant Surgeon General and Director, Division of Dental Health, Bureau of Health Professions Education and Manpower Training, NIH, Woodmont Building, Bethesda, Md.

Birthplace and date: Baltimore, Md., February 9, 1922.

Education: Western Maryland College, 1940–42 (interrupted by Army service, World War II); Pratt Institute of Engineering, 1943; Harvard University (predental), 1944; Baltimore College of Dental Surgery, Dental School, University of Maryland, 1949 (D.D.S.); Graduate School of Public Health, University of Pittsburgh, 1954 (M.P.H.); diplomate of the American Board of Dental Public Health, 1960.

Experience: 1966 to present, Director, Division of Dental Health, Bethesda, Md.; 1962–65, Deputy Chief, Division of Dental Health, Bethesda, Md.; 1959–61, Regional dental consultant, U.S. Public Health Service, Denver, Colo.; 1957–59, information officer, Division of Dental Public Health; 1956–57, Dental Recruitment and Personnel Officer, Division of Personnel, Office of the Surgeon General, Washington, D.C.; 1954–55, Assistant regional dental consultant, U.S. Public Health Service, Chicago, Ill.; Office of Personnel, Office of the Surgeon General, U.S. Public Health Service, Washington, D.C.; 1952–53, Dental public health field training, U.S. Public Health Service; 1950–52, various clinical assignments, U.S. Public Health Service; 1949–50, dental intern, U.S. Public Health Service hospital, Norfolk.

Assignments and offices: Dental Health Council, American Public Health Association, 1956–59; secretary of the Dental Health Council and member of the Governing Council, American Public Health Association, 1961–66; vice chairman of the Dental Health Council, 1965; chairman of the Dental Health Council, 1966; member of the Executive Board, Commissioned Officers Association, U.S. Public Health Service, 1963–65, and chairman of the Board, 1966–67; member Educational Advisory Board, Kettering Laboratory, University of Cincinnati, 1961 to present.

Honors: University of Maryland Gold Medal (Scholarship), 1949; magna cum laude, Dental School, University of Maryland, 1949; Omicron Kappa Upsilson,

1949; president of class at Graduate School of Public Health, University of Pittsburgh, 1954; Meritorious Service Medal, U.S. P.H.S., 1966; fellow, American Public Health Association; fellow, American Association for the Advancement of Science; fellow, American College of Dentists.

Scientific organizations: American Dental Association, American Public Health Association, American Association for the Advancement of Science, American Association of Public Health Dentists, American College of Dentists, American Board of Dental Public Health, and Federation Dentaire Internationale.

Mr. FLOOD. You have a statement, Doctor. How do you wish to proceed?

Dr. DIEFENBACH. With your permission, I would like to go through it with you and the committee and perhaps answer questions as I go, if you have any.

Mr. FLOOD. You may proceed.

GENERAL STATEMENT

Dr. DIEFENBACH. Mr. Chairman and members of the committee: The old priorities in dental health must be re-ordered. The dental problems we face today require a more efficient use of limited resources and a renewed commitment to reach higher national levels of dental health. Let me begin with a candid assessment of dental disease in this country. That assessment, to be blunt, is appalling.

Even before he enters school for the first time, nearly every child in the United States already has tooth decay or gum disease, yet one-half of our children are not even examined, much less treated, by a dentist before their 15th birthday. Poverty intensifies neglect. Compared to the average child, children from low-income families have five times the number of untreated decayed teeth. Among the underprivileged, 97 dental cavities out of every 100 go unchecked. Consequently, painful dental abscesses are common, and, when these children eventually do visit a dentist, they go for extractions six times as often as the average child. Dental problems of mentally retarded and physically handicapped children are of even greater magnitude.

For every 100 inductees, the Armed Forces provide 500 fillings, 80 extractions, 25 bridges, and 20 dentures. More than half of our young adult population has pyorrhea, 20 million people have lost one-half of their natural teeth, and another 25 million have lost all of theirs.

PYORRHEA AND GINGIVITIS

Mr. FLOOD. What is pyorrhea?

Dr. DIEFENBACH. Pyorrhea is a gum disease, Mr. Chairman.

Mr. FLOOD. A fungus, bacteria; what causes it?

Dr. DIEFENBACH. It is not a fungus but is more likely a bacterial disease. We do not know exactly what the cause of it is. It is a puzzling and unsolved condition.

Mr. FLOOD. Is anybody trying to find out?

Dr. DIEFENBACH. Yes, sir; the National Institute of Dental Research is undertaking several studies. It is a very complicated matter.

Perhaps it is more complicated even than dental caries. There appears to be more than one causative factor in the disease process. It quite often begins at a very young age, frequently in children of high school age.

Mr. FLOOD. Inherent?

Dr. DIEFENBACH. Inherent? Not in terms of heredity, but it is endemic if we could use that expression in terms of the disease's prevalence in high school age youngsters.

Gingivitis, as a matter of fact, affects about half of the high school population.

Mr. FLOOD. What is that?

Dr. DIEFENBACH. That is the earlier stage of gum disease which often leads to pyorrhea.

Mr. FLOOD. Does diet affect it?

Dr. DIEFENBACH. Diet may have an effect on gingivitis and pyorrhea, particularly when it lacks certain vitamins.

Mr. FLOOD. Contagious?

Dr. DIEFENBACH. Not so far as we know, sir.

Oral cancer will claim 23,000 new victims this year and will cause 5,000 to die.

Mr. FLOOD. Are pyorrhea or gingivitis necessarily a condition precedent to cancer?

Dr. DIEFENBACH. Not as far as we know, sir.

INADEQUACY OF DENTAL CARE PROGRAMS IN THE UNITED STATES

And yet American families are spending nearly $4 billion annually for dental services, although only 40 percent of the people even visited the dentist once last year. About half of them went for emergency care, and the other half—about 20 percent of the entire population—received complete care. Industry lost more than 100 million man-hours of production time because of absence for dental illness. Most distressing perhaps is the fact that the total dental care delivered did not offset the total new needs that developed, much less reduce the backlog of old, untreated needs. In short, millions of Americans are being denied adequate dental care, and the majority receive no care at all.

The preceding facts prevail despite America's envied world leadership in dental competence. The gap between promise and performance therefore exists not only because we lack professional knowledge or ability. The gap exists largely because we have failed to apply fully the scientific prevention and treatment knowledge we have, because we have failed to develop adequate distribution and financial systems to overcome delivery problems, and because we have not produced a sufficient supply of dental manpower. These problems must be better managed within the limited resources which can be made available.

FLUORIDATION OF DRINKING WATER

Certainly any reordering of priorities must give top priority to the implementation of nationwide decisive programs of prevention and control. At present, our most flagrant failure is the lack of universal fluoridation in the United States. If we made full use of this proven health measure, we could prevent tooth decay by 65 percent or more among the Nation's children, both rich and poor. But we fall far short of that goal today. Only 82 million people are using fluoridated water; almost as many are without its benefits. Through more technical aid and more vigorous promotion, we must revitalize the national movement to fluoridate all community water systems and rural school water supplies.

Mr. FLOOD. You must revitalize it.

Dr. DIEFENBACH. I believe we need to.

Mr. FLOOD. Do you not have about 75 million people now affected by it?

Dr. DIEFENBACH. There are about 72 million people drinking water to which fluoride has been added.

Mr. FLOOD. That is a lot of people.

Dr. DIEFENBACH. An additional 10 million people are drinking fluoridated water from natural sources. So the total is about 82 million.

The problem in the programs at this point, Mr. Chairman, is that these large figures have come about because most of the major cities in the United States are fluoridated.

Mr. FLOOD. What do you mean, the problem?

Dr. DIEFENBACH. The financial problem of instituting this measure in smaller cities and rural areas. Although the cost is not great, the purchase, installation and operation of equipment for a small community of five or 10,000 population, for example, it is a fairly large expenditure when compared to repairing the local fire truck. Not having the few thousand dollars readily available may block the implementation of this preventive measure.

Mr. FLOOD. That is to take care of children's teeth, to protect children?

Dr. DIEFENBACH. Yes, sir. Although the benefits of fluoridation continue throughout life.

Mr. FLOOD. What about me?

Dr. DIEFENBACH. As far as dental decay is concerned?

Mr. FLOOD. What about me, period. I want a glass of water. So I go to the tap and take a glass of water and there is sodium fluoride in it. I do not want sodium fluoride. What about that?

I understand there is absolutely no doubt that this will do what you say it will do for children.

Dr. DIEFENBACH. That is correct.

Mr. FLOOD. With this I agree, period. That is the end of that argument. You win. You are right. My compliments for you folks having made the discovery. What has that got to do with me?

Dr. DIEFENBACH. The most effective, safe, economic, and practical method of bringing dental health benefits to the Nation's children——

Mr. FLOOD. What about me? I am no child.

Dr. DIEFENBACH. In terms of bringing these benefits to you, Mr. Chairman, or to me either, it is too late to realize the benefits we would have derived had we had fluoridated water available to us in early youth.

Mr. FLOOD. When I say me, I am speaking of the American adult citizenry. You are so concerned with protecting the teeth of children by sodium fluorides in the water that everybody else is to be ignored. Here I am going to the water tap for a glass of water. I know it is going to take care of the children's teeth in the best interests of them, but I must drink the glass of water with fluorides in it.

You say do not worry about it, it is not going to hurt you anyhow, but I do not want it in the water I drink. What about that? What are my rights? Do I have any rights?

This is the position I am taking for the American citizen, let's say. I am the devil's advocate now. What about it?

Dr. DIEFENBACH. I think there are two points that need to be made in response to your question.

First of all, there is very good evidence that there is no harm whatsoever in the use of fluoridated water among the population at large.

Mr. FLOOD. I still do not want it in there. It is my water, I am paying for it.

Dr. DIEFENBACH. Very good. I just want to make clear for the record that as far as the evidence is concerned there is no medical problem here in terms of the safety of fluoridated water.

On the second part, you are talking about individuals' rights to have the same access to water supplies that are treated with fluoride or the access to waters that are free of fluorides if you so wish. I presume the same kinds of questions might be raised about many other treatment aspects of drinking water supplies.

Mr. FLOOD. I am not talking about any other treatment factors but the sodium fluoride in the water supply. I am the devil's advocate. I do not want it in there. I am an American citizen. To what extent are you violating my constitutional rights?

Dr. DIEFENBACH. This matter is a local decision of your city council or health department or State government, and thus under State or local law. More than a dozen State supreme courts have upheld fluoridation. The Supreme Court has refused seven times to review cases citing water fluoridation as a violation of individual freedom. It is not a matter of jurisdiction for the Federal Government. We urge all communities to fluoridate at the earliest possible time. We have presented all of the evidence with scientific substance showing the facts in the most open fashion.

Mr. FLOOD. I did not realize the Supreme Court had gotten into this.

Dr. DIEFENBACH. The decision to fluoridate is a local option. When an individual is a part of a fluoridated community, he is expected to abide by its laws and regulations or appeal to the courts.

USE OF FLUORIDATED WATER IN HEMODIALYSIS

Mr. FLOOD. Have you gone back to all of the local councils to which you have over a long period of years presented very openly, very strongly, the arguments for fluoridation to bring to their attention the alarming discoveries regarding using fluoridated water in kidney dialysis?

Dr. DIEFENBACH. In my testimony before city councils and other audiences——

Mr. FLOOD. Have you?

Dr. DIEFENBACH. I have not included such statements in any presentation I have made on fluoridation.

Mr. FLOOD. Why?

Dr. DIEFENBACH. Because there is no relation between water fluoridation and the use of fluoridated water in hemodialysis.

Mr. FLOOD. You are aware there is a possibility?

Dr. DIEFENBACH. I am aware of recent reports on the use of fluoridated water in artificial kidney machines in hemodialysis.

Mr. FLOOD. The clinicians say you should take a very careful look at the use of fluoride in that water being used for kidney dialysis as having a potential of danger to the kidneys and to bones of the patient.

Dr. DIEFENBACH. As a matter of fact, the National Institute of Arthritis and Metabolic Diseases for a number of years has recommended that water used for hemodialysis be specially treated and that elements contained in it, not just fluoride but other elements as well, be removed prior to use in the artificial kidney.

Mr. FLOOD. I am talking about fluoride only.

Dr. DIEFENBACH. Fluoride can easily be removed from the water supplies where hemodialysis treatments are done.

Mr. FLOOD. There is no doubt that fluorides or anything else can be removed from that water being used in this hardware. There is no doubt about that. But is fluoride in the water being removed before the water is used for dialysis to treat a kidney condition?

What about the water supplies containing fluoride which are there to protect children's teeth, which now we discover have a potential of endangering the kidneys or the bones of these people. What about that?

Dr. DIEFENBACH. No, Mr. Chairman. We have had long discussions on the subject of kidney disease and fluoridation with scientists at the National Institutes of Health. They have studied this matter carefully and have assured us of the safety of fluoridation. You may have seen a recent statement by the Surgeon General supporting this point. There is no association or relationship between the use of fluoridated water in artificial kidneys and the use of fluoridated water in drinking water supplies.

Mr. FLOOD. Very well.

So that he who runs may read and for those who may be concerned, we will insert at this point in the record from the Washington Star of March 2, 1969, the column of James J. Kilpatrick, "Some Fresh Facts on Fluoridation."

And also an article from the U.S. Department of Health, Education, and Welfare, Public Health Service, entitled "Fluoridation and the Use of Fluoridated Water in Artificial Kidneys."

(The articles follow:)

[From the Washington (D.C.) Star, Mar. 2, 1969]

SOME FRESH FACTS ON FLUORIDATION

(By James J. Kilpatrick)

If it were possible to put a copy of the current Saturday Review in the hands of every newspaper editor and member of a city council in the country, a blow for freedom might be struck in the matter of the fluoridation of public water supplies. Some fresh facts have come in.

John Lear, the magazine's science editor, has stuck his neck out in returning to the issue. Proponents of fluoridation, notably the U.S. Public Health Service, have done an excellent job of brainwashing the public and smearing the critics. As a consequence, any person who raises an objection runs the risk of being tagged as a quack, food faddist, or plain nut.

Yet the philosophical and medical objections that have been raised against fluoridation, from the inception of the program nearly 20 years ago, have an enduring validity.

Philosophically speaking, the program simply is incompatible with the principles of a free society. These principles hold that in the field of public health, compulsory measures should not extend beyond protection against contagious disease and the prevention of tragic social burdens. The reduction of tooth decay in children falls in neither of these classifications.

When sodium fluoride is added to a public water supply, everyone in the community, as a practical matter, is compelled to take the stuff into his system. The highly toxic chemical is not like chlorine, which treats the water itself; sodium fluoride is added to the water to treat human beings. There is no longer much question that it does improve children's teeth.

But what else does sodium fluoride do? Skeptics have been urging that medical question for years, and have been brushed aside for their pains. The promoters of fluoridation, determined to impose their own notions of good dentistry upon everyone, have insisted that sodium fluoride is utterly harmless—that its side effects are nil. Is this true?

In a long article, Lear summarizes some recent research in the field. Persuasive evidence is beginning to pile up, both in the United States and in Canada, that sodium fluoride may have far more serious effects upon kidneys and bones than the promoters have believed.

One especially significant finding is credited to Dr. Donald R. Taves and his colleagues at the University of Rochester. They discovered that once it enters the body, fluoride takes not one form, but two. Most of the fluoride stays "bound." About 15 percent appears as "a free ion, able to enter into any number of potential reactions." When fluoride is added artificially to a public water supply, "the rise in total blood fluoride concentration is approximately 36 percent; but the rise in free fluoride is 250 percent."

The findings of Dr. Taves in Rochester, and of Dr. Gerald Posen in Montreal and Ottawa, have been fully reported to learned societies. Dr. Posen's sobering paper on the dangers of using fluoridated water in the dialysis baths of artificial kidneys was presented late in January to the Royal Canadian College of Physicians and Surgeons in Vancouver.

These reports are important to every editor and city councilman concerned with the fluoridation issue. They revive all the old philosophical questions. Granted, for the sake of argument, that sodium fluoride is good for children's teeth: Is it therefore wise and necessary that every citizen be compelled to ingest it?

Almost 4,000 American communities, comprising 72 million persons, now are adding sodium fluoride to their public water supplies. In the view of old-fashioned conservatives, the practice is plainly an intrusion upon personal freedoms. Put that aside. Is artificially fluoridated water also an intrusion upon the bones and kidneys of susceptible persons compelled to drink it?

U.S. Department of Health, Education, and Welfare
Public Health Service

FLUORIDATION AND THE USE OF FLUORIDATED WATER IN ARTIFICIAL KIDNEYS

Recently questions have been raised about the use of fluoridated water in artificial kidneys. The Public Health Service, would like to issue some facts relative to the use of water fluoridation as a public health measure and the use of water containing fluoride and other elements in artificial kidneys.

Consumers of public water supplies enriched with minute quantities of fluoride in order to prevent tooth decay should not be misled by news articles which mention medical problems that may arise from using tap water in the artificial kidney. There is no relationship between the daily consumption of fluoridated water and the use of such water in artifical kidneys for the treatment of patients with total kidney failure.

The National Institute of Arthritis and Metabolic Disease (NIAMD), National Institutes of Health of the Public Health Service is responsible for research related to the use of artificial kidneys. The NIAMD estimates that 1,800 persons in the United States depend upon "hemodialysis" by artificial kidney equipment for the preservation of life. These are persons who have suffered critical failure of natural kidney function through disease or accident. In hemodialysis, the blood of the patient with kidney failure is passed through a unit containing permeable tubing or membranes immersed in a water solution of special composition so that blood impurities will be removed. During this process, there is also transfer of dissolved substances from the water solution into the blood. The dialysis techniques that have been developed permit patients to continue such treatments for years.

Under average circumstances such a patient's blood is "washed" in an artificial kidney two or three times a week for from 6 to 14 hours. In this process, in most cases, about 300 quarts of water to which helpful chemicals have been added are

used to purify the patient's blood during a dialysis session. Thus the patient's bloodstream is exposed to tremendous amounts of water each week (which amounts in most cases to about 900 quarts). In many parts of the country it has long been necessary to purify the local tap water before using it in artificial kidneys in order to remove iron, calcium, magnesium, and other natural or added solutes before its use in dialysis. Such purification may be accomplished by distillation or by passing the tap water through a special device, not unlike a water-softener, which "deionizes" it. In the United States the overwhelming majority of dialysis treatments are given in special hospital centers, and most of these are using such specially purified water for their artificial kidneys.

The desirable fluoride content of water to be used in dialysis has not been finally determined. Some clinicians have suggested that a small quantity of fluoride may counteract to a degree, undesirable bone demineralization that occurs in patients with kidney failure. There are also some indications that the absorption of fluoride during dialysis from the approximately 900 quarts of water used each week, an amount of water 50 to 100 times the amount of fluid consumed by the average person, can result in increased storage of fluoride in the skeleton.

Because various solutes may be absorbed from the water as it is normally supplied during long term dialysis, most water used in dialysis should be deionized.

It should be pointed out again that the need to process some water supplies before therapeutic use in large quantities in artificial kidneys has no bearing on the ingestion by anyone of optimally fluoridated water from community water supplies, recommended by health authorities as a medically safe procedure for the reduction of dental caries.

The U.S. Public Health Service endorses water fluoridation as a safe and effective public health measure and urges all communities to make its benefits available to people at the earliest possible time.

WILLIAM H. STEWART, M.D., *Surgeon General.*

Dr. DIEFENBACH. Mr. Chairman, I ask that you also consider reviewing another article that appeared in the Washington Star very recently, which followed the previous one to which you referred. This one, called "Fluorides: The Facts and the Fury," appeared on the editorial page of the March 27th issue of the Star and it discusses, from another viewpoint, the subject of fluoridation and hemodialysis to which you have made reference.

Mr. FLOOD. Without objection, that will be inserted in the record.

Mr. SHRIVER. Was that an editorial?

Dr. DIEFENBACH. It was an editorial written by Miss Judith Randal.

(The article follows:)

[From the Evening Star, Washington, D.C., Mar. 27, 1969]

WASHINGTON CLOSE-UP—FLUORIDES: THE FACTS AND THE FURY

(By Judith Randal)

A reader writes: "Why don't you tell it like it is and report the several deaths that have occurred from the use of flouridated water in patients being treated with artificial kidneys? Why are the news media keeping this information from the public?

This charge, stimulated by a recent article in The Saturday Review by its science editor, John Lear, would be a serious one if the situation were as simple as the above question makes it appear. But, as so often happens when the emotion-laden topic of fluoridation comes up, it is marred by a heavier emphasis on sound and fury than on facts.

Treatment by an artificial kidney—or hemodialysis, as it is called—is accomplished by inserting a hollow tube into the patient's wrist which permits his blood to flow from an artery into a cleansing bath and then return to his body through a vein.

During the process, which usually takes place overnight, the wastes that have accumulated as a result of kidney failure are removed from the circulation and substances dissolved in the water of the bath may pass through the permeable membranes of the "washing machine" into the blood.

* * *

In the course of the typical three-times-a-week treatment, the patient's circulation is exposed to about 900 quarts of water. This, allegedly, is how fluoride poisoning could take place. There is no such thing as fluoride-free drinking water, but if the concentration of the mineral were unusually high, bodily harm might ensue.

In most parts of the country, however, the water used in artificial kidneys is not the ordinary tap variety, but a liquid which has been purified either by distillation or by processing it with a device which "softens" it and removes fluoride and other minerals. While some patients who undergo dialysis at home instead of at a hospital may not have access to such water, there seems no reason why it could not be made available.

* * *

Indeed, there is some question whether some fluoride, at least, might not actually be beneficial rather than hazardous to patients whose own kidneys no longer work.

At a medical meeting not long ago, Dr. George Schreiner of Georgetown University School of Medicine, a kidney disease specialist, referred to hemodialysis as "one of the last remaining forms of general practice" and cited the tendency of patients to become fracture-prone as an example. Since this is due to the bone demineralization that is a concommitant of repeated treatment by the artificial kidney, some scientists have suggested that small quantities of fluoride taken regularly might have a compensatory effect.

Furthermore, to attack fluorides as the chief danger inherent in artificial kidneys is to miss an important point. Although these machines are, indeed, life-saving, they are by no means perfected. And perhaps their major disadvantage is that the membranes they employ to filter the blood are indiscriminate in the substances they take from and return to the circulation.

Physiologists are not sure which chemicals should be discarded and which should be retained and until such knowledge is forthcoming, properly selective materials cannot be designed.

Meanwhile, it is becoming increasingly evident that fluoridation of local water supplies can decrease the risk of two kinds of widespread disorders: one, dental decay and gum disease; the other, farctures in the elderly.

Study after study has shown that children who drink fluoridated water have fewer cavities than those who drink water poor in this mineral and are less likely, too, to develop inflamed gums—the major cause of loss of teeth in later life.

* * *

And there are more and more reports in medical journals that the regular intake of minute quantities of fluoride forestalls osteoporosis, the bone fragility that makes most women and many men who have passed their 60th birthday susceptible to broken hips.

Finally, these disorders—besides the suffering and disability they impose upon millions—call for treatment by two categories of specialists which are in especially short supply: dentists and orthopedic surgeons.

If the Nation is really concerned about providing the highest quality health care at the least possible cost, the fluoridation of public drinking water is one of the best buys around.

Mr. FLOOD. Go ahead.

Dr. DIEFENBACH. For those children who have no access to a fluoridated water supply, we should see to it that they receive the newest topical fluoride applications.

We know that periodontal disease can be prevented, controlled, and treated particularly when detected among children and young adults. We are testing prototype programs which will be given wider application in the future.

ORAL CANCER

Oral cancer can be successfully cured in almost every case if it is detected early enough. The best hope for the successful management of oral cancer is the early detection of lesions by dentists, who have the unusual opportunity of examining millions of people when they visit their offices every year.

Mr. FLOOD. How do you treat oral cancer if you discover it early enough?

Dr. DIEFENBACH. I am not a specialist on oral cancer, Mr. Chairman, but these lesions are referred to oral and maxillo-facial surgeons and to those who provide radiological treatment. Most oral cancer is subject to successful treatment by surgery if detected and treated early enough.

Mr. FLOOD. Is oral cancer of a high incidence?

Dr. DIEFENBACH. It is of relatively high incidence. It accounts for approximately 5 percent of all types of cancer occurring in the United States.

Mr. FLOOD. Is there a high incidence of fatality?

Dr. DIEFENBACH. Usually it does not have a high fatality rate, perhaps because it is readily visible on examination and easily treated. However, malignancies in the floor of the mouth spread rapidly and do have a rather high fatality rate unless detected and treated early.

Mr. FLOOD. What would cause oral cancer?

Dr. DIEFENBACH. There are a number of factors associated with oral cancer. We are not certain what causes any type of cancer. Most frequently associated with oral cancer is the heavy use of tobacco, either in the form of pipe smoking or tobacco chewing. Occasionally trauma from broken teeth or faulty dentures are connected with oral cancer.

Mr. FLOOD. Malocclusion?

Dr. DIEFENBACH. Prolonged malocclusion and prolonged trauma to surrounding structures may have an effect.

Mr. FLOOD. Is the cause the tobacco or the pipe itself as a piece of hardware in the mouth, on the lip and teeth and gums?

Dr. DIEFENBACH. Again, we are not sure—it may be partially a result of both. We are inclined to think tobacco is a special contributor to the cause of oral cancer.

Mr. FLOOD. Of course, with dentures, because of trauma from the denture, it can follow I suppose.

Dr. DIEFENBACH. That is correct. Poorly fitting dentures or ones that have been broken and mended and no longer fit well can cause chronic irritation that can become malignant.

We will continue to support cancer detection programs and will look for improved methods for use by dentists.

CLEFT LIP AND PALATE

Studies at our Dental Health Center in San Francisco, have shown that more than 250,000 Americans are marked by a cleft lip or palate for life and about 6,000 babies are born each year with these deformities. Our efforts are now focusing on comprehensive studies of twins affected by oral clefts.

Mr. FLOOD. Are the twins both affected?

Dr. DIEFENBACH. In the studies we are carrying out, no. Not necessarily. In fact, we are looking for the difference in the rate of occurrence between the identical twin of an affected child and the non-twin brothers and sisters of affected children as a clue to impact of genetic and nongenetic forces on cleft causation.

Mr. FLOOD. Not necessarily? It would be rather unusual, would it not?

Dr. DIEFENBACH. No, it is not uncommon for one twin to have a cleft and the other not to have one.

Mr. FLOOD. Did you say yes or no?

Dr. DIEFENBACH. I said it was not unusual for one twin to have a cleft and the other to be born without a cleft.

These studies and the complementary laboratory and hospital based investigations of the National Institute of Dental Research will provide a better understanding of the familial and environmental factors influencing the occurrence of clefts. Concurrently plans are being formulated to coordinate and organize treatment and rehabilitation programs for children with oral clefts.

BACTERIAL EXCHANGE BETWEEN DENTISTS AND PATIENTS

Also at the Dental Health Center we are investigating the potential hazards of airborne bacterial exchange between patients and dentists during treatment procedures. The findings may be relevant to future designs of dental offices, dental clinics, and dental school laboratories.

Mr. FLOOD. You mean dentists should wear masks when treating patients?

Dr. DIEFENBACH. We do not understand, Mr. Chairman, the implications of bacterial exchange between patient and dentists and other people in the dental operating area.

Mr. FLOOD. Is anybody trying to find out?

Dr. DIEFENBACH. That is what we are trying to find out in a specially designed laboratory at the Dental Health Center.

In addition, our work will continue on new dental filling materials, devices and techniques which have direct application to treatment procedures in dentists' offices.

Although programs like these do much to improve the management of dental problems, they are not the whole solution. Good dental health protection still depends upon direct treatment provided to individual patients in dental offices. During the next decade we expect demands for dental care to rise to unprecedented heights. If these demands are to be met adequately and if everyone is to have access to care, we must organize dental services more efficiently and improve present methods of financing dental care.

DELIVERY OF DENTAL SERVICES

Our next high priority, therefore, is to develop methods of facilitating the delivery of dental services to more people. As an important part of the solution, we are emphasizing dental care for children, especially children who are underprivileged and those who have physical and mental handicaps. Such an approach offers both immediate and long-term value because the dental health of adults in large part is determined by the dental protection afforded them as children. Our national goal should be the development of a school-based network of preventive and treatment programs for all school children.

Cost being the single greatest barrier to dental care, we must develop financial systems for helping families to budget and pay for the dental services they need. We are studying prototypes of dental insurance including all forms of prepaid plans.

We are encouraging the formation of State dental service corporations and evaluating different organizational patterns of private practice.

In addition, we are working to find ways of delivering dental services in the inner city and in the sparsely populated rural areas through our involvement in the poverty programs.

But the prospect of providing more dental care of high quality and extending treatment services to more people intensifies another serious problem—the increasing deficit of dental manpower. Already acute in some areas, the shortage of dentists and their auxiliaries will inevitably grow worse unless we expand the capacity of dental and allied schools and otherwise improve our dental educational capability.

Consequently, another high priority is to increase the supply of dental manpower, modernize, expand, and develop existing facilities where they are educated, enrich the educational programs offered them, and increase the productivity of dental graduates. The Division provides professional direction to the dental aspects of the Health Professions Educational Assistance Act, including the construction grants program and the basic and special improvement grants program. The Division also provides the professional input for public health dental traineeships and the new program in preventive dentistry.

The Division's education research and continuing education programs of the Dental Health Center are developing more efficient dental teaching methodology. We are evaluating self-teaching machines, audiovisual media and computer-assisted teaching programs for use by dental students and auxiliaries and for the continuing education of dental practitioners outside the university setting.

Grant programs are creating new centers for research training in applied dental science, research fellowships for students in those centers, and hubs for disseminating continuing education to practitioners. Problems related to the recruitment of well-qualified students, teachers, and researchers are being studied for better ways of attracting bright young people to dental careers.

The employment of greater numbers of auxiliaries in dental offices and their more efficient use offers great promise of partially solving the dental manpower shortage. The Division supports through grants to all dental schools the dental auxiliary utilization program which teaches students the effective use of trained clinical auxiliaries. To date, these programs have been limited to chairside dental assisting, often referred to as "four-handed dentistry." This year some programs will be expanded to include efficient use by students of dental hygienists and laboratory technicians as well. The Division's studies at the Louisville Manpower Development Center indicate that work output of dentists can be at least doubled by delegating additional clinical procedures to auxiliaries. Companion studies to the Louisville research project are being conducted in several dental schools through contracts.

The Division will place its priorities on (1) further developing, improving, and applying preventive and control measures; (2) improving the organization, delivery, and financing of dental services; and (3) increasing the Nation's supply of dental manpower. In all of these areas, our primary emphasis will be on elevating the dental health of children and youth for therein we will realize the largest and most important health benefits from our investment.

29-867 O—69—pt. 4——68

SUMMARY OF BUDGET

In conclusion, Mr. Chairman, the request is for $11,888,000, an increase of $1,703,000 over the 1969 operating level of $10,185,000. Included are increases of $1,220,000 for dental auxiliary utilization grants, $106,000 for research training grants, $100,000 for continuing education grants, $80,000 for research grants, and $197,000 for direct operations.

Thank you. I shall be happy to answer any questions.

RELATIONSHIP TO NATIONAL INSTITUTE OF DENTAL RESEARCH

Mr. FLOOD. What would be the advantages and disadvantages of combining this appropriation with the appropriation for the National Institute of Dental Research?

Dr. DIEFENBACH. Yes; and we have been giving that considerable attention and thought within the National Institutes of Health.

Mr. FLOOD. I would hope so.

Dr. DIEFENBACH. I might add that Dr. Marston, Dr. Kreshover, Dr. Sherman, and myself, have had several meetings on the subject and Dr. Marston has already projected a schedule upon which we will have further discussions on this matter. I believe they will continue soon after the appropriations hearings are completed.

Mr. FLOOD. I am glad to hear it.

INCREASE IN TRAINING PROGRAMS

In the Institutes, less funds are requested for training programs in 1970 than in 1969, but almost all of your requested increase is for training, an increase of $1,426,000, a 40 percent increase. They are going one way and you are going the other.

Why the big difference, between you and the Institutes?

Dr. DIEFENBACH. To get done what needs to be done in this country to improve the level of dental health, I believe we need to put greater emphasis on the development of auxiliaries and the development of their efficient use by graduating dental students.

Mr. FLOOD. The institutes have big problems. They are not doing this.

Dr. SHERMAN. May I suggest, Mr. Flood, that the difference here is one between the training of individuals for research and its conduct, that is in the research institutes and divisions of the so-called old NIH, and the programs in the Bureau, including that of Dr. Diefenbach's division, which are concentrating at this point in time primarily on the training of people to apply the results of that research.

Mr. FLOOD. But, my friend, 40 percent. In a year like this?

Dr. DIEFENBACH. The largest amount of that increase you refer to in training is the $1.220 million for developing the dental auxiliary utilization program.

Mr. FLOOD. Would you settle for 20?

Dr. DIEFENBACH. I think this would be unwise. There will be two new dental schools, for example, that will be operating and will be requiring funds to start programs. And in addition, many of the programs now in effect in dental schools provide students very limited exposure to the use of auxiliaries and certainly need to be broadened to include dental hygienists and laboratory technicians.

We believe that this investment will have an important payoff as compared to other considerations that we rejected.

DENTISTS ATTITUDE ON USE OF DENTAL AUXILIARIES

Mr. FLOOD. A great many dentists have resisted, the whole idea of dental auxiliaries. Is there any change on that attitude?

Dr. DIEFENBACH. I am pleased to say there is a very favorable change over the past several years.

Mr. FLOOD. It is about time.

Dr. DIEFENBACH. Perhaps the dental societies led by the American Dental Association, are demonstrating leadership in this important area superior to that of the other health professions.

Mr. FLOOD. This committee has been pounding on that for 10 years. They are seeing the light, are they?

Dr. DIEFENBACH. Thirty-some State dental societies this past year have reevaluated their dental practice acts for the purpose of modernizing them. This certainly reflects their belief that auxiliaries are here to stay, and they are being used in dental offices and practices more extensively.

Mr. FLOOD. What about the dental schools? Do they have a definite positive attitude?

Dr. DIEFENBACH. I think the best evidence of that is the current status of the DAU programs which are now operating in all of the dental schools.

Mr. FLOOD. They were no help either for several years.

Dr. DIEFENBACH. For some years the schools were dragging their feet, sir.

Mr. FLOOD. That is an understatement.

Dr. DIEFENBACH. At the present time these grants are an essential part of the dental education of students. The Council on Education of the American Dental Association, which accredits the programs, now insists that schools teach dental students how to use auxiliaries. Formerly this was not required. I am confident that the leadership in dental education and in the dental profession is committed to the expanded use and functions of auxiliaries.

Mr. FLOOD. By the way, you better have the record show what an auxiliary is. Somebody may not know.

Dr. DIEFENBACH. May I insert the definitions of various types in the record.

Mr. FLOOD. Sure.

(The information follows:)

DEFINITIONS OF DENTAL AUXILIARIES

The dental hygienist works under the supervision of the dentist and assists both the dentist and the patient by providing dental health information, and by performing preventive dental treatments, such as oral prophylaxis. The dental hygienist is the only one of the three auxiliary members of the dental health team who must be licensed to practice. Formal training programs for dental hygienists have existed longer than for either of the other dental auxiliaries.

There are two types of programs for the education of dental hygienist. A 2-year program leads to a certificate (or diploma) in dental hygiene or to an associate degree in arts or applied science.

A 4-year program of study leading to a baccalaureate degree may qualify dental hygienists as teachers or clinical instructors in schools of dental hygiene, as well as employment in private practice.

The dental assistant's most valuable role is that of the chairside assistant where she serves as the dentist's second pair of hands during dental treatment procedures. The dental assistant may also serve as a secretary-receptionist and in some dental offices will perfom certain laboratory procedures. In recent years, formal training programs for dental assistants have been started and the number of such programs is growing rapidly.

The dental laboratory technician makes and/or repairs dental appliances such as partial and full dentures, and makes restorations such as inlays and crowns. The technician works under the direction, or according to the prescription, of a licensed dentist. A few of them are employed full time by dentists, but the great majority work in commercial laboratories. There are now a few formal training programs and more will be developed in the future. However, most dental laboratory technicians are now trained on-the-job in dental laboratories.

DENTAL BEHAVIORAL SCIENCE PROGRAM

Mr. FLOOD. You mention on page 78, "a new program in dental behavioral science."

What is that all about?

Dr. DIEFENBACH. I am referring to a project to interest and train people for research in the behavioral science areas that are related to dentistry. For example, the attitudes of people toward personal hygiene and community dental health measures, why people resist going to the dentist, how to motivate more and better students to apply for training as dentists or dental auxiliaries, and how to choose, educate and keep the most capable of these—all these areas need study.

I might also say that studies are needed regarding the attitudes and behavior of dentists toward patients, which are perhaps even more important. Perhaps we can learn why some people refuse to go back to their dentist.

Mr. FLOOD. You have to almost drag people into a dentist's office. Why?

Dr. DIEFENBACH. Money of course is part of the block, but assuming that the money barrier is eliminated, there is a resistance of people to have their dental needs taken care of. There are apparently psychological factors involved.

Mr. FLOOD. Do something about the drill and you will cut the problem in half.

Dr. DIEFENBACH. It would be nice if we could eliminate that instrument.

Mr. FLOOD. Will the laser help?

Dr. DIEFENBACH. At its present stage of development the laser has very limited potential in dentistry.

On the other hand, I would expect that as the technology of the laser is improved, it may very well begin to have a very important application in clinical dentistry.

RESEARCH ON CLEFT LIP AND PALATE

Mr. FLOOD. What is the difference between the research that you do with regard to the cleft lip and the cleft palate, and that done by the National Institute of Dental Research?

Dr. DIEFENBACH. This is a serious dental deformity for many people and the impact on the affected individual, his family and community is great from an economic and psychological standpoint.

Mr. FLOOD. No doubt about that.

Dr. DIEFENBACH. With your permission, I would like to ask Dr. John Greene, the Deputy Director, to respond to your question.

Mr. FLOOD. All right.

What is the difference?

Dr. GREENE. The work we are doing is complementary to the NIDR program.

The studies that we are conducting in San Francisco are based largely on a survey of birth certificates in the various States that have information on birth defects included on the birth certificates.

Mr. FLOOD. You do not insist that this is included on the birth certificate?

Dr. GREENE. No, sir. What we are trying to do is to get information from birth certificates to identify factors associated with the occurrence of clefts.

Mr. FLOOD. Do the laws of the various States require that this condition be reported on a birth certificate?

Dr. GREENE. In some of them; yes sir.

Mr. FLOOD. Shouldn't you be working on that to see that all of them do?

Dr. GREENE. We certainly would like to see it done. We did participate in the redrafting of the standard birth certificate form with the National Center for Health Statistics.

Mr. FLOOD. Are you pushing this? Are you for this?

Dr. GREENE. We are for it, but have not been pushing it. We do not feel that it is within our area of jurisdiction.

Mr. FLOOD. Whose area is this? Who handles this?

Dr. GREENE. The National Center for Health Statistics of the Public Health Service designs the standard certificates and promotes its use. Our activities, in San Francisco, have been directed toward a followup of the data that we have gathered from the birth certificates. The activities of the Institute of Dental Research are largely of three types: one, is based on studies of types of treatment of cleft cases; another includes genetic studies of a selected population group, an Indian population. These studies are based on hospital births in Indian hospitals. The third type is laboratory-oriented. They are studying ways to cause clefts to form in laboratory animals.

Mr. FLOOD. Thank you.

PAYMENT TO NIH MANAGEMENT FUND

Now, in 1969 you have $6,000 budgeted for payment to the National Institutes of Health management fund, $6,000. For 1970 it is $62,000. Now, what services account for that big jump?

Mr. HAMBLETON. In 1969 we were paying a share to the National Institutes of Health, a small share for the work that they did for us in processing our research grants.

Mr. FLOOD. Is this inflation?

Mr. HAMBLETON. No. In 1970 we will have moved out to the NIH campus for the full year, and as a result we pay a full share of many central services that they will furnish.

This is worked on a formula and it is justified in the management fund budget for the National Institutes of Health.

Mr. FLOOD. Mr. Michel.

DENTIST-PATIENT RATIO IN THE ARMED FORCES

Mr. MICHEL. Doctor, these are pretty shocking statistics you cite here at the very beginning of your testimony. I am wondering particularly with respect to those inductees going into the Armed Forces, what is the ratio of dentists to patients in the Armed Forces as against what it is in civilian life? Are there any comparable figures?

Dr. DIEFENBACH. There are figures on the ratio of dentists in the Armed Forces and elsewhere. I do not have the records with me. I can provide them.

(The information follows:)

RATIOS OF DENTISTS AND PHYSICIANS TO PATIENTS IN THE ARMED FORCES COMPARED TO CIVILIANS

	Non-Federal/ civilian	Active clinical/duty personnel (not administrative) (dependents not included)
Dentists	1/2,150	1/650–1/700
Physicians	1/650	1/200

Dr. DIEFENBACH. As the data show, dentist-patient ratios are more favorable for the armed forces than for the population at large. There are very good reasons for this. With the urgency and speed with which the troops who are on the move need to be treated, you have to have the manpower available to deliver full services on short notice.

The ratio, therefore, is more favorable and I would be very glad to provide that information.

Mr. MICHEL. I am reminded of my own personal case. I don't think that I had to go to the dentist more than three times before I entered the service. I always felt that I had good teeth because of the training we had at home with respect to dental care. But when you are in the service, unfortunately during wartime—well, I was in the infantry and not particularly giving attention to my teeth like I should. I came back out of the service and I needed three pulled and 14 cavities filled. I always felt that I did not really give the attention to them that I should have in the service. However, being at a base and not fighting a war, it is a lot easier to take care of your teeth.

PROMOTION OF FLUORIDATION

I note that you say that at present our most flagrant failure is the lack of fluoridation in the United States and if we made use of this proven health measure we could prevent tooth decay by 65 percent or more among the Nation's children. What are we doing to get this story across to the people? You say it. We know it because you tell us, as a professional. Then I say "How do we get this communicated out to the people, to take advantage of this?" Is it a matter of cost? I don't think that is so much of a problem. Why can't we get this point across? Or is it the propaganda that is abroad that this is part of a Communist conspiracy to fluoridate? I remember the jazz I used to get in letters from a couple of the smaller communities that were about to do that. I had all of the silliest reasons you could imagine thrown at me.

How do we break this down and get this little thing done? It would seem to me this is one of the cheaper things we could do, isn't it, relatively speaking?

Dr. DIEFENBACH. From a cost-benefit analysis it is probably the best bargain there is in health today. However, just because something is inexpensive and practical doesn't necessarily mean that people are going to accept it; nor does it mean because some of us are experts in fluoridation that people will always accept the things that we recommend they adopt. It has been a slow process, as you know. The Public Health Service recommended this measure in 1951 and all of the major scientific health organizations throughout the world have now endorsed it.

So I think some of the resistance is the resistance to change. To institute a health measure which eventually will affect everyone is a rather broad and sweeping thing to do. The public is not always prepared to accept these recommendations.

Furthermore, the opponents of fluoridation have never given up. They seem to come in waves at times. The pressure will increase, then ebb, and then flow again. I predict that we will be going into a perod of intensified resistance to fluoridation perhaps because of some of the recent releases that have been appearing in the magazines—popular journals, I might add, and also because I think some people in our country are looking for ways to resist change or to be conservative.

Mr. MICHEL. You say here this is a flagrant failure. That would suggest to me that that would be an area where you would really be putting some of your money. What have you in this budget, any amount of money that would be earmarked for getting this story told? When you get one television program on hunger, and that wasn't even very factual, the whole country goes sky high. You get one television program and you get people all fired up about it.

Now, if this is such a flagrant failure and that much can be accomplished with so little, I would be willing to put up $1 million. I would think it was money well spent, money spent getting the story told professionally.

Now, drug addiction is another problem. We know what tremendous losses there are and what are some of the things that ought to be done about it. Sometimes it takes a shocker to wake up the people to the fact that something has to be done.

Is the dental society, are the dentists around the country conscious of this? For example, would they move locally with respect to their local television stations to put on prime time a good professionally done job to apprize people of this problem and how simply it could be done?

Dr. DIEFENBACH. To answer your several questions, probably in reverse order, first of all the local dental societies, as well as the national groups, have been some of the prime movers in the promotion of fluoridation. You will be interested in the movement in Allentown, Mr. Flood, particularly where the dentists have been pushing for fluoridation very vigorously.

They have asked for our assistance and we have provided it. Local dentists are really spending money out of their own pockets to buy time.

The American Dental Association, too, has been vigorous in urging fluoridation for prevention of dental caries. Regarding your point concerning making money available to get the story told—there is no doubt that a better job of informing the public could be done and that a well financed program would have an impact. However, I believe making money available in the form of Federal grants to purchase fluoridation equipment would have even greater payoff. The small cost involved is a roadblock to fluoridation in many of the Nation's small communities. Lastly, you asked how much money we're now spending on fluoridation. This amounts to approximately $160,000 at the present time.

We certainly should support an intensified promotional effort as you have implied, Mr. Michel.

Mr. MICHEL. Are there any metropolitan centers in the country that are not fluoridated?

Dr. DIEFENBACH. Yes, there are a number.

Mr. MICHEL. I can understand where some of the smaller communities do not fluoridate, although there is no reason why they should not also, but particularly our big cities, the metropolitan centers, that is where the people are and that is where the law of averages says you are going to save the most.

I would like to see that spread out in the record a little bit more clearly. Maybe we can give a little leadership here. We count on you folks, obviously, to lead the way in these areas when you come before us with testimony saying that is a flagrant failure on our part. Your failure is in part our failure. We may try to push you at times. Once we give you a nudge and see that nothing happens, then we get a little bit more bitter about it, I guess.

Dr. DIEFENBACH. I have a list before me, which I will be glad to supply for the record which includes the major cities that are fluoridated and the major cities that are not fluoridated.

Mr. MICHEL. All right. I would like to have that for the record.

(The information follows:)

MAJOR CITIES FLUORIDATED AND NOT FLUORIDATED

MAJOR CITIES FLUORIDATED

New York City	1965	Fort Worth	1965
Chicago	1956	Oklahoma City	1954
Philadelphia	1954	Rochester	1952
Detroit	1967	Toledo	1955
Baltimore	1952	St. Paul	1952
Cleveland 19	1956	Norfolk	1952
Washington, D.C	1952	Miami	1952
St. Louis	1955	Tulsa	1953
Milwaukee	1953	Richmond	1952
San Francisco	1952	Des Moines	1959
Dallas	1966	Providence	1952
Pittsburgh	1952	Mobile	1958
Buffalo	1955	Charlotte, N.C	1949
Denver	1954	Syracuse	1965
Minneapolis	1957	Atlanta	1969
Indianapolis	1951	San Juan	1954
Louisville	1951	Flint	1966

(Memphis, Seattle, and Omaha have approved but have not started yet.)

SOME OF THE MAJOR CITIES NOT FLUORIDATED

Los Angeles
Boston
Newark
Birmingham
Cincinnati
Columbus
Wichita
Kansas City, Mo.
New Orleans
Albuquerque
Houston
San Antonio
Long Beach
Oakland
San Diego
Honolulu
Portland

STATES REQUIRING FLUORIDATION BY LAW

Connecticut, communities 20,000 and over.
Minnesota, all communities by January 1, 1970.
Illinois, all communities.
Michigan, all communities within 5 years unless local community acts against fluoridation by council action or vote.
Delaware, board of health given authority to order fluoridation.
South Dakota, all water supplies serving 500 or more.

EARLY DETECTION OF ORAL CANCER

Mr. MICHEL. Now, I see oral cancer can be successfully cured in almost every case if it is detected early enough.

I go back again to that Pap test that we talked about so much years ago and have been not so much recently. There I find only 25 percent of the women taking advantage of it. Would oral cancer be detected only if one saw a dentist?

Dr. DIEFENBACH. That would not necessarily have to be the case, sir. It could be done by physicians as well as dentists. This is a very simple test to do and it is patterned after the Pap test. Fundamentally the approach is exactly the same. But it requires a plan and organization to provide a laboratory service which is competent to read the smears. I might say that the oral mucosa cells are different from the cells of the uterus and consequently the technology of reading oral cancer cells is a little different from the Pap smear. But basically, the process is the same.

We have advocated and supported demonstration projects, a number of them, in various parts of the country, both rural and urban, to determine the feasibility of dentists taking smears on a broad scale. In a number of instances the programs have met with success; in other places they have not been as successful.

I believe that we could do much here if we could educate dentists to routinely examine for oral cancer and be prepared to take a smear on every patient who walks into his office, regardless of whether he is there for an emergency or not.

When you stop to think that 40 to 45 percent of the people in America walk through dentists' doors every year, this opportunity is one of the best screening devices that we could possibly conceive. I do not believe that all of the things that could be done are being done.

Mr. MICHEL. When you say 45 percent, does that really mean 45 percent of the population or does that take numbers into consideration only? If I go in three or four times a year am I considered to be four as against the whole?

Dr. DIEFENBACH. No. I am speaking of 45 percent of the population who visit a dentist at least once a year. People walk into dentists' offices and out again for many reasons. Now, this is a tremendous oppor-

tunity in my opinion which is not being fully exploited to apply simple diagnostic screening tests for a variety of purposes which, could be carried out efficiently and economically.

Mr. MICHEL. You say that we will continue to support the cancer detection program. How much goes into that?

Dr. DIEFENBACH. We have been supporting programs in the past at approximately $60,000 each year. This is through contracts.

Mr. MICHEL. Kind of peanuts, isn't it?

Dr. DIEFENBACH. It is limited, definitely.

TRAINING OF DENTAL HYGIENISTS

Mr. MICHEL. In the manpower requirements you say that you wanted the demands to be met adequately, there are going to be tremendous requirements in the future.

Now, when I go to the dentist today there is a dental hygienist who cleans my teeth twice a year and the dentist himself will come in afterwards and give me a good going over to make sure that everything else is all right. If I need some extra care or treatment, that I will get.

I remember way back when, when there were no dental hygienists and this professional dentist was doing all those things himself.

What support do we give, if any, to these students going into this field to become, for example, dental hygienists? Do we do anything?

Dr. DIEFENBACH. At the present time it is rather small. The support that is available is under the Allied Health Training provisions. We do have a current listing of those grants in support of students, for training that can be identified for this purpose. May I submit that for the record?

Mr. MICHEL. All right.

(The information follows:)

Grant awards made to dental auxiliary programs in fiscal year 1968 under the Allied Health Professions Personnel Training Act of 1966

Basic improvement grants:	
Dental hygiene, 46 schools in 27 States	$1,181,973
Dental assisting, 18 schools in 4 States	299,478
Dental laboratory technicians, 10 schools in 7 States	142,545
Total	1,623,996
Traineeships for advanced (teacher) training:	
Dental hygiene, 17 trainees	83,024
Dental assisting, 2 trainees	8,440
Total	91,464

In addition to the above, $34,287 was awarded under section 306 of the Public Health Service Act to dental hygienists for studies leading to a baccalaureate degree in dental public health hygiene.

Mr. MICHEL. Do you know how many there are in schools around the country now in this field who will become dental hygienists? I suspect most of them, if not all of them, are women, are they not?

Dr. DIEFENBACH. Yes. I think without exception they are all women, both for dental hygienists and dental assistants training. I don't have the census on either of those at hand but we have it at the office.

Mr. MICHEL. Would you supply those for the record?
Dr. DIEFENBACH. Certainly.
(The information follows:)

Schools enrollmeent 1968–69 year

	Number of students
Dental hygienists	5,150
Dental assistants	4,500

Mr. MICHEL. From my querying the girls that I have known who have done the work on my own teeth, I gather that, at either Southern Illinois University or Northwestern, they can qualify with about 2 years of college level training and then be certified or certificated as hygienists.

Dr. DIEFENBACH. For hygienists there are two types of programs. There is a 2-year program, a certificate program, which trains a girl to be a clinician, for the cleaning of teeth, topical fluorides and other clinical procedures. The 4-year program leads to a baccalaureate degree and usually a teaching certificate as well. So then the young lady, in addition to being a clinical hygienists, is also qualified for teaching in a classroom, working with teachers, organizing health programs in the community, and so forth.

DENTAL SERVICES FOR THE POOR

Mr. MICHEL. Your next point here, is with respect to getting into the ghetto to those who normally do not have the facility or the wherewithal to go to a dentist to get an examination or get their teeth taken care of. We hear and know, as a matter of fact, that in the medical profession, though very unheralded, doctors give of their time and professional services to those unable to pay. We probably never would be able to get statistics to show to what extent this is done. But we know about it, we know it is being done by physicians.

Is anything being done in this area by the dentists themselves?

Dr. DIEFENBACH. The figures we have on dentists are no better than those on physicians, but there is no question that a large amount of time is donated by practicing dentists for treating people who are medically or dentally indigent and would not otherwise receive care.

Mr. MICHEL. Now, I can see it is different. Even as well as I know my own dentists for many, many years, I would have a problem calling up today or tomorrow for an appointment unless he pushed somebody else out of an appointment. People have to wait a considerable time. It strikes me that in that selection process, whether or not you have an opening, pure economics will dictate where the doctor will say "I am going to take the cash-paying customer first, and take the one who makes me wait second or those who will not pay at all." How do you get around this? Is there any way of meeting this without transgressing on normal practices?

Dr. DIEFENBACH. In the long run, Mr. Michel, I think the delivery of dental services to people who are in the ghettos and rural areas has to be financed adequately to attract dentists to deliver services there. It is fine for us to have missionary spirit, and I think most of us do in the dental and other health professions; but that is not really the answer to the problem. I would encourage dentists to continue giving

their services and, I might say, many of them give a considerable amount of time. In fact, some who are affiliated with certain church groups give up their private practice for an entire year to work for charity to alleviate the problems for people who otherwise would not have dental care at all. But that, in the long run, is certainly not the answer that we must have for serving these people.

I believe that we are learning much about organizing care programs through our work with the Headstart program, Neighborhood Health Centers, and Job Corps Centers. More recently we have been negotiating an arrangement with the followthrough programs in the Office of Education. Through these projects we are learning a great deal about what patterns of organization work in certain circumstances for dentists, what clinical locations will work, to what extent the private office of a dentist can be used, and what the handicaps are that affect each of these arrangement. In addition, I might add that in Chattanooga, Tenn. we initiated during this past year a project to determine how we might be able to organize a rural dental care program in seven counties that fan out from Chattanooga, using Chattanooga and the neighborhood health centers there as one base and providing care for schoolchildren, preventive services principally, in this rather difficult manpower area.

We have a mobile unit down there. We have a full-time dental officer assigned to the project but principally the practicing dentists in the area are the manpower resources being used to treat the children. I might add that in one of those counties there is no practicing dentist at all. So we are trying to take on the job of learning more about organizing programs under difficult circumstances to deliver dental care and services needed by youngsters.

Mr. MICHEL. Did you spell out for the record heretofore how you divide up your work with the National Institute of Dental Research?

Dr. DIEFENBACH. In previous years or here today?

Mr. FLOOD. We did put some comment into the record on it.

Mr. MICHEL. All right.

I think that is all I have.

Mr. FLOOD. Mr. Natcher.

PERIODONTAL TREATMENT

Mr. NATCHER. Doctor, is the periodontist generally well received in the dental profession?

Dr. DIEFENBACH. The periodontist, yes, I would say he is. These are dentists who have taken advanced training beyond dental school and who limit their practice to periodontics.

Mr. FLOOD. What is a periodontist?

Dr. DIEFENBACH. He is a dentist who has advanced training and limits his practice to the treatment of the gums and supporting tissues of the teeth.

Mr. FLOOD. The record should show these things.

Mr. NATCHER. Doctor, some 10 or 15 years ago was there some question about the treatment of pyorrhea and the system used by the periodontists? Was there some question about whether or not it was the type of treatment that we should have?

Dr. DIEFENBACH. The treatment of pyorrhea and related conditions of the gums has received continuing discussion among specialists as to what is the more efficacious treatment and, I should include, drug therapy. I might also add that in some dental schools there are certain periodontal treatment procedures that are stressed over others. This is not peculiar to periodontal practices. I think it is also the case in prosthetics, different techniques, procedures and it is also the case in orthodontics practices. What I am leading to is that there is probably no one best treatment procedure for all situations. This is what makes the periodontist important and perhaps why his services are so expensive. His judgment is needed to determine the best course to follow in handling a particular case to achieve the best results.

Mr. NATCHER. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Shriver.

DENTAL PROBLEMS OF THE HANDICAPPED

Mr. SHRIVER. Thank you, Mr. Chairman.

On the first page of your statement you say the dental problems of mentally retarded and physically handicapped children comprise one of the worst areas of dental illness.

Now, I can see it would be a terrific problem. How are you meeting that problem? What are you doing?

Dr. DIEFENBACH. We have through contracts conducted hospital- and institution-based studies on providing treatment to the mentally retarded and for some of the other physically handicapped children, including spastic youngsters who have difficulty even sitting still at any time; much less for a dental operation.

What we are trying to do for the handicapped is to develop and make available suitable portable equipment that can be taken to these institutions and used effectively by practicing dentists. In some instances we have urged State dental societies to purchase a portable unit which can be used by all of the dentists in the community and becomes a property of the local or State health department.

This is one approach to extending the services of dentists to the handicapped.

A second approach, and perhaps more important than the matter of equipment or the organization of the services, is to prepare dental students to cope with these special kinds of patients and their problems. We supported in dental schools for a number of years 12 programs to train students in treating the physically handicapped and mentally retarded.

In this connection, the senior dental students in some instances visited the hospitals and treated the children where they were institutionalized. In other instances the children were bused to the dental school or to a special clinic where they were given treatment.

This is a problem of great size, virtually untouched in this country. We need to do much more than we are now doing.

PREPAYMENT FOR DENTAL CARE

Mr. SHRIVER. Based on studies of your Division, do you have any recommendation on any particular form of prepayment or insurance

plan? Have your studies been sufficiently advanced so that you could recommend such a plan? Should it be compulsory or voluntary?

Dr. DIEFENBACH. We don't have any specific form of insurance to recommend. We do know that successful group plans can be administered by nonprofit organizations as efficiently as those in the commercial groups. Consequently, in a number of instances the nonprofit route is less expensive because it has a lower overhead charge.

We have found that State dental service corporations which have been organized to provide services on a statewide basis through members of the dental profession, are well accepted by union and management groups, as well as by the profession, because they give freedom of choice to both the patient and the dentist as to whom shall be treated by whom.

We have no special tailored model that we would recommend to any one particular group that was seeking dental care. We do provide direct technical advice and consultation. We have experts on our staff who know the prepaid dental subject very well. They frequently sit down with groups such as schoolteachers or milk truck drivers, labor unions, et cetera, interested in developing dental plans and help them work out the specifications.

There are many variations of plans as to what coverages certain groups wish to have included and how much they are willing and able to pay.

Mr. SHRIVER. In the justifications it is stated that research emphasizing special population groups will be undertaken.

Dr. DIEFENBACH. Yes. In this particular connection I was referring to children, particularly of elementary school age.

There are, as you know, public funds to help defray some of the costs or in some cases pay all the costs of dental care for some indigent children. But there are large numbers of children whose families cannot afford to pay cash on the barrelhead at the time services are needed. What I am referring to here is that we need to devise financial methods for families to budget and to pay in small amounts, as they can, probably in advance of the treatment, premiums for the dental care of elementary school children eventually and soon all of our youngsters can be included in the program, not just the very poor or the very rich.

COST OF USING DENTAL AUXILIARIES

Mr. SHRIVER. In the justifications you discuss a study in which one dentist and five chairside assistants are used to deliver care and that there was a considerable increase in productivity of the dentist. Now, if that were used in private practice, if you had that many people involved, wouldn't that increase the cost of the service?

Dr. DIEFENBACH. I would think not.

Mr. SHRIVER. Not even if you had that many?

Dr. DIEFENBACH. Well, the overhead costs, if you are taking a group of five people plus a dentist, for running the operation might appear higher at first glance. But actually when you look at it in terms of work output, by the total group, this one dentist and five auxiliaries, when we predict that the work output of one dentist can at least be doubled over what he is now doing with two assistants, the

cost of services would not increase and it would not indicate to me that the unit cost for a given piece of work would be higher. In fact I don't think the unit prices of dental care are going to decline. But one of the results of using more auxiliaries might be to help stabilize the cost of dental care rather than seeing them increase as other medical costs. The multiple use of auxiliaries in the long term will not only be more efficient from a manpower point of view but more economical from the country's dental bill point of view.

Mr. SHRIVER. Your statement mentioned $1,220,000 for dental auxiliary utilization grants. How does that work? Does the institution ask for it? Is it a school that asks for it?

Dr. DIEFENBACH. These programs are supported through project grants. The teachers or heads of the departments of these particular programs develop the projects, proposing how they are going to teach the dental students, to utilize auxiliaries, and so forth. These projects are submitted to us. They are reviewed by an outside advisory committee, are given priority ratings and therefore are competitive one with the other for funding. It has only been recently that all 50 schools have been included in the program. The reasons for that have been two: first, there have not been sufficient funds in the past to actually support the projects that had been submitted; second, some of the proposals that were submitted did not compete favorably in terms of quality standards when compared with other programs.

Now for the first time all 50 existing schools are included. As I indicated earlier, there will be two new dental schools ready for support in the next fiscal year.

Mr. SHRIVER. Is this additional money for the new schools?

Dr. DIEFENBACH. Yes, but not only that. As a matter of fact, the projects that we are now supporting this past year have only been supported at 71 cents for each dollar approved by Council. So you see we have a long way to go to meet the needs and realize the full potential of this program.

Mr. SHRIVER. Thank you, Doctor.

Mr. FLOOD. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Dental Health

Amounts Available for Obligation

	1969	1970
Appropriation	$10,224,000	$11,888,000
Comparative transfer to "Office of the Secretary, salaries and expenses"	-39,000	---
Cutback required by P.L. 90-364	-102,000	
Total currently authorized for obligation	10,083,000	11,888,000
Plus: Proposed release of reserves for increased pay costs	102,000	
Total available for obligation	10,185,000	11,888,000

Disposition of cutback:
To be used for pay costs in this account..... 102,000

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
76	1. Grants:						
	(a) Research	---	$1,259,000	---	$1,339,000	---	+$80,000
	(b) Fellowships	---	150,000	---	150,000	---	---
	(c) Training	---	3,850,000	---	5,276,000	---	+1,426,000
79	2. Direct operations	243	4,926,000	243	5,123,000	---	+197,000
	Total NOA available	243	10,185,000	243	11,888,000	---	+1,703,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	243	243	---
Full-time equivalent of all other positions	20	20	---
Average number of all employees	257	258	+1
Personnel compensation:			
Permanent positions	$2,545,000	$2,570,200	+$25,200
Positions other than permanent	194,000	194,000	---
Other personnel compensation	4,000	4,000	---
Total personnel compensation	2,743,000	2,768,200	+25,200
Personnel benefits	315,000	316,500	+1,500
Travel and transportation of persons	200,000	200,500	+500
Transportation of things	30,000	30,000	---
Rent, communications, and utilities	162,000	162,800	+800
Printing and reproduction	67,000	67,000	---
Other services	1,245,000	1,423,000	+178,000
Supplies and materials	94,000	94,000	---
Equipment	70,000	61,000	-9,000
Grants, subsidies, and contributions	5,259,000	6,765,000	+1,506,000
Total obligations by object	10,185,000	11,888,000	+1,703,000

Summary of Changes

1969 estimated obligations	$10,185,000
1970 estimated obligations	11,888,000
Total change	+1,703,000

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay raise	---	---	---	$5,000
B. Program				
1. Research grants	---	$1,259,000	---	80,000
2. Dental auxiliary utilization grants	---	3,200,000	---	1,220,000
3. Research training grants	---	450,000	---	106,000
4. Continuing education	---	200,000	---	100,000
5. Direct operations	243	4,920,000	---	139,000
Total program increases	---	---	---	1,645,000
C. Payment to "National Institutes of Health management fund" for centrally furnished services	---	6,000	---	62,000
Decreases				
A. Built-in				
1. Non-recurring program costs	---	---	---	-9,000
Total net change requested	---	---	---	+1,703,000

Explanation of Changes

Research grants

The requested increase of $80,000 is for continuation of research projects already underway in the most critical areas of dental health in need of research.

Dental auxiliary utilization grants

The requested increase of $1,220,000 will permit the initiation of developmental programs in three new dental schools and will strengthen existing programs by lengthening the time of clinical experience and broadening the scope to include other types of auxiliaries.

Research training grants

The requested increase of $106,000 will provide for the continuation and orderly progress of the five long-range, training programs now under way and thus, will permit realization of the planned return on the investment in terms of production of well-qualified researchers in dental public health.

Continuing education grants

The requested increase of $100,000 will support two additional projects adding approximately 4,000 dentists who will receive direct benefits from the program. Five projects were supported in 1969.

Direct operations

The requested program increase of $139,000 will enable us to provide for extension of dental manpower survey activities; continuing development of dental health programs for children; and further epidemiologic investigations into causes of oral malfunctions and periodontal diseases and evaluation of new restorative materials. These will largely be carried out through contracts.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301-Research Grants, Research Training Grants and Research Fellowships.....	Indefinite
Section 422-Dental Auxiliary Utilization Training Grants and Grants for Continuing Education of Dentists.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Title III - General Powers and Duties of Public Health Service

Part A - Research and Investigations

Research Grants, Research Training Grants, and Research Fellowships

Section 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impariments of man, including water purification, sewage treatment, and pollution of lakes and streams. In carrying out the foregoing the Surgeon General is authorized to--...

(c) Establish and maintain research fellowships in the Service with such stipends and allowances, including traveling and subsistence expenses, as he may deem necessary to procure the assistance of the most brilliant and promising research fellows from the United States and abroad;

(d) Make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for such research or research training projects as are recommended by the National Advisory Health Council, or, with respect to cancer, recommended by the National Health Advisory Cancer Council, or, with respect to mental health, recommended by the National Advisory Mental Health Council, or with respect to health diseases, recommended by the National Advisory Heart Council, or, with respect to dental diseases and conditions, recommended by the National Advisory Dental Research Council, and include in the grants for any such project grants of penicillin and other antibiotic compounds for use in such project; and make, upon recommendation of the National Advisory Health Council, grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs: PROVIDED, That such uniform percentage, not to exceed 15 per centum, as the Surgeon General may determine, of the amounts provided for grants for research or research training projects for any fiscal year through the appropriations for the National Institutes of Health may be transferred from such appropriations to a separate account to be available for such research and research training program grants-in-aid for such fiscal year;....

Title IV - National Research Institutes

Part C - Dental Disease Research Training

Dental Auxiliary Utilization Training Grants
and
Grants for Continuing Education of Dentists

Appropriation

Section 422. In carrying out the purposes of section 301 with respect to dental diseases and conditions the Surgeon General, through the Institute and in cooperation with the National Advisory Dental Research Council (hereafter in this part referred to as the "Council"), shall--...(if) provide training and instruction and establish and maintain traineeships, in the Institute and elsewhere in matters relating to the diagnosis, prevention, and treatment of dental disease and conditions with such stipends and allowances (including travel and subsistence expenses) for trainees as he may deem necessary, the number of persons receiving such training and instruction, and the number of persons holding such traineeships, to be fixed by the Council, and, in addition, provide for such training, instruction, and traineeships through grants, upon recommendation of the Council, to public and other nonprofit institutions.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to "Office of the Secretary, salaries and expenses"	$39,000	---	To support four positions for program services.

Dental Health

	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1962	$2,182,000	$2,182,000	$2,500,000	$2,500,000
1963	2,506,000	2,506,000	3,006,000	3,006,000
1964	6,287,000	6,270,000	6,270,000	6,270,000
1965	6,719,000	6,708,000	7,228,000	7,228,000
1966	7,903,000	7,903,000	8,383,000	8,383,000
1967	9,196,000	9,193,000	9,693,000	9,693,000
1968 1/	9,783,000	9,635,000	9,635,000	9,635,000
1969	11,173,000	10,224,000	11,173,000	10,224,000
1970	11,888,000			

1/ Included in Health Manpower Appropriation in Fiscal Year 1968.

Justification

Dental Health

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	243	$3,058,000	243	$3,084,700	---	+$26,700
Other expenses.....	---	7,127,000	---	8,803,300	---	+1,676,300
Total.....	243	10,185,000	243	11,888,000	---	+1,703,000

General Statement

Three broad program areas--manpower, community programs, and technology--have been chosen for major emphasis by the Division. These programs are carried out: (1) By staff in Bethesda; (2) at the Dental Health Center, applied research facility in San Francisco; (3) at the Dental Manpower Development Center in Louisville; and (4) by dental consultants stationed in the nine Regional offices.

The Division's manpower activities are aimed at increasing the size and quality of the dental manpower pool so it will be better able to cope with the Nation's dental needs. Facts about supply and demand for dental care, geographic distribution of manpower and population, and dental productivity are being collected continuously. From such data estimates are made of future manpower requirements. Present and future needs for dentists, auxiliary personnel and for teaching facilities are being identified and constantly updated for use in program planning.

Tomorrow's citizens are expected to create unprecedented demands for dental services. To meet these demands, anticipated for many years, many more dentists and supportive dental auxiliary personnel will be needed. The Division administers or participates in grants programs for the construction of new and expansion of existing dental schools. Over the past four years funds have been made available for modernizing and expanding 20 existing dental schools and for building five entirely new schools.

Valuable as these new facilities will be as a means of increasing the dental work force of the future, school expansion alone cannot provide enough manpower to handle the anticipated growth in demands for care. Dentists are therefore being taught how to use auxiliary personnel effectively and productively. All dental schools now participate in this Division-supported activity. Through the 1968 school year, this training has been provided to over 24,000 dental graduates.

To help dental practitioners keep abreast of advances in dentistry, and thus provide the highest quality care, the Division is exploring a variety of means of bringing education to the dentist in his own setting. Programmed instruction, for example, has been adapted to serve the practicing dentist in his own community. Teaching machine courses covering a variety of dental subjects are now available, and such media as educational TV and computer-assisted instruction are being tested as ways of bringing continuing advanced education to the busy practitioner.

Education research is an important part of the Division's manpower program. This program area includes studies of methods of recruitment and selection of dental students, selection, recruitment and development of dental teachers, design of instructional facilities and methods of instruction.

In addition to its intramural program, the Division stimulates and supports research in areas of Division responsibility through research grant funds. The Division supports research projects, research training, and research fellowships through grants for activities which complement intramural programs. Dentists and investigators from other fields are being prepared for research in areas such as dental administration, economics, statistics, epidemiology, and the health aspects of urban planning.

The community programs portion of the Division is directed towards developing dental disease prevention programs at the community level and improving and strengthening public dental health programs. The promotion of community water fluoridation is a prime example of the activities in this area. Since 1967, more than half the population in the United States with access to public water supplies has been receiving the benefits of this public health measure. Children who drink fluoridated water as their teeth are developing benefit greatly, with tooth decay reduced by 60 percent. Studies supported by the Division have shown that dental bills are cut in half when a population has the advantage of fluoridation.

Public health specialists believe that without fluoridation the dental manpower shortage would be even greater than it is now. They also anticipate that wider application of controlled fluoridation will have a marked effect on dental manpower requirements of the future, in addition to obvious economic benefit.

The Division also promotes the development and evaluation of preventive periodontics and orthodontics programs and promotes and evaluates cytologic methods for early detection of cancer of the mouth.

Publicly supported dental care programs, including cooperative programs with the Office of Economic Opportunity, are also a responsibility of the staff working in the community programs area. Through a reimbursable agreement, technical assistance and consultation is being provided to the dental programs of the Office of Economic Opportunity. Project Head Start, for example, has brought dental care to more than two million pre-schoolers.

As more and more people come to expect regular dental care, prepayment plans that provide a means to pay dental bills will become of increasing interest. The Division maintains a clearinghouse of information on the planning and operation of prepaid dental care plans as well as costs of services, patterns of use of services, and dental care needs. Presently, about four million Americans are enrolled in prepaid dental care plans. In contrast, approximately 85 percent of the population has the protection of medical insurance.

The technology program of the Division encompasses research and development activities such as dental epidemiology and clinical evaluation of dental materials and techniques.

Periodontal disease, the gum disorder which is the major cause of tooth loss among adults, is a long-term interest of the Division's epidemiologists, who are concerned not only with biological factors but with the social and environmental aspects of this pervasive disease.

Because of the particular susceptibility of school-age children to tooth decay, Division scientists are concentrating on studies which will lead to improved decay-resistance among these young people. In this major effort to develop effective methods for controlling dental decay, the Division is experimenting with a number of topically applied agents in search for the agent that is both effective and economical in preventing tooth decay and requires a minimum expenditure of professional time for application.

Congenital clefts of the lip and palate, which are present in at least one of every 700 new births, present another challenge to dental epidemiologists. To learn more about these disfiguring congenital malformations, scientists at the Division's Dental Health Center have analyzed birth certificates from 29 states and two cities over a four-year period and from four states for a ten-year period. These statistics form a new base from which to build a better understanding of the significance of such variables as age of parents, birth weight of the child, season of birth, race and geographic location. Follow-up studies of twins identified from the birth certificates are now being conducted to learn more about the relative importance of genetic and non-genetic factors in cleft causation.

Applied clinical research to evaluate and compare new and conventional dental materials, procedures and devices is another important activity underway at the Dental Health Center. Relatively few studies have tested, in the complex oral environment, the many new materials now available to the practitioner. Research is helping to provide valid standards by which dental practitioners and researchers can judge the relative merits of new products.

A corollary to this effort is the development and testing of reproducible systematic data-gathering methods which must be available if clinical evaluation of pertinent characteristics is to be meaningful. The clinical measurement systems being perfected will be useful in other testing laboratories as well. The training of clinical researchers in the use of measurement systems is still another facet of this program.

Grants

	1969 Estimate	1970 Estimate	Increase or Decrease
Research	$1,259,000	$1,339,000	+$80,000
Fellowships	150,000	150,000	-0-
Training grants	3,850,000	5,276,000	+1,426,000
Total	5,259,000	6,765,000	+1,506,000

RESEARCH GRANTS

	1969 Estimate	1970 Estimate	Change
New and competing	$361,000	$361,000	-0-
Non-competing continuations	898,000	978,000	+$80,000
Total	1,259,000	1,339,000	+80,000

The authority for this program is contained in Section 301 of the Public Health Service Act with an indefinite authorization for 1970.

In 1969 research projects relevant to the Division's mission have been supported at 32 universities and non-profit agencies. Several of these projects are to conduct research in dental health with the purpose of increasing and improving the supply of dental and allied manpower and developing ways of

increasing their productivity. Three new projects were funded to extend efforts to provide for more effective treatment and prevention of oral diseases through improved dental practice techniques: (1) Determination of the extent to which dental practitioners utilize new technological developments; (2) study of long-range effects of post-graduate training and experience on preventive dentistry programs; (3) study of extent of patient compliance with dentist's advice. Also, support was provided for the continuation of research to determine ways of extending dental services to more people. One project is finalizing testing and refining an outline of methods for establishing service coverage and premium charges for dental care prepayment plans.

The requested increase of $80,000 is for continuation of research projects already underway in these most critical areas of dental health in need of research. In addition, much-needed research emphasizing special population groups will be undertaken. A study of selection factors and success criteria for dentists will be supported. One high-quality proposal designed to facilitate the selection of the most promising dental hygiene students will be funded, leading to a goal of better-educated dental hygienists, in greater numbers, working more years after graduation. Another project that will be undertaken in 1970 will study patient responses to different methods of dental clinic organization and operation. Such a study may result in more efficient utilization of personnel and facilities, better attitudes of patients toward dental health, and improvement in dental services without comparable increase in costs.

FELLOWSHIPS

	1969 Estimate	1970 Estimate	Change
New and competing	$80,000	$45,000	-$35,000
Non-competing continuations	70,000	105,000	+35,000
Total	150,000	150,000	-0-

The authority for this program is contained in Section 301 of the Public Health Service Act with an indefinite authorization for 1970.

In 1969 a budget of $150,000 supported 13 fellows pursuing advanced degrees in research specialties, such as dental health administration, epidemiology, computer methodology, dental economics, statistics and the behavioral sciences.

Individuals, none of whom have completed training as yet, will be prepared to conduct research to help improve dental health by obtaining information about preventive dentistry, dental diseases, dental education and more effective methods of delivering dental services.

TRAINING GRANTS

	1969 Estimate	1970 Estimate	Change
DENTAL AUXILIARY UTILIZATION GRANTS	$3,200,000	$4,420,000	+$1,220,000

The authority for this program is contained in Section 422 of the Public Health Service Act with an indefinite authorization for 1970.

One of the most productive activities of the Division of Dental Health is the Dental Auxiliary Utilization program. This program is helping dental schools to develop formal classroom and clinical instruction in the effective utilization of dental auxiliaries. By teaching the concept of greater productivity through

proper use of auxiliary personnel while dental students are in school and at the time their patterns of practice are developing, future practitioners are being trained who can effectively treat many more patients. Recent studies indicate that a dentist who uses one chairside assistant can increase his productivity by nearly 30 percent.

In fiscal year 1969 grant funds in the amount of $3,200,000 will be awarded to 49 dental schools for the training of approximately 8,600 students in the concepts of dental auxiliary utilization. A total of $4,420,000 in grant support for fiscal year 1970 will permit the initiation of developmental programs in three new dental schools, and will permit present dental auxiliary utilization programs to lengthen the training and include other types of auxiliaries such as dental hygienists. A direct correlation between hours of instruction in auxiliary utilization and actual use in practice after graduation has been demonstrated. The need to increase length of exposure to the concept of dental assistant utilization is evidenced by the fact that many of today's dental graduates are still not fully incorporating these concepts in their practice. An increase in hours of instruction and consequent increase in auxiliary utilization in the practices of future dentists will assure continued progress toward providing adequate dental care for the Nation.

RESEARCH TRAINING	1969 Estimate	1970 Estimate	Change
New and competing	$150,000	$150,000	-0-
Non-competing continuations	300,000	406,000	+$106,000
Total	450,000	556,000	+106,000

The authority for this program is contained in Section 301 of the Public Health Service Act with an indefinite authorization for 1970.

The appropriation of $450,000 in fiscal year 1969 provides support for five research training grants, including a new program in dental behavioral science. Eighteen full-time students participated directly in these programs. Also sponsored in this year was a research training conference-institute designed to identify areas of dental education urgently in need of research and to develop solutions to problems of conducting educational research in dental schools. At the same time the institute provided a formal, academic introduction to educational research methodology for thirty young dental school faculty members interested in continuing this type of training and in conducting research in dental education.

The increase of $106,000, requested for 1970, will provide for the continuation and orderly progress of the five long-range, training programs now under way and, thus, will permit realization of the planned return on the investment in terms of production of well-qualified researchers in dental public health.

CONTINUING EDUCATION GRANTS	1969 Estimate	1970 Estimate	Change
New and competing	-0-	$100,000	+$100,000
Non-competing continuations	$200,000	200,000	-0-
Total	200,000	300,000	+100,000

The authority for this program is contained in Section 422 of the Public Health Service Act with an indefinite authorization for 1970.

These grants instituted in 1967 are laying the groundwork for the development of a much-needed national continuing education network of schools to provide instruction for dental practitioners in both urban and rural areas. Five projects are currently being supported. These are Tufts University, University of Iowa, University of California at San Francisco, University of Pittsburgh and Temple University. Over the next three to seven years, existing projects will contribute to up-grading the skills of 29,000 dentists and auxiliaries. Two additional projects will be funded in 1970 adding approximately 4,000 dentists who will receive direct benefits from this program. Materials, such as programmed courses, audio-visual tapes, and teaching machine material, developed by these programs will reach another 20,000 dental workers of all types each year.

Direct Operations

	1969 Estimate		1970 Estimate		Increase or Dec.	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	243	$3,058,000	243	$3,084,700	---	+$26,700
Other expenses	---	1,868,000	---	2,038,300	---	+170,300
Total	243	4,926,000	243	5,123,000	---	+197,000

The annual attack of dental disease in the United States reaches epidemic proportions--a continuous dental plague to which almost everyone eventually falls victim.

Because of the unique nature of dental problems, solutions sufficient for other health problems often are inadequate to meet dental needs. Dental diseases are not self-healing or curable with drugs. They begin at an early age, recur throughout life and, unless treated, become progressively more severe. Dental diseases are universal and the massive backlog of untreated defects increases daily. The Division activities are carried out under these principal programs: (1) Manpower and Education; (2) Community Programs; and (3) Dental Technology.

Manpower and Education

Basic to the Division's manpower operations is the continuing analysis of current supply and demand of dental services, of economic factors relating to dentistry and the characteristics of dental manpower. A State-by-State survey of registered dentists and a study seeking basic data on active and inactive licensed hygienists is now providing information on the distribution and characteristics of a portion of the dental manpower problem. Studies confirm that rural America has long-suffered as a result of a poor dentist-population ratio and inability to support dental services. Financial difficulties are being alleviated with new public programs for deprived rural and ghetto areas, but the dental manpower problem in these areas still exists. A pilot study underway in Kentucky will determine additional factors needed to launch a minimal program in 1970, designed to attract the dentist to rural areas.

Major progress in dental productivity is dependent upon continued exploration of those functions that can be delegated to dental auxiliaries and devising methods of training auxiliaries to undertake these functions in conjunction with the dentist. The studies in Louisville, Kentucky are exploring the use of teams composed of one dentist and five chairside assistants to deliver dental care. Preliminary data from this study indicates that the dentist's productivity can be increased by 50 to 60 percent by increased use of auxiliary personnel. It is time now to begin training dental leaders and teachers in the latest concepts and techniques being developed for greater auxiliary utilization.

New knowledge is accruing so fast that dental and dental auxiliary schools are hard-pressed to include all relevant information in undergraduate curriculums. The practicing dentist, unaided, finds it impossible to keep up-to-date. Division education research programs focus on the development or adaptation of time-saving teaching materials and techniques. They range from the production of self-instruction manuals to the programming of courses for self-teaching machines, television and the development and evaluation of computer-assisted teaching techniques. The need for training of teachers in new educational practices is recognized by dental educators. Of some 6,700 teachers in dental schools and schools of dental hygiene, the Division has been successful in reaching less than one percent with a single summer institute for teachers and two programs offered in university settings. In response to this need for teacher-training, training sessions will again be offered in 1970, supplemented with a series of short course offerings at the Dental Health Center in San Francisco.

An increase of $81,000 is requested for this activity (including $44,000 for payment to"National Institutes of Health management fund"for centrally furnished services) to provide for the extension of the Dental Manpower Survey Activities described above.

Community Programs

Coordinated statewide efforts have extended benefits of fluoridation to a greater portion of our population. Approximately 82 million people now have access to public water supplies containing fluoride. However, about 48 percent of the population on public water supplies still lack this scientifically sound dental decay-preventive measure. In 1970 emphasis will be given to: (1) Expanding technical assistance to support coordinated statewide action; (2) providing increased information and technical assistance to small communities (a vast majority of unfluoridated communities are under 10,000 population); and (3) developing school fluoridation programs in rural communities where community water supplies are not available. The goal of this expanded effort is to bring this proven health measure to at least 50 percent of the population by the end of fiscal year 1970.

Scientific evidence gathered to date, demonstrates a positive association between poor oral hygiene and periodontal disease (pyorrhea). Currently the Division is supporting two projects to demonstrate the effectiveness of prophylaxis, toothbrushing, dental health education and professional education to diminish the periodontal disease problem. In 1970 a project will be undertaken in a selected community applying proven successful periodontal preventive and control measures developed through current research to demonstrate their effectiveness in the community setting.

Requests for consultation and technical assistance from communities and the private sectors in the development of administrative mechanisms necessary for organizing, financing and delivering dental health care services continue to increase. Prepaid or insured dental care coverage may be expected to nearly double in the next two or three years. In 1969 it is anticipated that the number of prepaid or insured plans will increase from the current estimate of 1,100 plans covering about 4.5 million persons to 1,500 plans with a membership of over six million. Additionally, the number of mechanisms to provide insurance required to meet increased consumer needs and demands for dental services in both the public and private sectors of the economy may be expected to increase. In the past year, at least six new dental service corporations were activated as a direct result of the need for administrative mechanisms to serve new publicly-funded care programs. Several of the Nation's largest labor unions are currently negotiating for dental health benefits.

The protection of children against the ravages of dental diseases could, within a generation, be reflected in higher levels of dental health among young people and eventually raise the dental health of the Nation. In 1968 the Division instituted a contract with the Tennessee Department of Public Health, designed to provide a coordinated dental health program for school-age children in seven counties in Tennessee. This project will be continued in 1970 utilizing direct technical assistance from the Division.

An increase of $18,000 is requested for this program to provide for the continuing development of these dental health programs for children.

Dental Technology

The evaluation of new and conventional dental materials, procedures and devices will make it possible for practicing dentists to improve their treatment regimen and clinical effectiveness. Studies of bacterial aerosol exchange between patients, dentists and auxiliaries are yielding practical data regarding bacterial hazards to dental personnel and their patients. These studies are expected to document the need to modify dental school construction requirements, clinical procedures, equipment and to develop precautionary measures. New uses of intermediate, restorative materials in children's care programs show considerable promise as a time and money saver. These will be evaluated in 1970.

The epidemiologic studies of cleft lip and palate have provided new information about this malformation. A follow-up study of twins in California, since 1967, is providing clues to the relative importance of genetic and non-genetic forces in the causation of clefts. In 1969 this study was expanded to three additional States of high incidence in the midwest. The data collection phase of a three-year study to determine if good oral hygiene effectively retards the initiation and progression of periodontal disease was completed early in fiscal year 1969. Data based on the first two-years of the study shows that there is marked retardation of the disease with good oral hygiene practices. Studies now are underway to determine ways of preventing calculus formulation and the optimum frequencies for professional cleaning of the teeth.

Studies to develop and evaluate new topically-applied fluoride agents and efficient methods for their application as dental caries preventatives are continuing.

An increase of $98,000 is requested for this activity (including $18,000 for payment to "National Institutes of Health management fund" for centrally furnished services) to provide for further epidemiologic investigations into the causes of oral malformations and periodontal diseases and the evaluation of new restorative materials.

Construction of Health Educational, Research, and Library Facilities

WITNESSES

DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JOSEPH A. GALLAGHER, DEPUTY DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
DR. VIRON L. DIEFENBACH, DIRECTOR, DIVISION OF DENTAL HEALTH
THOMAS D. HATCH, ASSISTANT DIRECTOR, DIVISION OF ALLIED HEALTH MANPOWER
DAVID F. KEFAUVER, ASSOCIATE DIRECTOR FOR EXTRAMURAL PROGRAMS, NATIONAL LIBRARY OF MEDICINE
DR. FRANK W. McKEE, DIRECTOR, DIVISION OF PHYSICIAN MANPOWER
MISS JESSIE SCOTT, DIRECTOR, DIVISION OF NURSING
DR. THOMAS G. BOWERY, ACTING DIRECTOR, DIVISION OF RESEARCH FACILITIES AND RESOURCES
JOHN W. HAMBLETON, FINANCIAL MANAGEMENT OFFICER, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
LELAND B. MAY, ASSISTANT DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Teaching facilities:			
(a) Medical, dental, and other health personnel	150,799	130,196	141,000
(b) Nurses	19,382	18,781	8,000
(c) Allied health professions personnel	1,792	3,008	----------
2. Health research facilities	38,368	20,640	----------
3. Medical libraries	10,000	1,250	----------
Total program costs, funded—obligations	220,341	173,875	149,000
Financing:			
Comparative transfer from other accounts	−10,000	−1,250	----------
Unobligated balance available, start of year	−74,666	−102,324	−22,900
Unobligated balance available, end of year	102,324	22,900	----------
Budget authority (appropriation)	238,000	93,200	126,100
Distribution of budget authority by account:			
Construction of health educational facilities	203,000	84,800	----------
Grants for construction of health research facilities	35,000	8,400	----------
Construction of health educational, research, and library facilities			126,100
Relation of obligations to outlays:			
Obligations incurred, net	210,341	172,625	149,000
Obligated balance, start of year	408,144	511,381	556,534
Obligated balance, end of year	−511,381	−556,534	−539,939
Adjustments in expired accounts	27	----------	----------
Outlays	107,131	127,472	165,595
Distribution of outlays by account:			
Construction of health educational facilities	60,689	89,230	120,305
Grants for construction of health research facilities	46,442	38,242	45,290

Mr. FLOOD. We now have the appropriation item "Construction of health educational, research and library facilities." As the witness we have Dr. Leonard D. Fenninger, who is the Director, Bureau of Health Professions Education and Manpower Training.

Do you have anybody here we do not know?

Dr. FENNINGER. Mr. Kefauver from the National Library of Medicine.

Mr. FLOOD. We have met him before. In fact I don't see a stranger in the room.

You have a statement, Doctor? How do you wish to proceed?

Dr. FENNINGER. May I proceed by reading it?

Mr. FLOOD. Yes.

GENERAL STATEMENT

Dr. FENNINGER. Mr. Chairman and members of the committee; I would like to discuss the construction programs which are administered by the Bureau of Health Professions Education and Manpower Training in support of its primary responsibilities to increase the numbers and quality of capable men and women who will minister to the health needs of the American people. The passage of Public Law 90–490, the Health Manpower Act of 1968, which will become effective on July, 1, 1969, provides for the extension of the several separate construction authorities for educational and research facilities for health professional education and training. It will also provide for a more uniform administration of the construction of such facilities. One of the principal amendments in this legislation provides for Federal assistance in constructing multipurpose facilities which, in addition to the primary concern for teaching space, may also include space for research and library activities.

The construction of new facilities, and appropriate expansion and refurbishing of existing facilities, is an essential ingredient in supporting educational and training programs to produce vitally needed health manpower. With the increasing scope and complexity of health services, the educational preparation of those who will render these services also changes, and the associate facilities must keep pace with and reflect this progress.

Obsolescent and overloaded facilities are a major deterrent to expanding the manpower so essential to meeting the needs of an expanding population including the aged, the young, and the disadvantaged, which requires improved health services. Planning and construction is always a long term process, even more so for a new medical or dental school which may encompass 10 years from planning to the productive yield of its first graduating class. Initial construction costs of health professions schools are high, but are justifiably related to design of buildings for most effective and economical programs of education in the health professions. Expansion and renovation of established schools generally requires less time, but costs often may be equal to or exceed costs of new construction, particularly in rundown urban areas or in more isolated rural situations.

We are deeply concerned, as are all responsible Americans, that medical facilities and manpower are least available in areas of greatest need. The concentration of health workers and practicing physicians, like other professional people, is in the suburbs or away from urban

population centers, and the inner city and rural citizens are consequently being deprived of immediate attention and left with inadequate health services and aging facilities. Contemporary education in the health professions, with a coordinated approach to providing health services largely replacing the former self-sufficiency of the solo practitioner, has increased the importance of facilities for adequate and efficient housing of the instruments and human talent on which we depend and of which we are so justly proud, both for the provision of education and training, and for the ultimate service to people. Because these facilities are presently supported by several specific Federal programs, I should like to speak to the progress and needs for each of these important assistance programs.

HEALTH PROFESSIONS EDUCATIONAL FACILITIES

From the beginning of the program in 1965 through December 31, 1968, 242 applications for construction assistance have been received from 144 schools. Of these, 157 project applications from 125 schools have been approved and awarded grants. The total teaching construction costs for these projects, including applicants' share and Federal assistance, is $841,475,676. The Federal assistance amounted to $456,480,069. Upon completion of construction of these projects, 4,507 new first-year student places will be created in addition to the 20,000 places which existed prior to 1965. The 4,507 places include 1,879 student places in medicine and 871 in dentistry. These places will make it possible to admit an additional 4,507 students year after year, resulting in a substantial increase in the number of health professionals. $154,100,000 of these funds have made possible the establishment and development of 12 new medical schools, five new schools of dentistry, two new schools of nursing (funded prior to the first appropriation under the Nurse Training Act of 1964) and one new school of public health. In addition, 44 existing medical schools, 21 dental schools, two schools of osteopathy, five schools of public health, five schools of optometry, 12 schools of pharmacy, 14 schools of nursing and two schools of veterinary medicine have received construction funds enabling them to expand their enrollments substantially and to improve their educational programs.

As of December 31, 1968, 30 applications requesting $185,385,746 in Federal assistance have been approved for funding. Seventeen applications in the amount of $61,100,000 have been received and await review. In addition, 181 institutions have indicated their intention to request assistance in constructing facilities under this program within the next 4 or 5 years.

These applicants would require an estimated $777 million Federal share and would provide approximately 6,600 first-year student places. Our request for construction funds for health professions educational assistance during fiscal year 1970 is $118,100,000, an increase of $43,100,000 over the fiscal year 1969 appropriation.

NURSING EDUCATIONAL FACILITIES

Construction funds for schools of nursing are needed (1) to enable those educational programs in nursing which are capable of expansion to do so, and (2) to replace and renovate obsolete facilities so

that the quality of education will be improved and enrollments will be maintained. During the past few years some nursing schools have been unable to admit qualified applicants because of lack of space. There is evidence that additional thousands of students could be admitted to nursing programs if urgent needs for improvement and expansion of schools are met.

Many nursing education programs occupy makeshift buildings, such as military barracks, dormitories, former hospitals, and basements. Many are poorly ventilated, noisy, and structurally unsafe. It is essential that these obsolete educational facilities be replaced with modern teaching facilities. Every year the need for construction funds for schools of nursing becomes more critical as existing facilities deteriorate and the need for expansion of enrollments increases.

Through fiscal year 1969, $73 million in Federal funds will be awarded for construction of nursing educational facilities under Public Law 88–581.

As of December 31, 1968, and during the 40 months of operation under Public Law 88–581, 187 applications have been received, 102 of these have been funded representing a total construction cost of $101,454,068 and Federal participation totaling $57,580,858. Upon completion of construction these projects will provide 4,037 additional first-year places, and maintain approximately 14,500 existing places in nursing education facilities. Twenty-one new schools of nursing will have been built and many more expanded. Twenty additional applications representing $16,399,259 in Federal funds have been approved but not yet funded. Twenty-two other applications requesting Federal funds of $9,207,915 are awaiting Council action. As of December 31, 1968, 129 letters of intent show that many more institutions are actively planning to submit applications. These institutions indicate that they will request Federal participation amounting to $88 million. Our request for fiscal year 1970 of $8 million is the same as in fiscal year 1969.

ALLIED HEALTH PROFESSIONS EDUCATION FACILITIES

The Allied Health Professions Personnel Training Act of 1966 authorizes construction for eligible allied health programs similar to that for the health professions. These grants will assist in increasing the number, improving the quality, and enlarging the training opportunities for allied health personnel.

Under the new Health Manpower Act of 1968, the current program is extended through fiscal year 1970. Thereafter, based upon 2 years experience, new legislation may be requested to modify, revise and improve the act. As of December 31, 1968, eight applications have been received and one has been funded. The total teaching facility cost for the funded project is $3,004,800 with Federal participation tot[illegible]g $1,791,920. Of the remaining seven applications, three reques[illegible]g $2,323,209 in Federal participation are approved but unfunded [illegible]d four requesting $3,766,014 in Federal participation are awaiting council review. Upon completion of construction the project which has been funded will provide 337 additional first-year student spaces. Through the balance of fiscal year 1969, $3,008,080 in Federal funds is available for awarding grants. We are not requesting construction funds under the allied health program for 1970.

HEALTH RESEARCH FACILITIES

Since its inception, the program has made 1,467 awards totaling $460 million for 1,159 projects throughout the country. About 55 percent of the funds have gone to medical schools, 25 percent to other academic institutions and 20 percent to nonacademic biomedical research institutions.

A substantial amount of critical research space has been constructed and remodeled with the aid of health research facilities grants. But the national biomedical research community continues under heavy pressure to accommodate expanding student enrollments in the health sciences and to expand research programs to take advantage of the burgeoning opportunities to pursue important research objectives.

As of December 31, 1968, there was 83 projects totaling $85 million which had been recommended for funding by the National Advisory Council on Health Research Facilities. $20,639,433 is available for obligation in fiscal year 1969. There is no request for construction funds for this purpose for fiscal year 1970.

SUMMARY OF REQUEST

To summarize our construction request for fiscal year 1970, the estimate is $126,100,000, a net increase of $32,900,000 over the appropriation available in fiscal year 1969. This increase includes $43,100,000 for construction of educational space in health professions schools, offset by decreases for research ($8,400,000) and allied health facilities ($1,800,000). The nursing construction request of $8 million remains at the same level as in 1969.

Thank you, I shall be happy to answer any questions.

UNOBLIGATED BALANCES

Mr. FLOOD. For this item the unobligated balances are almost as significant as the appropriation. I want to be sure you understand the situation on this side of the table this year. We are looking at unobligated balances carried forward with the finest kind of microscope, not only this subcommittee but all subcommittees.

You show $102,324,292 was carried forward from 1968 to 1969. Why was such a large balance unused in 1968? That is a large balance, even for the Defense Department.

Mr. HAMBLETON. That was a part of the Department's plan, to defer obligations under a congressional directive, Public Law 90–218 that set a ceiling on obligations in fiscal year 1968. We deferred obligations in 1968 for that reason.

Mr. FLOOD. In other words, it is not your fault; it is ours. Is that it? If it hadn't been for the congressional fiat, this condition would not have existed, would it?

Mr. HAMBLETON. The Department set the obligation level for this program under the overall controls imposed by Public Law 90–218. We usually have a balance but not as large as that, Mr. Chairman.

Mr. FLOOD. About how large?

Mr. HAMBLETON. Each year we usually have $10 to $20 million.

Mr. FLOOD. There is a lot of difference between $10 or $20 million and $102 million, and you suggest the reason for that wide discrepancy in this unobligated balance is because of the congressional action?

Mr. HAMBLETON. It was the overall ceiling on obligations under Public Law 90–218 under which the Department set the obligation level for this program.

Mr. FLOOD. You show only $22.9 million will be carried forward from 1969 to 1970. Is that still a pretty good estimate?

Mr. HAMBLETON. That is a pretty good estimate. Each year many good projects that we fully expect to fund are deferred because of various reasons. We sometimes need more information or the applicants are awaiting matching funds, or something of that sort.

Mr. FLOOD. You will stand by that figure?

Mr. HAMBLETON. I think that is a pretty good estimate.

Dr. GALLAGHER. It is quite a close figure.

Mr. FLOOD. Do you stand by it?

Dr. GALLAGHER. Yes, sir.

Mr. FLOOD. In total, you had $173,874,292 available for obligation this year. How much have you actually obligated?

Mr. HAMBLETON. We have obligated a little over $80 million out of $173 million.

PRIORITIES IN THE BUDGET

Mr. FLOOD. Suppose you give us the reasons for the priorities in your budget. For instance, you have no funds allocated for medical libraries, health research facilities, or allied health professions' teaching facilities. Why not? People are crying about these things. Not a dime. Why not?

Dr. FENNINGER. Sir, if I may start the answer, there are at least two factors involved in this.

First of all, there is the whole question of availability of resources for these particular purposes, which we talked about at some length yesterday. That has to do with the great demands for many other functions that have to be carried out within the country. I think this is an overriding consideration.

Under the new legislation for the multi-purpose facilities, for the first time institutions can be planned so that those portions of the institution that are involved with research and with the creation of a library or its expansion, where the research and the library purposes are primarily concerned with education—and, of course, these are absolutely vital to any institution of higher education—these facilities may be provided for under the multipurpose provision of the act.

So, where the emphasis is on the educational purposes, libraries and laboratories can be included in the applications submitted by schools of the health professions, for primarily educational purposes. It also leaves, obviously, major unmet needs in research and in library development in the United States.

REDUCTION IN NURSING SCHOOL CONSTRUCTION

Mr. FLOOD. I openly and notoriously and unblushingly am an advocate of nurses. You have told us for several years that we must do something for nurses. I have just heard you this morning give a fine presentation about nurses.

So, this is what you do in construction: 1969 estimate, $18,781,034. 1970 estimate, $8 million. Decrease, $10,781,034.

You wear your love lightly on your shoulder, don't you?

Dr. FENNINGER. I am not sure I wear my love lightly on my shoulder, sir. At any rate, with $8 million of new obligational authority we can do some of the things that need to be done.

Mr. FLOOD. Sure, but why did you cut the nurses $10 million, from $18 million to $8 million? That is a hefty cut. Why nurses? Couldn't you spread that around a little bit?

Mr. HAMBLETON. $10 million of the $18 million was a carryover balance from 1968 into 1969. $8 million was appropriated——

Mr. FLOOD. I know, but they are still American dollars. You are budgeting $18 million for this year and $8 million for next year.

Dr. GALLAGHER. Our request is not any different than it was the year before, Mr. Chairman.

Mr. FLOOD. That leaves me cold. Why not?

Mr. GALLAGHER. We were attempting with a certain amount of money available to spread it in the areas that had priority, and this was our best judgment.

Mr. FLOOD. This was your best judgment?

Dr. GALLAGHER. Yes.

Mr. FLOOD. Of course, that is a good answer. You have to exercise your judgment. How much did you ask the Secretary for?

Mr. HAMBLETON. We asked the Secretary for $11 million.

Mr. FLOOD. You asked for $11 million. How much did he ask the Budget Bureau for?

Mr. HAMBLETON. $18.8 million.

Mr. FLOOD. So, he asked the Budget Bureau for $18 million?

Mr. HAMBLETON. $18.8 million. That is correct, sir.

Mr. FLOOD. And the Budget Bureau in its classical lack of judgment, came out with $8 million, is that it?

Mr. HAMBLETON. That is right, sir.

Mr. FLOOD. So you are not the devil in the piece, really, are you? It is our friends in the Bureau of the Budget. Is that where it came from? The Secretary asked for $18 million and you came out with $8 million.

Mr. HAMBLETON. The Bureau of the Budget cut us to $8 million.

Mr. FLOOD. Could you use more for nurses if you got it?

Dr. FENNINGER. Yes, sir.

Mr. CARDWELL. Mr. Chairman, could I say something? I do not want to appear too much on the side of the Bureau of the Budget, but there are two values they were trying to exercise in the review of this budget, and they came into play in this item.

The first was, under a restrained budget you should pull back on construction.

Mr. FLOOD. That has been going on since the War Between the States. Everybody knows that. I know that.

Mr. CARDWELL. Then there is also a conclusion which may not, in the view of some of our witnesses here today, be validated: that of all the chairs open today in nursing schools compared to other kinds of health facilities, they are not being used at the same rate that they would be in other areas. Thus, they gave at this point in time nursing a lower priority in terms of construction, not in terms of unmet needs

as a profession. The conclusion is still that this is a very high priority area, but the problem is matching the facilities with the demand. The demand has not been growing as fast as had been hoped.

This is the position of the Bureau of the Budget. As I say, I am not sure everyone at this table thinks that is valid.

Mr. FLOOD. Will you develop that last part of your statement a bit for the record?

Mr. CARDWELL. Yes, sir.

(The information follows:)

When dealing with the question of capacity of schools of nursing unused and unusable space must be considered. The schools where places are available are not usually those where students want to study. Applicants are looking for a certain type of program (diploma, associate degree, baccalaureate) accreditation status, adequacy of facilities and other criteria that guide them in choosing a school. The type of program is most significant as students increasingly select collegiate programs. The expansion and consequent need for facilities, is in the associate degree programs.

There have been misleading statements regarding existing vacant places in schools of nursing. (p. 8, "Human Investment Programs: Nursing Manpower Programs." March 1968 USDHEW, Office of the Assistant Secretary (Planning and Evaluation), prepared by Jeffrey H. Weiss, and p. 22, Report of the National Advisory Commission on Health Manpower, vol. I, Nov. 1967). These were based upon a June 1967 postcard survey made for purposes of referring potential students not to determine "capacity". In this survey schools indicated 7,600 places were still available. Almost all of these schools also indicated they would accept students until September or October. While these schools were as yet undersubscribed other schools were oversubscribed and had already turned away over 5,000 qualified applicants. It cannot be assumed that schools which do not attract sufficient applicants to fill their spaces provide a reservior of unused capacity for use by applicants turned away at other schools which could not accept additional applicants.

If admissions to schools of nursing are to increase, new places for additional first-year students must be constructed. Of equal significance is the need for construction funds to replace unusable and deteriorating facilities. A large proportion of the Nation's 1,300 schools of nursing are housed in inadequate structures.

The applications for construction grants under the Nurse Training Act represent a definite commitment to construction on the part of schools which must provide almost half of the total construction funds and the attendant costs of planning, and are indicative of the need for these educational facilities.

PRIORITIES FOR SCHOOLS OF MEDICINE, DENTISTRY, ETC.

Mr. FLOOD. For schools of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine, and public health you are requesting an increase from $130,195,745 to $141 million.

You and I are having trouble about priorities. Will you set forth your priorities there? You can do that for the record. That will give you a little more time.

(The information follows:)

CONSTRUCTION PRIORITIES

Experience in program operation has established the following order of demands for funding, and there is no indication of change foreseen.

1. Medicine, including osteopathy.[1]
2. Dentistry.
3. Public health.
4. Pharmacy.
5. Optometry.
6. Veterinary medicine.
7. Podiatry.

FUNDS AVAILABLE COMPARED WITH DEMAND

Mr. FLOOD. Will you place in the record a table showing for each category under your appropriation (1) the funds available at the beginning of the year; (2) the amounts now obligated; (3) the amount of the approved but yet unfunded applications that you have down there; and (4) the amount of the applications that you have on hand that have not been processed.

Mr. Michel.

Mr. MICHEL. Thank you, Mr. Chairman.

Would there be any way of following that kind of table with figures to reflect the number of students in each category that might be affected?

Dr. FENNINGER. Yes, we would be glad to supply that.

Mr. MICHEL. I think that would be a significant figure to include with that.

(The information follows:)

[1] For program purposes, osteopathy is considered as a part of medicine.

Category construction appropriation	Dollars available fiscal 1969 (1)	Obligations to date, Mar. 31, 1969 (2)	Approved and unfunded applications, Mar. 31, 1969 (3)	Applications on hand being processed (4)	Estimated obligations, Mar. 31, 1969 to June 30, 1969 (5)	Estimated total applications approved and unfunded, June 30, 1969 (6)	1st year student places expected columns 3+4−5 (7)	Estimated unobligated balances, June 30, 1969 (8)
Medical and other	$104,695,745	$37,196,206	$171,799,728	$37,349,379	$53,524,950	$155,624,157	844	$1,000,000 to $2,800,000 held and not obligated as representing too small amount for applications pending. Will be carried to 1970 for funding.
Dental	25,500,000	12,379,588	36,953,720	3,408,287	23,250,369	16,111,638	113	
Nurse	18,781,034	10,205,594	16,372,652	16,782,649	8,575,440	24,506,000	1,541	
Allied	3,008,080	1,620,825	702,384	8,539,945	1,387,255	7,965,261	800–1,200	
Health research	20,639,433	20,619,624	86,741,694	11,000,000	0	97,000,000	(1)	
Library	1,250,000	1,222,679	13,952,392	4,415,624	27,321	18,368,016	(1)	
Total	173,874,292	83,244,516	326,522,570	81,495,884	86,765,335	319,569,072		

[1] Not applicable

EFFECTS OF REVENUE AND EXPENDITURE CONTROL ACT—CONSTRUCTION VS OTHER

Mr. MICHEL. On the over-all Revenue and Expenditure Control Act, we are aware, of course, that the first area that usually gets hit under this kind of procedure, which incidentally I did not support, is construction. This limitation that was imposed had to do with the whole Department of HEW, did it not?

Mr. CARDWELL. Yes, sir. We began to hold back construction.

Mr. MICHEL. I guess what I am leading up to is, What portion of the entire cutback in HEW was absorbed simply by the reduction in construction like these items we have been talking about?

Mr. CARDWELL. We can put it in the record. I think the main thing that happened in this particular appropriation, though, is that the holdback began in 1968, began prior to the literal imposition of the Revenue and Expenditure Control Act. It was the result of an administrative decision of the last administration to hold back expenditures in an effort to demonstrate to the Congress that the administration could on its own hold back expenditures. So, the cutback here started to occur in 1968.

We will supply for the record an analysis showing construction versus other kinds of activities.

(The information follows:)

In fiscal year 1968, Public Law 90-218 required that Federal obligations shown in the 1968 budget be reduced. The Department of Health, Education, and Welfare, as part of the overall Federal reduction, was required to decrease 1968 budgeted obligations by over $700 million. Since the fiscal 1968 level of obligation in construction programs was substantial, and construction obligations in 1966 and 1967 had also been at a high level, it was felt that 1968 obligations for construction programs could be reduced without having a long-term detrimental effect.

The Revenue and Expenditure Control Act of 1968 requires the new obligational authority and expenditures on the 1969 Federal budget be reduced. The Department of Health, Education, and Welfare was assigned a very small share of the total decrease. Since a reduction in construction programs would have had little or no effect on 1969 expenditures, the limited reductions which were made involved areas other than construction. No reductions have been made on 1969 construction programs as a result of the Revenue and Expenditure Control Act of 1968.

The only change affecting 1969 construction obligation levels has been in the higher education facilities loan fund. This program has been proposed for conversion from one in which direct Federal loans are provided to higher education institutions to one in which such loans are obtained from private financial sources and the interest subsidized by the Federal Government. This change in method of operation is not related to the requirement to reduce 1969 new obligational authority and expenditures.

ESTIMATED OBLIGATIONS IN 1969

Mr. MICHEL. In response to several of the earlier questions, you mentioned what is obligated and unobligated. Were you talking in terms of some current date?

Mr. HAMBLETON. February 28 is the last figure I have on obligations.

Mr. MICHEL. Let me develop that just a little bit, if I might. The chairman mentioned $173 million being the total available for the current fiscal year, 1969.

Mr. HAMBLETON. Yes, sir.

Mr. MICHEL. I think your response was that $80 million of it had been obligated.

Mr. HAMBLETON. A little over $80 million, that is right.

Mr. MICHEL. As of February?

Mr. HAMBLETON. February 28.

Mr. MICHEL. One step further than that, what is your prediction of what will be obligated between that date and the end of the fiscal year?

Dr. GALLAGHER. $50 or $60 million, at least, will be obligated, perhaps even more, between that date and July 1.

Mr. MICHEL. Let us say $50 million. Then we are talking about a carryover of roughly $40 million, in round, ball park figures, of the total that is available for this current fiscal year.

Dr. GALLAGHER. We are talking about the $80 million that has been obligated already. We are thinking here of the possibility of obligating another between $50 and $60 million, at least. A great deal depends——

Mr. MICHEL. Between now and the end of the fiscal year.

Dr. GALLAGHER. Yes.

Mr. MICHEL. Are there any particular priorities that you have in this obligating time remaining for the balance of the fiscal year?

Dr. GALLAGHER. As far as categories?

Mr. MICHEL. Yes.

Dr. GALLAGHER. We are going on the basis of the Council's action in establishing a priority for each application.

Mr. MICHEL. What is that?

Dr. GALLAGHER. Each applicant for a construction grant receives a site visit by a group of consultants to assess the application. Following the site visit the application is reviewed for its professional, educational and technical completeness and quality by a review committee which consists of consultants knowledgeable in the field. If the committee approves the application it also recommends a priority for it and refers it to the National Advisory Council for Education in the health professions, which is established by law. The Council after reviewing the application establishes its priority. The application is then placed in competition with all other approved and unfunded applications awaiting grant award.

Mr. MICHEL. A particular filing date has no bearing on the priority?

Dr. GALLAGHER. No, sir. One which comes in late has equal opportunity for receiving grant award, depending upon the quality of the application.

Mr. MICHEL. Going on the assumption of $80 million obligated and another $50 to $60 million to be obligated by the end of the fiscal year, we come up with a total of $130 million, or $140 million. Let us take the lower figure and be conservative here, $130 million. Then I match that against the $173 million-plus of total obligations for 1969, and my simple subtraction comes out to the neighborhood of $44 million.

Then at page 85 of the justifications I look at the unobligated balances brought forward into 1970, and I see an item of $22.9 million. There is quite a spread there.

Mr. CARDWELL. Could I get a shot at this, Mr. Michel?

The table on page 85, as I read it, says from the combination of the appropriation and balances brought forward into 1969, they would obligate roughly $150 million. The testimony given to you thus far today indicates $80 million has been obligated now, and another $50 million, perhaps, will be obligated in the remainder of this year. That gives you $130 million.

There is about $20 million worth of obligation that the budget calls for which is now not accounted for, a difference of about $20 million. That, I think, is the crux of your question. Where is that $20 million?

It could mean $40 million will be carried forward at the end of this year. The way the testimony comes out, as I hear it, we seem to be saying we are going to carry forward $42 million at the end of this year, rather than $22 million Is that true?

Mr. MICHEL. How can we clear that up? I do not know that it will be cleared up altogether in the table that will be submitted for the record.

Dr. FENNINGER. May we clarify the differences in the table that will be inserted in the record?

Mr. MICHEL. Yes. I just want the information.

That is all, Mr. Chairman.

Mr. FLOOD. Thank you, gentlemen.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

Construction of Health Educational, Research, and Library Facilities

Amounts Available for Obligation

	1969	1970
Appropriation	$93,200,000	$126,100,000
Comparative transfer from the National Library of Medicine	1,250,000	.....
Unobligated balance brought forward	102,324,292	22,900,000
Unobligated balance carried forward	-22,900,000	.....
Total available for obligation	173,874,292	149,000,000

Obligations by Activity
(Appropriation plus funds brought forward)

Page Ref.		1969 Estimate	1970 Estimate	Increase or Decrease
95	Teaching facilities:			
	Schools of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine and public health.....	$104,695,745	$141,000,000 1/	+$36,304,255
	Schools of dentistry..	25,500,000	.....	-25,500,000
	Nurses.....	18,781,034	8,000,000	-10,781,034
	Allied health professions.....	3,008,080	.....	-3,008,080
100	Health research facilities.....	20,639,433	.....	-20,639,433
101	Medical libraries.....	1,250,000	.....	-1,250,000
	Total obligations.....	173,874,292	149,000,000	-24,874,292

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Grants, subsidies, and contributions....	$173,874,292	$149,000,000	-$24,874,292

1/ Includes schools of dentistry.

Obligations by Activity
(Appropriation)

Page Ref.		1969 Estimate	1970 Estimate	Increase or Decrease
95	Teaching facilities:			
	Schools of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine and public health	$60,000,000	$118,100,000 1/	+$58,100,000
	Schools of dentistry	15,000,000	.....	-15,000,000
	Nurses	8,000,000	8,000,000	.....
	Allied health professions	1,800,000	.....	-1,800,000
100	Health research facilities	8,400,000	.....	-8,400,000
101	Medical libraries	.....	.....	.....
	Total new obligational authority	93,200,000	126,100,000	+32,900,000

1/ Includes schools of dentistry.

Summary of Changes

1969 estimated obligations	$173,874,292
1970 estimated obligations	149,000,000
Net change	-24,874,292

	Base	Change from Base
Increases		
A. Program		
1. Teaching facilities: (a) Schools of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine and public health	$130,195,745	+$10,804,255
Decreases		
A. Program		
1. Teaching facilities:		
(a) Nurses	18,781,034	-10,781,034
(b) Allied health professions	3,008,080	-3,008,080
2. Health research facilities	20,639,433	-20,639,433
3. Medical libraries	1,250,000	-1,250,000
Total decreases		-35,678,547
Total net change requested		-24,874,292

Explanation of Changes

Teaching facilities:

(a) Schools of medicine, osteopathy, dentistry, pharmacy, optometry, podiatry, veterinary medicine, and public health.

Funds requested for 1970, $118,100,000, together with funds brought forward from 1969, $22,900,000, will permit construction awards of $141,000,000. This compares with planned awards in 1969 of $130,195,745. The estimated obligations will provide 1,016 new first-year places in 1970 and 840 in 1969.

(b) Nurses

Funds requested for 1970, $8,000,000, provide the same appropriation level as in 1969. The funds brought forward into 1969, $10,781,034, together with the $8,000,000 appropriation, provide planned awards of $18,781,034, for 1,174 new first year places and for maintaining 3,522 existing student places. In 1970 the estimated obligations of $8,000,000 will provide approximately 500 new first-year places, and maintain approximately 1,500 student places by modernizing facilities in existing schools.

(c) Allied health professions

Funds available in 1969, $3,008,080 ($1,800,000 in funds appropriated in that year with $1,208,080 brought forward from 1968), will assist in providing approximately 400 new student places. No obligations are planned in 1970.

(d) Health research facilities

Funds available in 1969, $20,639,433 ($8,400,000 in funds appropriated with $12,239,433 brought forward from 1968) will provide for 500,000 net square feet of research space. No obligations are planned in 1970. Research space primarily for teaching purposes may be funded from the allocation made for the construction of teaching facilities under the multipurpose provisions of the Health Manpower Act of 1968.

(e) Medical libraries

The funds available in 1969 are $1,250,000 brought forward from 1968 which will fund one project. No obligations are planned in 1970. Library space primarily for teaching purposes may be funded from the allocation made for the construction of teaching facilities under the multipurpose provisions of the Health Manpower Act of 1968.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 720--Construction Program for Medical, Dental and Other Health Professions Schools	$170,000,000
Section 791--Grants for Construction of Teaching Facilities for Allied Health Professions Personnel.	10,000,000
Section 801--Grants for Expansion and Improvement of Nurse Training	25,000,000
Section 701--Construction of Facilities for the Conduct of Research in the Sciences Related to Health	20,000,000
Section 393--Assistance for Construction of Medical Library Facilities	10,000,000

PUBLIC HEALTH SERVICE ACT

Title VII--Health Research and Training Facilities and Training of Professional Health Personnel

Part B--Grants for Construction of Teaching Facilities for Medical, Dental, and Other Health Personnel

Appropriation

Section 720. There are hereby authorized to be appropriated $480,000,000 for the three fiscal years in the period beginning July 1, 1966, and ending June 30, 1969, of which not more than $160,000,000 may be available for grants before July 1, 1967, and not more than $320,000,000 may be available for grants before July 1, 1968, for--

(1) grants to assist in the construction of new teaching facilities for the training of physicians, pharmacists, optometrists, podiatrists, veterinarians, or professional public health personnel;

(2) grants to assist in the construction of new teaching facilities for the training of dentists; and

(3) grants to assist in the replacement or rehabilitation of existing teaching facilities for the training of physicians, pharmacists, optometrists, podiatrists, veterinarians, professional public health personnel, or dentists.

For such grants there are also authorized to be appropriated $170,000,000 for the fiscal year ending June 30, 1970, and $225,000,000 for the next fiscal year. Sums so appropriated for any fiscal year shall remain available for obligation through the close of the next fiscal year.

Part G--Training in the Allied Health Professions

Grants for Construction of Teaching Facilities
for Allied Health Professions Personnel

Appropriation

Section 791. (a)(1) There are authorized to be appropriated for grants to assist in the construction of new facilities for training centers for allied professions, or replacement or rehabilitation of existing facilities for such centers, $3,000,000 for the fiscal year ending June 30, 1967; $9,000,000 for the fiscal year ending June 30, 1968; $13,500,000 for the fiscal year ending June 30, 1969; and $10,000,000 for the fiscal year ending June 30, 1970.

(2) Sums appropriated pursuant to the paragraph (1) for a fiscal year shall remain available for grants under this section until the close of the next fiscal year.

Title VIII--Nurse Training

Part A--Grants for Expansion and Improvement
of Nurse Training

Appropriation

Section 801. (a) There are authorized to be appropriated--

(1) for grants to assist in the construction of new facilities for collegiate associate degree or diploma schools of nursing, or replacement or rehabilitation of existing facilities for such schools, $25,000,000 for the fiscal year ending June 30, 1970, and $35,000,000 for the fiscal year ending June 30, 1971.

(b) Sums appropriated pursuant to subsection (a) for a fiscal year shall remain available for obligation through the close of the next fiscal year.

Title VII--Health Research and Teaching
Facilities and Training of Professional Health Personnel

Part A--Grants for Construction of Health Research Facilities

Appropriation

Section 704. There is hereby authorized to be appropriated for the fiscal year ending June 30, 1957, and for each of the nine succeeding fiscal years, not to exceed $50,000,000, for the fiscal year ending June 30, 1967, and the two succeeding fiscal years, an aggregate of not to exceed $280,000,000, $20,000,000 for the fiscal year ending June 30, 1970 and $30,000,000 for the next fiscal year, for making grants-in-aid for the construction of facilities for research, or research and related purposes, in the sciences related to health; and any sums appropriated pursuant to this section shall remain available until expended.

Title III--General Powers and Duties of
Public Health Service

Part I--Assistance to Medical Libraries

Appropriation

Section 393. (i) For the purposes of carrying out the provisions of this section, there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1967, and ending with fiscal year ending June 30, 1970, such sums, not to exceed $10,000,000 for any fiscal year, as may be necessary.

Explanation of Transfer

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer from: "National Library of Medicine"	$1,250,000	---	To consolidate NIH construction activities in this account.

Construction of Health Educational, Research, and Library Facilities

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	$30,390,000	0	0	0
1965	85,782,000	$85,782,000	$110,782,000	$110,782,000
1966	90,599,000	90,599,000	90,599,000	90,599,000
1967	160,794,000	160,727,000	160,727,000	160,727,000
1968	203,000,000	203,000,000	203,000,000	203,000,000
1969	84,800,000	84,800,000	84,800,000	84,800,000
1970*	126,100,000			

* In prior years the appropriation included only funds for construction of health educational facilities; beginning in 1970 the appropriation also includes health research facilities and medical library funds.

Construction of Health Educational, Research, and Library Facilities

Year	Estimate to Bureau of Budget	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	$30,435,000	$30,390,000	0	0	0
1965	85,782,000	85,782,000	$85,782,000	$110,782,000	$110,782,000
1966	90,664,000	90,599,000	90,599,000	90,599,000	90,599,000
1967	185,794,000	160,794,000	160,727,000	160,727,000	160,727,000
1968	219,000,000	203,000,000	203,000,000	203,000,000	203,000,000
1969	201,000,000	84,800,000	84,800,000	84,800,000	84,800,000
1970 *	149,100,000	126,100,000			

* In prior years the appropriation included only funds for construction of health educational facilities; beginning in 1970 the appropriation also includes health research facilities and medical library funds.

Justification

Construction of Health Educational, Research, and Library Facilities

	1969 Estimate	1970 Estimate	Increase or Decrease
Schools of medicine, dentistry, osteopathy, pharmacy, optometry, podiatry, veterinary medicine, and public health (obligations).....	$130,195,745	$141,000,000	+$10,804,255

The Health Manpower Act of 1968 (PL 90-490) approved August 16, 1968, extends the Health Professions Educational Facilities construction program for another two years through June 30, 1971. This program was originally established by the Health Professions Educational Assistance Act of 1963 (PL 88-129), extended by the Health Professions Educational Assistance Act Amendments of 1965 (PL 89-290) and modified by the Veterinary Medical Education Act of 1966 (PL 89-709). The Health Manpower Act of 1968 amends PL 89-290 to provide Federal assistance for construction of multipurpose teaching facilities including research space, medical library space and areas for advanced and continuing education as they relate primarily to education. It also provide for increased Federal participation percentages (up to 66 2/3 percent in areas previously authorized for 50 percent) under special circumstances. The total authorization for this 1968 Act is $395,000,000: $170,000,000 for 1970 and $225,000,000 for 1971.

The Health Professions Educational Facilities construction program has provided effective incentive to schools to increase their undergraduate enrollment, particularly in the field of medicine and dentistry. Through December 31, 1968, of a total of $456,000,000, $300,000,000 had been awarded for construction projects for medical schools providing 1,879 new first year student places and $107,000,000 for dental schools providing 871 new first year student places.

Although the supply of physicians has increased annually during the past ten years, the ratio of total active physicians has remained at about 150 per 100,000 total population. The graduates of Canadian and other foreign medical schools have contributed significantly to our physician manpower. It is estimated that in 1968, 311,000 physicians were available and estimates indicated a need for approximately 363,000 physicians to supply adequate health services. Similarly in 1975 approximately 358,000 physicians will be available when estimates indicate a need for approximately 400,000.

Dentists, like physicians, are not being produced in sufficient numbers to even maintain a current ratio of approximately 49 active dentists per 100,000 total population. It is estimated that in 1968, 100,000 dentists were available and estimates indicated a need for approximately 109,000 dentists to supply adequate dental services. In 1975 approximately 109,000 dentists will be available when estimates indicated a need for 137,000. The Nation's supply of dental manpower has been lagging behind the growth of the population for more than a third of a century. At the same time, the public's desire and ability to purchase dental care is at an all time high. It is estimated that a minimum increase of 22,000 practicing dentists, over and above presently projected expansions, will be needed if we are to achieve continued progress in the field of dental health. To realize such an expansion would require not only an acceleration of present efforts to expand training facilities, but would also require continued increases in dentist productivity.

Critical shortages of qualified personnel exist in all other health disciplines as well.

To meet the current and future demand of the American people for better health services we must plan ahead to meet health manpower requirements. In some fields as many as nine-to-ten years lead time is necessary to provide qualified personnel. A primary goal is the expansion of the collective enrollments of the Nation's health professions schools to a level that permits all qualified applicants to be admitted.

It has been demonstrated that some schools cannot exist, much less expand their student enrollment, without assistance. Increased emphasis must be given to the support of medical center activities with the intent that the production of physicians and other health personnel be given highest possible priority.

It is, therefore, of the utmost importance that construction funds be made available to existing health professions educational institutions to assist in expansion of their enrollment in replacing or renovating obsolete facilities, adding space where overcrowding occurs, as well as to provide assistance in the establishment of new schools.

A summary of the accomplishments of the Health Professions Educational Facilities construction program from its inception in 1964 through December 31, 1968, is shown in the following table:

Type	No. of Schools Assisted	No. of Projects	No. of First Yr. Places Provided
Medical	56	79	1,879
Osteopathy	2	2	17
Dental	26	33	871
Pharmacy	12	13	367
Optometry	5	5	157
Public Health	6	7	357
Veterinary Medicine	2	2	80
Nursing *	16	16	779
Total	125	157	4,507

* Funded prior to passage of the Nurse Training Act of 1964.

Funds requested for 1970, $118,100,000 together with funds brought foward from 1969 of $22,900,000 will permit construction awards of $141,000,000 in 1970 compared to planned awards in 1969 of $130,195,745, based on appropriated funds in 1969 of $75,000,000 and $55,195,745 in funds brought forward from 1968. The estimated obligations will provide funding for approximately 840 new first year student places in 1969 and 1,016 in 1970.

The program has also provided essential assistance in the creation of 20 new schools as follows: Medical 12, Dental 5, Public Health 1, and Nursing 2.

The backlog of approved but not funded construction projects as of June 30, 1969, is estimated at approximately $263,000,000. The following table indicates the total pending and currently anticipated requests for assistance from eligible institutions including applications which have been reviewed, approved and are awaiting funding; applications pending review; and expressions of intent to submit applications.

Construction - Schools of Medicine, Osteopathy, Dentistry, Pharmacy,

Optometry, Podiatry, Veterinary Medicine, and Public Health

As of December 31, 1968

	Approved Not Funded		Pending Review		Expressions of Intent		Total Anticipated Need	
	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share
Medical	16	$133,765,304	10	$39,798,344	88	$554,300,000	114	$727,863,648
Dental	6	35,281,237	2	10,991,606	24	96,400,000	32	142,672,843
Other	8	16,339,205	5	10,277,441	69	126,400,000	82	153,016,646
Total	30	$185,385,746	17	$61,067,391	181	$777,100,000	228	$1,023,553,137

	1969 Estimate	1970 Estimate	Change
Nursing educational facilities (obligations)	$18,781,034	$8,000,000	-$10,781,034

The shortage of nurses is reaching a critical stage. Currently 141,000 more nurses are needed, and by 1975 the shortage will almost double. Available data indicate that many qualified applicants are being rejected for lack of adequate space at some nursing schools. It is also a fact that at some schools places for students are not being used for lack of applicants. In many such instances the available places are in schools which do not attract students because of their locations, or other shortcomings of the schools. Facilities must be increased in locations where there are inadequate numbers of places and improved at some of the schools where unused places persist.

Construction of new schools, modernizing facilities in existing schools, and building of additional teaching facilities at strong, successful schools which will thereby be enabled to increase their enrollments are essential to achieve the goals of the nurse education program for sustaining and increasing the number of nurse graduates, raising the quality of nurse education and improving the geographical distribution of nurse education facilities.

Construction funds are particularly needed for replacement of inadequate facilities. The fact is that a large proportion of the Nation's 1,300 schools of nursing are housed in inadequate structures. Many of them are not only unattractive in appearance and lacking in conduciveness to excellence in education, but are also considered unsafe.

Under the Nurse Training Act, PL 88-581, as of December 31, 1968, 102 projects were assisted by Federal funds, of which 21 were new schools. These institutions submitted 187 applications requesting Federal funds in excess of $98,000,000. The schools provided the matching portion of funds to construct 4,037 new student places, and maintain 14,500 student places in existence. As of December 31, 1968, 129 letters of intent to construct nursing school facilities are on file which include cost estimates totalling $88,000,000 for the Federal share. Funds requested in 1970 under the Health Manpower Act of 1968, PL 90-490, of $8,000,000 will provice approximately 500 new student places and maintain approximately 1,500 student places by modernizing facilities in existing schools. The $8,000,000 for 1970 is the same appropriation level as in 1969. In 1969 there was a carry-over balance of $10,781,034; there is no carry-over into 1970.

The Health Manpower Act of 1968 extended the nursing school construction program for two years, 1970 and 1971. The amounts authorized are $25,000,000 and $35,000,000 respectively. The new Act provides for inclusion in the construction project of spaces for advanced training activities that are not degree oriented.

Nursing Educational Facilities
As of December 31, 1968

	Approved Not Funded		Pending Review		Expressions of Intent		Total Anticipated Need	
	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share	No. of Projects	Estimated Federal Share
Total	20	$16,399,259	22	$9,207,915	129	$88,000,000	171	$113,607,174

	1969 Estimate	1970 Estimate	Change
Allied health educational facilities grants (obligations)	$3,008,080	---	-$3,008,080

The Allied Health Professions Personnel Training Act, PL 89-751, authorized a program of matching grants for the construction of new allied health training centers and the renovation and rehabilitation of existing educational facilities for the allied health professions. This was extended into 1970 by the Health Manpower Act of 1968, PL 90-490, with an authorization of $10,000,000.

The first construction grant was awarded in 1968 and will assist in the construction of teaching facilities for an increase in enrollment of 337 students. This was the only project supported in 1968 as it required $1,791,920 of the $2,000,000 available for obligations that year. It is expected that based on applications now being considered, the 1969 obligations of $3,008,080 ($1,800,000 appropriation; $1,208,080 carry-over) will assist in providing approximately 400 new student places at four to six schools. Three projects requesting $2,323,209 in Federal participation are approved and unfunded as of December 31, 1968. Four projects requesting $3,766,014 in Federal participation are awaiting Council review. No funds are requested for 1970.

	1969 Estimate	1970 Estimate	Change
Health research facilities (Obligations - includes $8,400,000 appropriation and $12,239,433 carry-over from prior years)	$20,639,433	---	-$20,639,433

The major objective of Health Research Facilities grants are to meet the needs for new and replacement facilities for this Nation's research program in the health sciences, including construction of biomedical research facilities in new and expanding medical schools and the construction and renovation of animal facilities. This program as amended by PL 90-490, "Health Manpower Act of 1968," authorizes $20,000,000 for fiscal year 1970 and $30,000,000 for fiscal year 1971. Grants are awarded for up to 50 percent of the cost of the facility but in certain instances where the Secretary, DHEW, deems a project has special national or regional significance, the maximum grant may be 66 2/3 percent of the cost of a facility. Not more than 25 percent of the funds appropriated may be utilized for projects of special national or regional significance. Facilities constructed with these funds are dedicated to research in the health sciences for a minimum of ten years by the recipient.

Research facilities are essential to the numerous health objectives; to increase qualified faculty, including those needed to staff planned new medical schools; to provide career opportunities for outstanding scientific talent to work on problems of national significance as these individuals emerge from research training programs; to provide facilities within which humane care of laboratory animals used in research may be provided and to house certain critical research programs including those judged by the Secretary, DHEW, to be of special national or regional significance.

A number of major research programs have been identified by the National Institutes of Health and the Congress as meriting special attention. These include centers for cardiovascular research and training, cancer research and training, research on aging, growth and development, research and training in pharmacology-toxicology, and dental research institutes.

During the period of the existence of this program over $460,000,000 in Federal funds have been awarded to 406 institutions to construct or remodel over 18,000,000 net square feet of space. The total construction cost of these research facilities, including the non-Federal share is over one billion dollars. Since the inception of the program 1,992 applications have been received representing a total of over $895,000,000.

It is of interest to note that the passage of the Laboratory Animal Welfare Act, PL 89-544, dated August 24, 1966, has had a significant impact on the Health Research Facilities program. In fiscal year 1966, ten animal facilities applications totalling $5,496,000 were received which amounted to 5.1 percent of all Health Research Facilities applications. In 1968 this increased to 23 applications totalling $12,631,000 for ten percent of the total Health Research Facilities requests.

Eighty-three projects requesting $84,753,372 in Federal participation are approved and unfunded as of December 31, 1968. Twenty-two projects requesting $23,390,910 in Federal participation are awaiting Council action. No construction projects will be funded in fiscal year 1970. Research space primarily for teaching purposes may be funded from the allocation made for the construction of teaching facilities under the multipurpose provisions of the Health Manpower Act of 1968.

	1969 Estimate	1970 Estimate	Change
Grants for construction of library facilities.....	$1,250,000	---	-$1,250,000

Under the Medical Library Assistance Act, PL 89-291, to assist in the construction of new, and the renovation, expansion, or rehabilitation of existing medical library facilities there was authorized to be appropriated for each fiscal year beginning with fiscal year ending June 30, 1967, and ending with the fiscal year ending June 30, 1970, such sums as might be necessary, not to exceed $10,000,000 for any fiscal year.

Grants are made to public and other non-profit institutions. No construction projects will be funded in 1970. Funds available in 1969 will support one construction project. Nine projects were supported in 1968. Library space primarily for teaching purposes may be funded from the allocation made for the construction of teaching facilities under the multipurpose provisions of the Health Manpower Act of 1968.

From the beginning of the program through December 31, 1968, institutions have submitted 44 applications requesting a total of $44,166,715. A total of nine grants for $10,000,000 have been awarded.

NATIONAL LIBRARY OF MEDICINE

THURSDAY, APRIL 3, 1969.

WITNESSES

DR. MARTIN M. CUMMINGS, DIRECTOR
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. RUTH M. DAVIS, DIRECTOR, LISTER HILL NATIONAL CENTER FOR BIOMEDICAL COMMUNICATION
DAVID F. KEFAUVER, ASSOCIATE DIRECTOR FOR EXTRAMURAL PROGRAMS, NATIONAL LIBRARY OF MEDICINE
GEORGE F. RUSSELL, JR., EXECUTIVE OFFICER, NATIONAL LIBRARY OF MEDICINE
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	4,161	4,806	5,029
Positions other than permanent	60	208	223
Other personnel compensation	53	83	85
Total personnel compensation	4,275	5,096	5,337
Personnel benefits: Civilian employees	326	387	402
Travel and transportation of persons	118	147	173
Transportation of things	8	14	17
Rent, communications, and utilities	194	621	1,612
Printing and reproduction	−29	310	230
Other services	2,698	4,950	5,762
Supplies and materials	207	348	388
Equipment	258	366	444
Grants, subsidies, and contributions	5,192	7,483	7,608
Total costs, funded	13,246	19,723	21,973
Change in selected resources	3,869	452	909
Total obligations	17,115	20,175	22,882

PERSONNEL SUMMARY

Total number of permanent positions	536	470	492
Full-time equivalent of other positions	12	22	21
Average number of all employees	456	485	491
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,966

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
1. Grants:			
(a) Training	612	1,137	1,021
(b) Special scientific projects	41	89	100
(c) Research	980	1,285	1,442
(d) Library resources	2,670	2,994	2,458
(e) Regional medical libraries	517	1,750	2,211
(f) Publications support	372	228	376
Total, grants	5,192	7,483	7,608
2. Direct operations:			
(a) Library operations	2,929	7,465	6,493
(b) Toxicology information	586	1,153	1,549
(c) National Medical Audiovisual Center	1,438	1,451	2,175
(d) Lister Hill National Center for Biomedical Communications	187	526	2,058
(e) Research and support contracts	1,032	248	
(f) Review and approval of grants and contracts	545	480	621
(g) Program direction	1,337	917	1,469
Total, direct operations	8,054	12,240	14,365
Total program costs, funded [1]	13,246	19,723	21,973
Change in selected resources [2]	3,869	452	909
Total obligations	17,115	20,175	22,882
Financing:			
Comparative transfers to other accounts	10,151	1,402	
Unobligated balance available, start of year	−10,567	−4,117	−700
Unobligated balance available, end of year	4,117	700	
Unobligated balance lapsing	858		
Budget authority	21,674	18,160	22,182
Budget authority:			
Appropriation	19,912	18,160	22,182
Transferred from other accounts	1,762		
Appropriation (adjusted)	21,674	18,160	22,182
Relation of obligations to outlays:			
Obligations incurred, net	27,266	21,577	22,882
Obligated balance, start of year	8,098	22,070	21,338
Obligated balance, end of year	−22,070	−21,338	−20,815
Adjustments in expired accounts	−182		
Outlays	13,112	22,309	23,405

[1] Includes capital outlay as follows: 1968, $258,000; 1969, $366,000; 1970, $444,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $3,168,000; 1968, $7,037,000; 1969, $7,489,000; 1970, $8,398,000.

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name: Martin Marc Cummings.

Position: Director, National Library of Medicine.

Birthplace and date: Camden, N.J., September 7, 1920.

Education: B.S., Bucknell University, 1941; M.D., Duke University School of Medicine, 1944; mixed internship, Boston Marine Hospital, 1944–45; assistant resident, medicine, Boston Marine Hospital, 1945–46.

Experience: Director, National Library of Medicine, 1964 to present; Associate Director for Research Grants, NIH, 1963; Chief, Office of International Research, NIH, 1961–63; chairman and professor, Department of Microbiology, University of Oklahoma School of Medicine, Oklahoma City, Okla., 1959–61; Director, Research Services, Veterans Administration Central Office, Washington, D.C., 1953–59; special lecturer in microbiology, George Washington University School of Medicine, Washington, D.C., 1953–59; Chief, Tuberculosis Research Laboratory, Veterans Administration Hospital, Atlanta, Ga., 1949–53; associate professor of bacteriology, 1953, and instructor through associate professor of medicine at Emory University School of Medicine, Atlanta, Ga., 1948–53; Director, Tuberculosis Evaluation Laboratory, Communicable Disease Center, U.S. Public Health Service, Atlanta, Ga., 1947–49.

Association memberships: American Academy of Microbiology, Inc.; American Federation for Clinical Research—emeritus; American Society for Clinical Investigation—emeritus member; American Thoracic Society and National Tuberculosis Association; Association of American Medical Colleges; Medical Library Association; the Society of the Sigma XI; American Documentation Institute; Council of Biology Editors, Inc.; American Clinical and Climatological Association; American Association for the History of Medicine; American Board of Microbiology; board of directors, Gorgas Memorial Foundation; board of directors, Association of Research Libraries; board of visitors of the Medical Center of Duke University; board of directors, Association of Research Libraries.

Special awards, citations, or publications: VA Exceptional Service Medal; DHEW Superior Service Award; DHEW Distinguished Service Award; honorary degree, doctor of science, Bucknell University.

Mr. FLOOD. Now we have the National Library of Medicine, Dr. Martin M. Cummings, Director.

You have a statement. How would you like to proceed?

Dr. CUMMINGS. I would like to read the statement into the record, if I may.

Mr. FLOOD. All right, Doctor.

GENERAL STATEMENT

Dr. CUMMINGS. Mr. Chairman, and members of the committee, the National Library of Medicine serves as a national resource for biomedical information. Traditionally one of the world's great research libraries, the National Library of Medicine in recent years has become the principal focus within the Federal Government for national planning to improve communications in the health sciences.

It is the function and statutory purpose of the National Library of Medicine to support the national health effort by improving the communications processes through which medical knowledge is generated, transmitted, and utilized.

Congress assigned this mission to the library in recognition of the existence of a problem. Simply stated, the problem is this: the complexity and the mass of health information produced by our advanced scientific society has outstripped our ability to store, retrieve, and deliver information to the people who need to use it.

At the frontier of interdisciplinary research, traditional information services are no longer adequate. New ways of organizing and presenting information must be developed. At the educational frontier, where students must learn so much in so little time, modern technologies for information transfer must be employed. At the health service frontier there is an even greater challenge, that of communicating the new medical knowledge to those who minister daily to the Nation's health.

The library's mission requires it to address such large and important health communications problems. We are doing so through a broad array of programs and services. I should like to highlight some of our accomplishments over the past year.

In our core library operations, we provided a quarter of a million services to readers and users of the library. Some 127,000 of these were loans in support of medical libraries across the country. Our collections increased by 117,000 medical publications; our holdings now represent the equivalent of a million and a quarter volumes.

MEDLARS SYSTEM

Through the Medlars system we provided to scientists and physicians throughout the country over 10,000 computer-based searches of the literature. We now share the retrieval power of Medlars with 11 university-based bibliographic search centers and regional medical libraries across the country; this constitutes, in fact, a prototype computer-based service network. Using Medlars also, we have continued to expand our index publication activities, producing over 125,000 pages of the Index Medicus, Current Catalog, and 11 specialized indexes in various fields of medicine. Over 20,000 subscriptions to these publications have been sold through the Government Printing Office and other outlets.

The service loads we have placed on Medlars long ago exceeded the design limitations of the original system. Our request includes funds to continue the acquisition of a larger second generation system, which we began in 1968.

The transfer to the National Library of Medicine of the National Medical Audiovisual Center greatly augmented the library's resources for the support of medical education; this last year the Center provided nearly 100,000 loans of audiovisual materials, primarily films, for educational uses.

Through our extramural program we made resource grants in 1968 to 110 libraries in 37 States, thereby strengthening their ability to provide local services.

We have also made grants to seven regional medical libraries which are associating themselves with us to form the nucleus of a national medical library system. The President's Science Advisory Committee called for planning for the development of a nationwide toxicology information system in 1966. This program, for which the Congress provided initial funding in 1968, is moving forward.

These are specific responses to meet the needs of the medical communities for strengthened and improved information services.

LISTER HILL NATIONAL CENTER

The Lister Hill National Center for Biomedical Communications (so designated by Public Law 90–456 of the last Congress) provides a Federal focus for the systems engineering essential to the development of a biomedical communications network.

The network will apply modern communications technology to improve access by users to the specialized information they require from existing information resources in the Federal, State, local, academic, and private sectors.

Of particular importance to the long-range solution of health communication problems has been the comprehensive planning accomplished over the past year toward development of the biomedical communications network. This planning is responsive to the recommendations of the House and Senate Subcommittees on Appropriations as well as the House Special Subcommittee on Investigation of the Department of Health, Education, and Welfare, which called for the systematic organization of an active biomedical communications complex as the most important goal of the library.

Our planning effort has progressed to the point where we have conceived the structure of this network, identified its major components, and prepared a preliminary technical development plan. We have involved elements of the medical community in providing statements of their requirements for improved health communications. We believe that the application of modern technology to assist in the transfer of information through a biomedical communications network represents a realistic and forward looking approach to solution of the health communications problems.

In summary, our request for 1970 is $22,182,000 and 492 positions, an increase of $4,021,500 in new obligational authority and 22 positions over the amounts appropriated in 1969. This increase will provide funds and positions needed to develop components of the biomedical information network, complete the acquisition of computer programing for Medlars II, implement a nationwide videotape acquisition and utilization program and improve the distribution capabilities at the National Medical Audiovisual Center, continue the planning and implementation of the toxicology information program, and generally enhance the National Library of Medicine's capability to serve as a national information resource for the libraries and other information agencies serving the national health effort.

I would be pleased, Mr. Chairman, to answer any questions that you may have.

UNOBLIGATED BALANCES

Mr. FLOOD. Here is the committee's bete noir again. Unobligated balance, $4,117,462 carried forward from 1968 to 1969. Suppose you were sitting over here, Doctor, and you see this long retinue of unobligated balances. It casts a doubt on the previous year's estimate and even on the budget request.

What is this one composed of?

Dr. CUMMINGS. I can see how you might look critically at that. In the case of the national library's unobligated balance carried forward, a major part of it was in the area of medical library construction. Actually, $1.25 million was carried forward after the money had been withheld by the Bureau of the Budget for the same purposes and reasons given earlier.

The other funds carried forward relate to the Revenue and Expenditure Control Act.

Mr. FLOOD. You estimate $700,000 will be carried forward from 1969 to 1970.

Dr. CUMMINGS. That is correct, sir.

Mr. FLOOD. What activities are involved there? Does that estimate still stand pretty firm? What activities, first?

Dr. CUMMINGS. This figure we believe is quite firm. It is a planned carryover to cover obligations particularly in the area of research grant continuations and for support of regional medical libraries in our extramural programs.

Mr. FLOOD. Extramural?

Dr. CUMMINGS. Yes, sir; grants programs.

LISTER HILL NATIONAL CENTER FOR BIOMEDICAL COMMUNICATIONS

Mr. FLOOD. Your largest increase is $1,163,000 for the Lister Hill National Center for Biomedical Communications.

Dr. CUMMINGS. That is correct.

Mr. FLOOD. The authorization for this was enacted last year. It is about a year old. Suppose you describe that a little bit.

Dr. CUMMINGS. I would be very pleased to describe the elements of this Center. I would like also the privilige of asking Dr. Davis, the Director of this new Center, to add to my testimony, if I may.

Essentially, the concept of the Lister Hill Center is to develop an integrated, nonredundant communications network through which existing information sources could transmit knowledge in all forms.

Mr. FLOOD. Are communications redundant?

Dr. CUMMINGS. I think to some degree, Mr. Chairman, the messages and communications channels are redundant.

Mr. FLOOD. The messages themselves?

Dr. CUMMINGS. The messages themselves. There are five elements proposed for this network. One has already been described to this committee, the library network. There will be an audiovisual component through which all audio-visual messages may be transmitted. There will be specialized information services, such as the toxicology information program, where poison information and other types of related data can be shared nationally. There will be an educational component primarily geared to the undergraduate, graduate, and continuing education of physicians. Finally, the last element will comprise the data transmission machinery, and in particular the computer machinery to handle these data.

I think Dr. Davis would be pleased to elaborate on any of these elements, if you would like her to do so.

Mr. FLOOD. Very well.

Dr. DAVIS. Mr. Chairman, I think, as you can see from Dr. Cummings' statement, what we mean by network is a structure, both within the Federal Government and external to the Federal Government, that will allow the sharing of resources and sharing of capabilities in the medical community, primarily through communications.

For example, there are a number of institutions such as medical schools and hospitals that have excellent educational resources, in terms of computer, audio-visual tape, and other teaching resources. There are hospitals that have excellent patient records, differential diagnosis systems, and other clinical application of computers. There are other centers that have large computer information data banks in medical schools, libraries and hospitals. These are not now available to other institutions nor to the majority of users within the medical community, the individual physicians scattered throughout the country.

One has two alternatives. First, all of these capabilities everywhere throughout the country can be duplicated as they are needed. There is a fair amount of overhead to doing this. Everyone then shares the problem and duplicates the cost of solving it, of people to run the equipment, to run the centers, and duplicates the cost of developing the resources. Moreover, there are also higher costs of going out to industry piecemeal and paying prime prices for very small numbers of special equipment and special manpower that would be needed.

The other alternative is to interested information sources and services and to link the people who have with people who do not have these kinds of resources. When we say link, we mean through every kind of mechanism. We mean through telephone lines. For example, there is a dial system in the State of Wisconsin, where you can dial a number and get a 5 to 10 minute lecture on some 270 different medical topics. This can be done in emergencies as fast as you can dial the telephone number. That particular capability will be very useful in the other States. There is no need to develop anything new to do this but a good, dedicated telephone system.

Mr. FLOOD. I think you have impressed the jury. This, of course, is an important thing, especially since it is named after our old friend and colleague in the Senate, Lister Hill. But this is what we are hearing all the time. "This is all very good, but let's do it next year. Why this year? We are having trouble. We have to give up some things during this period of fiscal difficulties." Why not put this off a year?

Dr. CUMMINGS. I think it is possible to defer the implementation of such a program, however the decision as to whether this should be done is obviously a judgment that has to be made by this committee. In my view, this program represents an urgent need, and I personally give this a high priority in terms of my own program priorities. I would have to agree that it could be deferred, as can perhaps other things that would be good for the country.

INCREASE FOR MEDLARS

Mr. FLOOD. You have a large increase of $1,018,000 for what you call development and partial implementation of the second generation Medlars. How much of this is for development and how much is for implementation?

First of all, you had better tell us what Medlars is. That is gobbledygook to the average person. What is Medlars?

Dr. CUMMINGS. Medlars is acronym for medical literature analysis and retrieval system. This is our computer-based information retrieval system that has been operational at the Library since January of 1964.

With respect to your question on development and implementation of the second generation Medlars, I presented to this committee a 5-year plan for replacement of our existing system. The Congress provided us with funds during the last fiscal year to acquire the basic software for conversion. The funds requested for fiscal year 1970 are to provide the hardware to implement operations.

I should have pointed out that the systems design was also included within the funding for the first year of the Medlars program.

We expect to be able to increase not only the number of services that we provide with this new system, but more importantly, we expect to have new capabilities in the handling of abstracts as well as citations. We should be able to deliver larger information packages with the new system than we have been in the past.

Mr. FLOOD. Can you finish the development job in 1970?

Dr. CUMMINGS. No, sir; we cannot finish the development job in 1970. I believe the schedule calls for it to be completed in 1971.

Mr. FLOOD. How much of the 1970 budget is for nonrecurring costs? This is the second generation of Medlars. How much is for nonrecurring costs in fiscal year 1970?

Dr. CUMMINGS. I would have to check this figure to be precise.

Mr. FLOOD. Check that and be sure on the figure.

Dr. CUMMINGS. I would like to be absolutely certain and shall provide the figures for the record.

The increase of $1,018,000 for development and partial implementation of Medlars II contains virtually no nonrecurring expenses. The major portion of the increase is $1,013,000 for rental of computer equipment and $129,000 to support 12 positions essential to development and operation of the new system. These major items and smaller amounts totaling $44,000 for consultative services, travel, printing, services of other agencies, and supplies are partially offset by a decrease in project contracts of $168,000 in 1970.

MIDDLE ATLANTIC REGIONAL LIBRARY

Mr. FLOOD. Take a look at page 112. You have a reference there to establishing the Library as the regional library for the Middle Atlantic area.

I am interested in the Middle Atlantic area. I am very parochial at times.

Dr. CUMMINGS. This refers, Mr. Chairman, to the distribution of regional libraries throughout the country. We now have regional libraries operating in Boston, New York, Philadelphia, Chicago, Detroit, Seattle, Los Angeles, and the beginning of a regional library in Atlanta to serve the Southeastern States.

It was my judgment that the District of Columbia, Maryland, Virginia, and West Virginia are so close to the National Library of Medicine itself that there would be no reason to create a regional library in this area. We have assumed the responsibility for serving as the regional library for this area.

Mr. FLOOD. This does not affect the Philadelphia setup?

Dr. CUMMINGS. No, it will not. The concentration of users in the Delaware Valley is so heavy that we felt they had to have their own local service.

Mr. FLOOD. That is a great medical center, probably the biggest in the world.

REDUCTION IN LIBRARY RESOURCES GRANTS

With regard to library resources grants, you show on page 123 the number of grants will go up from 390 in 1969 to 424 in 1970, but the dollar total goes down from $2.8 million to $2.350 million.

Dr. CUMMINGS. That is correct.

Mr. FLOOD. How do you explain that?

Dr. CUMMINGS. I believe I can explain this. The basic legislation requires the Library to provide its resource grants on a decreasing formula. That is to say, we are permitted to make a first-year award in a larger sum than in the second year, third year, and fourth year, so it is a reducing budget formula.

The intention of the legislation, as I understand it, was to prime the pump to upgrade the medical libraries that were in great need of resources, and then to have the institutions begin to pick up the

differential between the Federal and local support. Therefore, each grant will be smaller in size in successive years, and we will have the opportunity to make more awards to other institutions.

USE OF COMPUTERS COMPARED WITH SIZE OF TOTAL BUDGET

Mr. FLOOD. On page 130 you have this, and I quote: "In 1966, less than 4 percent of the Federal Government computers were in HEW, while HEW spent about 10 percent of the Federal budget."

What do you have that in your justification for? What is that to you? What do you care? Of what significance is such a comparison anyway?

Dr. CUMMINGS. I would like Dr. Davis to respond to that question, if she would. I believe it has relevance to how we plan the utilization of the computers that are available through HEW resources.

Mr. FLOOD. Why is it in your justification?

Dr. DAVIS. It is in our narrative but it is not basic to our justification, sir.

Mr. FLOOD. That is what I thought. That is the reason for the question.

Dr. DAVIS. The implicit reason for our interest is that one of the functions of the Lister Hill Center is to be the focal point within the Department, not just within the Library or NIH, but the focal point in the Department for the application of technology to biomedical communications.

Mr. FLOOD. Would you like the Library's allowance for computers to be based on the percentage your budget is of the total Federal budget?

Dr. DAVIS. By no means, sir. This was an indication only that an attempt was being made to become the focal point working with various other agencies such as GSA. It was an indication that computers had not yet permeated management.

Mr. FLOOD. Do you people buy any kind of hardware which the salesman has, or do you concern yourselves with initiating or pushing or demanding miniaturization and the most advanced equipment.

Dr. CUMMING. No, we do not buy all hardware that salesmen recommend, nor do we develop our own hardware. We seek to utilize the new technology that fits the need and that is economically feasible for our purpose.

Mr. FLOOD. You are not sure some city slicker isn't selling you the tail-end of the last generation, are you, with a new one coming up on Monday?

Dr. CUMMINGS. We hope that is not the case.

Mr. FLOOD. So do I.

Mr. Michel?

USER CHARGES FOR LIBRARY SERVICES

Mr. MICHEL. Thank you, Mr. Chairman.

Doctor, in the Medlars system, noting those 8,000 computer-based searches of the literature that have been provided to scientists and physicians around the country, who pays for that? Is there any participation on the part of the scientists or physician? Obviously,

this service is somewhat limited in scope. Are you able to take care of all the requests, or what priority is there as to who gets the service and who does not?

Dr. CUMMINGS. So far, with the decentralization of the MEDLARS program to the universities scattered across the country, we have been able to meet the requirements. In additions to the 8,000 demand searches that we have provided, the decentralized centers will provide about 12,000 searches to the regional users next year.

The answer to your question about who pays for the service is that these services are provided in the tradition of free public library services.

Mr. MICHEL. Do you think eventually we will get into a user charge kind of arrangement?

Dr. CUMMINGS. Yes, sir. I believe we may eventually have to arrange for some kind of partial basic subsidy with some cost to be assessed users for special purposes. I think all of the Federal agencies are beginning to examine this issue at this time.

Mr. MICHEL. Because the more specialized and finite it is, obviously the more difficult it is to come up with the information.

LIBRARY RESOURCES GRANTS

Can we have spelled out in the record how much money is going into the extramural resource grants in 1969? In 1968, you say there were 110 libraries in 37 States. What is expected in 1969?

Dr. CUMMINGS. I wonder if Mr. Kefauver would answer your question.

Mr. KEFAUVER. Referring to page 123, we expect to be able to make 424 grants in fiscal 1970, and perhaps 390 in fiscal 1969.

Mr. MICHEL. What is the size of these grants?

Mr. KEFAUVER. The size of the grant is based on the size of the operating budget of the applying institution. The law permits us to pay up to 60 percent of the operating budget. With the limited funds we have had, we have paid 25 percent of their operating budget. That is the first year.

Mr. MICHEL. Is that a flat amount determination you have made?

Mr. KEFAUVER. Yes.

Mr. MICHEL. Regardless of the size of the institution?

Mr. KEFAUVER. Yes, sir. That is the first year grant. As Dr. Cummings explained a moment ago, the year thereafter the grant must decrease.

Dr. CUMMINGS. The range in size of these grants, Mr. Michel is between $2,000 and $50,000, depending on the size of the institution providing services.

Mr. MICHEL. With that percentage that you have arbitrarily set in keeping within the limited funds available, do you think that percentage will ever be increased beyond 25 percent, the figure you have set now, or is it necessary?

Mr. KEFAUVER. The figure could be increased in two ways: by a larger appropriation or by making fewer awards.

We tried to base the program on a 5-year plan which would include the largest number of institutions. It seemed to be the figure that would enable us to do that.

GRANTS FOR PUBLICATIONS

Mr. MICHEL. Under what program do you give grants to provide financial assistance to nonprofit biomedical publications?

Mr. KEFAUVER. This program is authorized by section 399 of Public Health Service Act. It enables us to provide grants for the preparation and/or publication of certain types of specialized literature directed to the biomedical community. Most of the projects supported under this program are in the nature of secondary literature, handbooks, atlases, reviews.

Mr. MICHEL. How much in this last year was spent in that area? Can you supply that for the record, and what is projected for 1970?

Mr. KEFAUVER. Yes.

The amount projected for 1970 is $400,000.

Mr. MICHEL. And the 1969 figure?

Mr. KEFAUVER. The 1969 figure is $300,000.

NEED FOR MEDICAL LIBRARIANS

Mr. MICHEL. How did you come to the conclusion that the medical schools in the United States each need 10 professional medical librarians and other medical communication specialists wherever they are?

Dr. CUMMINGS. We have provided such data, so I suspect you found it in our budget justification.

Mr. MICHEL. It seems a little high.

Dr. CUMMINGS. This represents the data derived from several studies that have been made for the library, one by the Association of American Medical Colleges, and another one by the American Medical Association.

The situation with respect to manpower is simply this: that there are more than 6,000 medical libraries and only 3,000 trained professional medical librarians; roughly a half a librarian for each library. Those medical libraries, which have been carefully examined, which seem to be able to provide 80 to 90 percent of the services requested of them, have a professional staff that reaches the level you have identified here of 10 or more professional librarians.

So in the effort to upgrade the others, we have used that as a standard. In my own judgment, I think that is a minimal standard.

AMOUNTS BUDGETED FOR CONTRACTS

Mr. MICHEL. How much money is in your budget for contracts?

Dr. CUMMINGS. Do you have the figures, Mr. Russell?

Mr. RUSSELL. We have a total of $4.9 million for project contracts in 1970.

Mr. MICHEL. About how many contractors would that include? Do you have any idea?

Dr. CUMMINGS. It would be well over 25.

Mr. MICHEL. Would you list this in the record for us?
Dr. CUMMINGS. Yes.
(The information follows:)

NATIONAL LIBRARY OF MEDICINE—ESTIMATED NUMBERS OF CONTRACTORS AND DOLLAR AMOUNTS FOR PROJECT CONTRACTS IN 1970 BY PROGRAM

Program	Estimated number of contractors	Estimated amounts for project contracts
Decentralized medlars centers	5	$400,000
Other library operations and National Medical Audiovisual Center	15	1,618,000
Lister Hill National Center for Biomedical Communications	9	1,710,000
Toxicology information program	8	1,135,000
Total	37	4,863,000

Mr. MICHEL. Dollarwise, is that about standard for the year before or about the same figure?

Dr. CUMMINGS. The ratio would be similar. I think we provided these data for the record last year.

I should point out our Medlars centers, although university-based, are supported through contracts rather than grants.

There will be a mixture of universities and other groups who are recipients of our contracts.

Mr. MICHEL. That is all, Mr. Chairman.

Mr. FLOOD. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation
(New Obligational Authority Basis)

	1969	1970
Appropriation	$18,160,500	$22,182,000
Comparative transfer to "Salaries and expenses, Office of Director"	-136,000	---
Comparative transfer to "Salaries and expenses, Office of Comptroller"	-16,000	---
Unobligated balance carried forward	-700,000	---
Cutback required by P.L. 90-364	-162,000	---
Total currently authorized for obligation	17,146,500	22,182,000
Plus: proposed release of reserves for increased pay costs	162,000	---
Total obligations	17,308,500	22,182,000
Disposition of cutback: To be used for pay costs in this account	162,000	---

Obligations by Activity
(New Obligational Authority)

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
121	Grants:						
	Training	--	$655,500	--	$1,000,000	--	+$344,500
	Special scientific projects	--	---	--	100,000	--	+100,000
	Research	--	433,000	--	1,080,000	--	+647,000
	Library resources	--	2,500,000	--	2,350,000	--	-150,000
	Regional medical libraries	--	1,200,000	--	1,950,000	--	+750,000
	Publications support	--	300,000	--	400,000	--	+100,000
125	Direct operations:						
	Library operations	248	5,997,000	264	7,193,000	+16	+1,196,000
	Toxicology information	18	1,452,000	20	1,628,000	+2	+176,000
	National Medical Audiovisual Center	105	1,962,000	105	2,341,000	--	+379,000
	Lister Hill National Center for Biomedical Communications	11	577,000	15	1,998,000	+4	+1,421,000
	Review and approval of grants and contracts	33	664,000	33	594,000	--	-70,000
	Program direction	55	1,568,000	55	1,548,000	--	-20,000
	Total obligations	470	17,308,500	492	22,182,000	+22	+4,873,500

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation

	1969	1970
Appropriation	$18,160,500	$22,182,000
Comparative transfer to "Construction of Health Educational, Research, and Library Facilities"	-1,250,000	---
Comparative transfer to "Salaries and expenses, Office of Director"	-136,000	---
Comparative transfer to "Salaries and expenses, Office of Comptroller"	-16,000	---
Unobligated balance carried forward	-700,000	---
Unobligated balance brought forward	4,117,462	700,000
Cutback required by P. L. 90-364	-162,000	---
Total currently authorized for obligation	20,013,962	22,882,000
Plus: proposed release of reserves for increased pay costs	162,000	---
Total obligations	20,175,962	22,882,000
Disposition of cutback: To be used for pay costs in this account	162,000	---

Obligations by Activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
121	Grants:						
	Training	--	$1,088,962	--	$1,000,000	--	-$88,962
	Special scientific projects	--	100,000	--	100,000	--	---
	Research	--	1,321,000	--	1,480,000	--	+159,000
	Library resources	--	2,800,000	--	2,350,000	--	-450,000
	Regional medical libraries	--	2,088,000	--	2,250,000	--	+162,000
	Publications support	--	300,000	--	400,000	--	+100,000
125	Direct operations:						
	Library operations	248	5,997,000	264	7,193,000	+16	+1,196,000
	Toxicology information	18	1,452,000	20	1,628,000	+2	+176,000
	National Medical Audio-visual Center	105	1,962,000	105	2,341,000	--	+379,000
	Lister Hill National Center for Biomedical Communications	11	835,000	15	1,998,000	+4	+1,163,000
	Review and approval of grants and contracts	33	664,000	33	594,000	--	-70,000
	Program direction	55	1,568,000	55	1,548,000	--	-20,000
	Total obligations	470	20,175,962	492	22,882,000	+22	+2,706,038

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	470	492	+22
Full-time equivalent of all other positions	22	21	-1
Average number of all employees	485	491	+6
Personnel compensation:			
Permanent positions	$4,806,000	$5,029,000	+$223,000
Positions other than permanent	207,500	222,500	+15,000
Other personnel compensation	82,700	85,000	+2,300
Total personnel compensation	5,096,200	5,336,500	+240,300
Personnel benefits	386,400	404,200	+17,800
Travel and transportation of persons	147,000	173,300	+26,300
Transportation of things	14,500	16,600	+2,100
Rent, communications, and utilities	621,000	1,637,500	+1,016,500
Printing and reproduction	308,700	421,000	+112,300
Other services	5,174,500	6,454,700	+1,280,200
Supplies and materials	356,000	407,200	+51,200
Equipment	373,700	451,000	+77,300
Grants, subsidies, and contributions	7,697,962	7,580,000	-117,962
Total obligations by object	20,175,962	22,882,000	+2,706,038

Summary of Changes

1969 estimated obligations	$20,175,962
1970 estimated obligations	22,882,000
Net change	+2,706,038

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay act costs	--	---	--	$10,000
2. Development and partial implementation of second-generation MEDLARS	52	$2,107,000	12	1,018,000
B. Program				
1. Research grants	--	1,321,000	--	159,000
2. Regional medical library grants	--	2,088,000	--	162,000
3. Publications support grants	--	300,000	--	100,000
4. Library operations	196	3,516,000	4	171,000
5. Toxicology information	18	1,452,000	2	176,000
6. National Medical Audiovisual Center	105	1,962,000	--	377,000
7. Lister Hill National Center for Biomedical Communications	11	835,000	4	1,163,000
Total program increases	--	---	10	2,308,000
C. Payments to the "National Institutes of Health Management Fund" for centrally furnished services	--	449,000	--	67,000
Total increases	--	---	22	3,403,000
Decreases				
A. Program				
1. Training grants	--	1,088,962	--	-88,962
2. Library resources grants	--	2,800,000	--	-450,000
3. Review and approval of grants and contracts	33	584,000	--	-76,000
4. Program direction	55	1,199,000	--	-82,000
Total decreases	--	---	--	-696,962
Total net changes requested	--	---	+22	+2,706,038

Summary of Changes

(New Obligational Authority Basis)

1969 estimated obligations	$17,308,500
1970 estimated obligations	22,182,000
Net change	+4,873,500

	Base		Change from Base	
	Positions	Amount	Positions	Amount
Increases				
A. Built-in				
1. Annualization of 1969 pay costs...	--	---	--	$10,000
2. Development and partial implementation of second-generation MEDLARS	52	$2,107,000	12	1,018,000
B. Program				
1. Training grants	--	655,500	--	344,500
2. Special scientific project grants.	--	---	--	100,000
3. Research grants	--	433,000	--	647,000
4. Regional medical library grants...	--	1,200,000	--	750,000
5. Publications support grants	--	300,000	--	100,000
6. Library operations	196	3,516,000	4	171,000
7. Toxicology information	18	1,452,000	2	176,000
8. National Medical Audiovisual Center	105	1,962,000	--	377,000
9. Lister Hill National Center for Biomedical Communications	11	577,000	4	1,421,000
Total program increases	--	---	10	4,086,500
C. Payments to the "National Institutes of Health Management Fund" for centrally furnished services	--	449,000	--	67,000
Total increases	--	---	22	5,181,500
Decreases				
A. Program				
1. Library resources grants	--	2,500,000	--	-150,000
2. Review and approval of grants and contracts	33	584,000	--	-76,000
3. Program direction	55	1,119,000	--	-82,000
Total decreases	--	---	--	-308,000
Total net changes requested	--	---	+22	+4,873,500

Explanation of Changes

Research grants

An increase of $159,000 will bring the total for this program to $1,480,000 consisting of $1,080,000 in new obligational authority and $400,000 brought forward from 1969. The total amount for this program will support approximately 34 grants to support the investigation and development of new techniques in health information communication.

Regional medical libraries

A total of $2,250,000 in new obligational authority is requested for this program in 1970, an increase of $162,000 over amounts available for obligation in 1969. The requested amount will fund eight regional medical library grants in 1970.

Publications support grants

An increase of $100,000 for a total of $400,000 is requested, consisting entirely of new obligational authority. This amount will support 13 grants providing financial assistance to non-profit biomedical publications.

Library operations

An increase of four positions and $171,000 for a total of $3,687,000 is requested to improve and expand library operations exclusive of the MEDLARS II project. The increase will support expanded levels and expedition of bibliographic, reference, and loan services, particularly by establishing the Library as the regional medical library for the Middle-Atlantic Area.

Toxicology information

An increase of $176,000 and two positions for a total of $1,628,000 and 20 positions is requested. The increase will support user studies to determine appropriate products and services of the system.

National Medical Audiovisual Center

A total of 105 positions and $2,339,000 is requested for this program, an increase of $377,000. The increase will support: development and initial operation of a Videotape Distribution Center to produce, store, and distribute television tapes to schools of medicine, dentistry, nursing, and allied sciences providing an additional access to current knowledge of techniques, treatment, and therapy; expansion of the NMAC collection of motion pictures, audio and video tapes, and other audiovisuals for world-wide distribution; four major seminars in biomedical communications through which health science professionals will be exposed to the newer communications media and their use in the teaching-learning process; and, operation and maintenance of an automated audiovisual distribution system now under development.

Lister Hill National Center for Biomedical Communications

An increase of four positions and $1,163,000 for a total of $1,998,000 is requested for the Lister Hill National Center for Biomedical Communications. The increase will support development of a biomedical communications network utilizing advanced information science to bring biomedical information to doctors, other health specialists, and the general population. An increase of $310,000 is requested to support the Library Component and allow inter-netting of the Regional Medical Libraries, of the MEDLARS (bibliographic) search centers, and of the three National Libraries. An increase of $508,000 is requested to allow the planning and implementing of test program materials and technical capabilities in continuing medical education. Adequate capabilities for data processing and transmission, timely planning of remote processing support to medical libraries, and effective remote use of the MEDLARS system will require an increase of $300,000. In addition to these increases $100,000 is requested for the application of information sciences technology to other efforts to improve the delivery of health services. Decreases from the 1969 base of $45,000 in the Specialized Information Services component and

$10,000 in the Audio and Audiovisual Services component partially offset the increases described above.

Training grants

The amount requested for 1970 is $1,000,000 a decrease from the total available in 1969 of $88,962. The 1969 availability of $1,088,962 consisted of $655,500 appropriated in 1969 and $433,462 brought forward from 1968. The 1970 request will support approximately 17 grant awards compared to the same number in 1969.

Library resources grants

The request for 1970 is $2,350,000 consisting entirely of new obligational authority, a decrease of $450,000 from the amount available in 1969 which consisted of $2,500,000 in new obligational authority and $300,000 brought forward from 1968.

Review and approval of grants and contracts

The request of $508,000 in 1970 is $76,000 below the amount provided in 1969 reflecting reductions in estimated consultative services and contracts required in reviewing and processing new grant applications.

Program direction

In 1970 the request of $1,117,000 reflects a net decrease of $82,000 reflecting small increases in the costs of administrative support including postage and printing offset by decreases for services of other agencies and administrative contracts.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action taken or to be taken
1. Committee urges the Library to develop, within the limits of its resources, a Center for Biomedical Communications through which all elements of the health community may have ready access to information needed for its research, education, and service efforts (page 65 of the Senate Report).	1. By Joint Resolution (P.L. 90-456) signed by the President on August 8, 1968, the Congress resolved that a National Center for Biomedical Communications to be constructed and located as a part of the Library as an urgently required facility for the improvement of communications necessary for health education, research, and practice, be named and designated as the Lister Hill National Center for Biomedical Communications. On September 18, 1968, the Secretary, DHEW, announced the establishment of the Center as an organizational entity within the National Library of Medicine (A more detailed explanation of the Center's development appears in the Narrative Justification).

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act	
Section 301.(a)(c)(d) and (i)--Research and Investigation	indefinite
Section 393.(i)--Assistance for Construction of Facilities	$10,000,000
Section 394.(a)--Grants for Training in Medical Library Sciences	1,000,000
Section 395.--Assistance to Special Scientific Projects	500,000
Section 396.(a)--Research and Development in Medical Library Science and Related Fields	3,000,000
Section 397.(a)--Grants for Improving and Expanding the Basic Resources of Medical Libraries and Related Instrumentalities	3,000,000
Section 398.(a)--Grants for Establishment of Regional Medical Libraries	2,500,000
Section 399.(a)--Financial Support of Scientific Publications	1,000,000

PUBLIC HEALTH SERVICE ACT

Title III--General Powers and Duties of Public Health Service

Part A--Research and Investigation

Section 301. The Surgeon General shall conduct in the Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man, including water purification, sewage treatment, and pollution of lakes and streams. In carrying out the foregoing the Surgeon General is authorized to--

(a) Collect and make available through publications and other appropriate means, information as to, and the practical application of, such research and other activities;

(c) Establish and maintain research fellowships in the Service with such stipends and allowances, including traveling and subsistence expenses, as he may deem necessary to procure the assistance of the most brilliant and promising research fellows from the United States and abroad;

(d) Make grants-in-aid to universities, hospitals, laboratories, and other public or private institutions, and to individuals for such research or research training projects as are recommended by the National Advisory Health Council, or, with respect to cancer, recommended by the National Advisory Cancer Council, or, with respect to mental health, recommended by the National Advisory Mental Health Council, or with respect to heart diseases, recommended by the National Advisory Heart Council, or, with respect to dental diseases and conditions, recommended by the National Advisory Dental Research Council, and include in the grants for any such project grants of penicillin and other antibiotic compounds for use in such

project; and make, upon recommendation of the National Advisory Health Council, grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs: Provided, That such uniform percentage, not to exceed 15 per centum, as the Surgeon General may determine, of the amounts provided for grants for research or research training projects for any fiscal year through the appropriations for the National Institutes of Health may be transferred from such appropriations to a separate account to be available for such research and research training program grants-in-aid for such fiscal year;

(i) Adopt, upon recommendation of the National Advisory Health Council, or, with respect to cancer, upon recommendation of the National Advisory Cancer Council, or with respect to mental health, upon recommendation of the National Advisory Mental Health Council, or, with respect to heart diseases, upon recommendation of the National Advisory Heart Council, or, with respect to dental diseases and conditions, upon recommendation of the National Advisory Dental Research Council, such additional means as he deems necessary or appropriate to carry out the purposes of this section.

Part I--Assistance to Medical Libraries

Appropriation

Section 393.(i) For the purposes of carrying out the provisions of this section, there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1967, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $10,000,000 for any fiscal year, as may be necessary.

Section 394.(a) In order to enable the Surgeon General to carry out the purposes of section 390(b)(2), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $1,000,000 for any fiscal year, as may be necessary. Sums made available under this section shall be utilized by the Surgeon General in making grants--

(1) to individuals to enable them to accept traineeships and fellowships leading to postbaccalaureate academic degrees in the field of medical library science, in related fields pertaining to sciences related to health, or in the field of the communication of information;

(2) to individuals who are librarians or specialists in information on sciences relating to health, to enable them to undergo intensive training or retraining so as to attain greater competence in their occupations (including competence in the fields of automatic data processing and retrieval);

(3) to assist appropriate public and private nonprofit institutions in developing, expanding, and improving, training programs in library science and the field of communications of information pertaining to sciences relating to health; and

(4) to assist in the establishment of internship programs in established medical libraries meeting standards which the Surgeon General shall prescribe.

Section 395. In order to enable the Surgeon General to carry out the purposes of section 390(b)(3), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $500,000 for any fiscal year, as may be necessary. Sums made available under this section shall be utilized by the Surgeon General for the establishment of special fellowships to be awarded to physicians and other practitioners in the sciences related to health and scientists for the compilation of existing, or writing of original, contributions relating to scientific, social, or cultural, advancements in sciences related to health. In establishing such fellowships, the Surgeon General shall make appropriate arrangements whereby the facilities of the National Library of Medicine and the facilities of libraries of public and private nonprofit institutions of higher learning may be made available in connection with the projects for which such fellowships are established.

Section 396.(a) In order to enable the Surgeon General to carry out the purposes of section 390(b)(4), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $3,000,000 for any fiscal year, as may be necessary. Sums made available under this section shall be utilized by the Surgeon General in making grants to appropriate public or private nonprofit institutions and entering into contracts with appropriate persons, for purposes of carrying out projects of research and investigations in the field of medical library science and related activities and for the development of new techniques, systems and equipment, for processing, storing, retrieving, and distributing information pertaining to sciences related to health.

Section 397.(a) In order to enable the Surgeon General to carry out the purposes of section 390(b)(5), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $3,000,000 for any fiscal year, as may be necessary.

Section 398.(a) In order to enable the Surgeon General to carry out the purposes of section 390(b)(6), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $2,500,000 for any fiscal year, as may be necessary. Sums made available under this section shall be utilized by the Surgeon General, with the advice of the Board, to make grants to existing public or private nonprofit medical libraries so as to enable each of them to serve as the regional medical library for the geographical area in which it is located.

Section 399.(a) In order to enable the Surgeon General to carry out the purposes of section 390(b)(7), there are hereby authorized to be appropriated for each fiscal year, beginning with the fiscal year ending June 30, 1966, and ending with the fiscal year ending June 30, 1970, such sums, not to exceed $1,000,000 for any fiscal year, as may be necessary. Sums made available under this section shall be utilized by the Surgeon General, with the advice of the Board, in making grants to, and entering into appropriate contracts with, public or private nonprofit institutions of higher education and individual scientists for the purpose of supporting biomedical scientific publications of a nonprofit nature and to procure the compilation, writing, editing, and publication of reviews, abstracts, indices, handbooks, bibliographies, and related matter pertaining to scientific works and scientific developments.

(b) Grants under this section in support of any single periodical publication may not be made for more than three years.

(c) Payment pursuant to grants made under this section may be made in advance or by way of reimbursement and in such installments as the Surgeon General shall prescribe by regulations after consultation with the Board.

Section 399a. Funds appropriated to carry out any of the purposes of this part for any fiscal year shall remain available for such purposes for the fiscal year immediately following the fiscal year for which they were appropriated.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfer to:			
"Construction of Health, Educational, and Library Facilities".....	$1,250,000	---	To consolidate construction grant funds in a single appropriation to be administered by the Bureau of Health Professions Education and Manpower Training.
"Salaries and expenses, Office of Comptroller".....	16,000	---	To consolidate administration of indirect cost negotiations in the Office of the Assistant Secretary, Comptroller.
"Salaries and expenses, Office of Director".....	136,000	---	To provide funds covering expenses for the Office of Director, NIH, which were previously funded through the NIH Management Fund.

National Library of Medicine

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$1,566,000	$1,566,000	$1,566,000	$1,566,000
1961	1,738,000	1,738,000	1,738,000	1,738,000
1962	2,066,000	2,066,000	2,066,000	2,066,000
1963	3,335,000	3,335,000	3,335,000	3,335,000
1964	4,074,000	4,074,000	4,074,000	4,074,000
1965	3,678,000	3,858,000	4,058,000	3,958,000
1966	9,185,000	9,185,000	9,685,000	9,685,000
1967	19,231,000	20,092,000	20,192,000	20,192,000
1968	21,162,000	18,662,000	21,162,000	19,912,000
1969	19,172,000	17,149,000	19,172,000	18,160,500
1970	22,182,000			

Justification

National Library of Medicine

	1969 estimate		1970 estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	470	$5,482,600	492	$5,740,700	+22	+$258,100
Other expenses	--	14,693,362	--	17,141,300	--	+2,447,938
Total	470	20,175,962	492	22,882,000	+22	+2,706,038

General Statement

The mission of the National Library of Medicine is to promote the advancement of medical and related sciences through the conduct of programs designed to aid the collection, dissemination, and exchange of scientific information critical to the support of research, education, and medical practice. This mission and the NLM's established leadership in the application of new communications technology has made it the principal focus for the biomedical communications aspect of the national health effort.

Through the Medical Library Assistance Act of 1965 the National Library of Medicine has supported the strengthening of biomedical libraries and related institutions, exploitation of interlibrary relationships, improvement of information handling techniques, and the enhancement of the role of libraries as learning resources. Other achievements include the development of the computer based Medical Literature Analysis and Retrieval System (MEDLARS) and the initial efforts in the development of a Toxicology Information Program. At the same time the NLM has provided direct bibliographic and interlibrary loan services to thousands of users.

Along with these efforts the NLM has embarked on a long-range plan to develop and implement a national multimedia biomedical communications network utilizing advanced information science to bring biomedical information to doctors, other health specialists, and the general public. This effort, which began in 1967, was formally recognized in August 1968 when Congress authorized and the Secretary, DHEW, established the Lister Hill National Center for Biomedical Communications (LHNCBC) within the National Library of Medicine. This organization is responsible for the design, implementation, and management of the biomedical communications network.

The 1970 budget request includes funds in all categories of support authorized by the Medical Library Assistance Act of 1965 (with the exception of Medical Library Construction) to continue the development and support of the Nation's biomedical information resources. Increases are requested for research in medical library science, support of a system of regional medical libraries, and support of secondary publications.

Increases are requested in Direct Operations to develop and install a second-generation Medical Literature Analysis and Retrieval System (MEDLARS) to meet increasing demands for bibliographic services; continue development of the Toxicology Information Program; increase resources available to provide services through the National Medical Audiovisual Center; and, support design and testing activities for the biomedical communications network.

Grants

The Medical Library Assistance Act of 1965 authorizes a program of grants for the purpose of assisting the health community in the acquisition, organization, dissemination and application of medical knowledge. The purpose of this Act is to encourage and assist the development of medical libraries and related resources to provide for the improved flow of biomedical information throughout the areas of research, education, and medical practice, so that existing medical knowledge can be utilized to the fullest extent in improvement of health throughout the Nation.

Training and Fellowships

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	15	$794,000	17	$1,000,000	+2	+$206,000
New grants	2	294,962	--	---	-2	-294,962
Total	17	1,088,962	17	1,000,000		-88,962

A decrease of $88,962 in 1970 will allow the Library to support only non-competing continuation applications and will allow no funds for new grants. The amount available in 1969 was comprised of $433,462 in funds carried forward from 1968 and new obligational authority of $655,500.

The Medical Library Assistance Act authorization of $1,000,000 per year for training can support approximately 100 trainees per year for a total of approximately 500 during the five year period authorized by the Act.

As an example of the health sciences information manpower shortage and needs, it is estimated that the approximately 100 medical schools in the United States each need 10 professional medical librarians and other medical communication specialists, for a total need of 1,000. Several thousand hospital and other health related institutions each should have at least one trained librarian or other information resource specialist.

Since the fiscal authorization for training cannot provide fulfillment of the estimated total professional medical librarian manpower requirement, the program focuses on training persons for creative leadership in positions of major responsibility.

New training grant applications now in the review process and others in preparation propose innovative programs for the development of various new careers in biomedical communications. The increasing uses of complex automated systems and the potential applications of various new communications media require the training of biomedical communication specialists who have the capability for the design, development, and management of multimedia information systems. There is increasing interest in doctoral and post-doctoral training programs for biomedical communication specialists.

In 1969 the Library expects to support approximately 17 training grants to 16 institutions for the training of 119 persons.

Special Scientific Projects

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	--	---	2	$50,000	+2	+$50,000
New grants	3	$100,000	1	50,000	-2	- 50,000
Total	3	100,000	3	100,000	--	---

No increase is requested for this category in 1970.

The purpose and intent of the Special Scientific Project Awards program is to support outstanding scholars who can devote full time to analysis, evaluation, and documentation of major advances in the health sciences.

These studies result in the publication of important monographs on advances in medicine, including scientific, social, and cultural factors.

This program has been announced to medical school faculties and to other academic and research centers. Five awards have been made to outstanding scholars, and 50 persons have indicated interest in applying for these awards.

Research

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	26	$752,000	26	$948,000	--	+$196,000
New grants	9	569,000	8	532,000	-1	-37,000
Total	35	1,321,000	34	1,480,000	-1	+159,000

The growing national effort in health research, education, and service produces and requires a constantly growing amount of biomedical information. Achieving a rapid and effective flow of this information at favorable resource allocations is an important goal of biomedical information research. Such research takes the form of behavioral studies of information seeking patterns in the health sciences community, development of new methods of transferring information, and feasibility studies of sophisticated technological processing systems. The best efforts of many disciplines are needed to synthesize behavioral and technological research, and to contribute to designs of total information flow systems and biomedical communication networks.

The Extramural Research Program now supports a variety of studies in these areas. Many of the investigations require steadily expanding support over a long term as project design leads to data accumulation, experimentation, and, finally, testing and evaluation. The trend will probably continue, particularly when definitive testing of innovative methods or equipment is involved.

It is expected that a greater number of applicants will request higher levels of support in order to undertake investigations which, to realize potential value, necessarily involve complex research design as well as computerized data accumulation and analysis. Average grant awards have increased steadily: from $31,000 in 1967, to $45,000 in 1968, and to an estimated $52,000 in 1969. Further increases are expected for these larger, more comprehensive studies.

Support for 35 or more research projects is projected for 1969, and 34 in 1970. The decrease is based on the likelihood of supporting more of the relatively complex projects, at a higher average award. A slight decline in the total number of applications is also expected, however, with fewer proposals for the retrospective historical studies which this program also sponsors. Research projects being supported during 1969 which will require continued support in 1970 include studies on communications processes and the flow of medical information, the relationships between various biomedical information facilities and services, the cost-effectiveness of certain indexing techniques, the use of self-instructional materials, historical studies, and the introduction and evaluation of new techniques and systems in medical libraries.

Library Resources

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	373	$2,688,000	390	$2,142,000	+17	-$546,000
New grants	17	112,000	34	208,000	+17	+96,000
Total	390	2,800,000	424	2,350,000	+34	-450,000

Obligations for resources grants in 1969 consist of $2,500,000 in new obligational authority plus $300,000 brought forward from 1968. The $2,350,000 requested for 1970 represents a net decrease of $450,000 in obligational authority.

The purpose of the medical library resources program is to provide financial assistance and incentive for improving the basic materials, equipment, and services of medical libraries. Although it has been estimated that there are approximately 6,300 medical libraries in the United States, the resources grants program will focus on assisting only 10 to 15 percent of the major libraries which serve comparatively large and varied health science clientele. The amount of each resource grant is computed by a formula based on the annual operating budget of the library. A library receiving an initial award may request continued support for subsequent years in decreasing amounts.

This program is vital and essential for the immediate and rapid improvement of the several hundred medical libraries which are major stations and links in the development and operation of the national biomedical communications network.

During 1968 first year awards and renewals were made to 165 academic libraries in the amount of $2,482,217; 177 hospital libraries in the amount of $764,184; 31 medical societies and other institutions in the amount of $301,600 for a total of 373 awards amounting to $3,548,001. Estimated 1970 continuing commitments for these 373 awards will be made in 1969 in the amount of $111,000 which will generate an additional $93,000 in continuing commitments for 1970. Thus, approximately $2,142,000 will be required to fund continuing commitments for resources awards in 1970.

Regional Medical Libraries

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	3	$839,000	8	$2,250,000	+5	+$1,411,000
New grants	5	1,249,000	--	---	-5	-1,249,000
Total	8	2,088,000	8	2,250,000	--	+162,000

The Medical Library Assistance Act of 1965 authorized appropriations to assist in the development of a national system of regional medical libraries each of which would have facilities of sufficient depth and scope to supplement the services of other medical libraries within a specific region. Grants are awarded to improve, augment, and strengthen regional service in selected libraries which already have a sound base for providing expanded services in a defined region. These libraries will be critical service complexes for the developing biomedical communications network.

The intent of this program is to provide support to existing superior institutions, permitting them to extend their services in support of libraries (and individuals) in the agreed region. Statutory limitations on funding strictly limit the number of regional libraries which can be supported.

In 1967 the first regional library grant was made to Countway Medical Library of Harvard University. This enabled the activation of the New England regional medical library system. In 1968 two more regional medical libraries were established, in Seattle for the Pacific Northwest (including Alaska) and in Philadelphia for the Delaware Valley complex. In 1969 continuation support for the three awarded Regional Medical Library grants will amount to $839,081. The remaining balance of $1,248,919 will allow the awarding of five additional Regional Medical Library grants. In 1970 the Library expects to support the continuation of the eight Regional Medical Libraries at a cost of $2,250,000, with the increase of $162,000 covering expansion of services and increased operating costs within the eight regions.

Publications Support

	1969 estimate		1970 estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	7	$218,000	7	$225,000	--	+$7,000
New grants	3	82,000	6	175,000	+3	+93,000
Total	10	300,000	13	400,000	+3	+100,000

Secondary literature resources constitute essential bridges to the great annual outflow of new information from health research and practice. The Library's selective program for developing non-profit publications (such as bibliographies), to compile, synthesize, and repackage biomedical information, focuses toward more rapid and effective use of such knowledge by Americans in the health professions.

Much of this multidisciplinary information is accessible only through the use of such secondary resources, and the program has already sponsored a series of significant secondary tools of proven value to the health community.

An important focus for the Library's activities in the 1969 program will be a study covering the review and evaluation of the needs of American health sciences personnel for biomedical information originally published in a foreign language. During 1970 the Library will extend and implement the results of this study.

The $100,000 increase in this program will provide for three new awards in 1970.

DIRECT OPERATIONS

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	470	$5,482,600	492	$5,740,700	+22	+$258,100
Other expenses	--	6,995,400	--	9,561,300	--	+2,565,900
Total	470	12,478,000	492	15,302,000	+22	+2,824,000

Library Operations

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	248	$2,740,500	264	$2,933,400	+16	+$192,900
Other expenses	--	3,256,500	--	4,259,600	--	+1,003,100
Total	248	5,997,000	264	7,193,000	+16	+1,196,000

Development and partial implementation of second-generation MEDLARS

In 1968 the National Library of Medicine awarded a contract to Computer Sciences Corporation for the design and installation of a second-generation Medical Literature Analysis and Retrieval System (MEDLARS II) to replace the current system which was installed in 1964. The plan calls for a 3-4 year project of incremental upgrading, with first-phase operations on the new equipment scheduled for early 1970.

When fully operational the MEDLARS II computer system will incorporate: (1) increased processing capability; (2) intermediate access storage; (3) time-sharing; and, (4) on-line access to data bases from remote terminals. Translated into program capabilities, these new features will provide: (1) a greatly increased file capacity which will allow the maintenance of abstracts on the data record; (2) quicker response to an increasing volume of bibliographic service requests including demand searches and recurring bibliographies; (3) more current data through on-line record up-dating; (4) an automated acquisition and cataloging system with cataloging data availability to and from other medical libraries through remote terminal access to the NLM record files; (5) development of specialized information services supporting the toxicology information and drug literature programs through the addition of chemical structure search capabilities in the new system; and, (6) support of data processing and data transmission activities of the biomedical communications network.

The program increase of $1,019,000 will allow the continued phased implementation of MEDLARS II. Specifically, it will support: 12 new positions to provide additional project management for the MEDLARS II project and additional operating and software maintenance personnel for the augmented system; continuation of the contract for software development and equipment installation for the scheduled

phases of the project; and, lease costs for the equipment installed.

Other Library Operations

An increase of $177,000 and four positions is requested to begin full operation of the Mid-Atlantic Regional Library service, to provide for central operational management of the Regional Medical Library network, and to procure assistance in the development of augmented Medical Subject Heading vocabulary for MEDLARS II.

In developing the network of Regional Medical Libraries authorized by the Medical Library Assistance Act of 1965, the NLM facility appeared to be best suited to serve as Regional Medical Library for the Mid-Atlantic Region. Assumption of this function will require an additional position to provide improved and augmented services for interlibrary loans and bibliographic and reference services, training services to health science practitioners in the use of library resources, and back-up support to small hospital libraries.

Central management of the network of nine Regional Medical Libraries will require an additional two positions. Three of these Regional Medical Libraries were established in 1968, and the remaining six (including the Mid-Atlantic) were established in 1969. Central management functions include maintaining balanced interlibrary loan and demand search workloads among regions, providing indexing and demand search formulation training both at NLM and in the field, and formulation of standardized operating procedures.

The development of the more sophisticated MEDLARS II system will require augmented vocabulary for input and retrieval. This will require intensive review of a large number of thesauri and terminology authority files to provide the "mapping" and structuring of up to 200,000 biomedical concepts into relationships that can be programmed and maintained by the computer. Such activities are largely intellectual requiring highly skilled terminology specialists and scientists with comprehensive subject matter knowledge in the many scientific disciplines comprising the complex of biomedical sciences. This effort involves a substantial supplemental clerical support effort. The ability to make use of and to exploit fully the extensive and sophisticated capabilities of MEDLARS II is dependent on this intellectual input. The growing scope of health-related activities will provide continuing need for such developments in new areas. The dynamic nature of biomedical sciences results in radical changes in concepts over very short periods of time which require considerable revamping of terminology. Advances over the past decade in fields such as molecular biology, viruses, transplantation, immunology, genetic coding, etc., have literally created new vocabularies and concepts which must be incorporated and related to the existing body of concepts to provide ready access to the biomedical literature.

One professional terminology and subject specialist will be required for this activity in 1970. This direct staff increase will be complemented by an increase of $50,000 for contractual consultative services of qualified experts in various disciplines and fields to provide the high degree of scientific and technical expertise necessary to the success of this activity.

Toxicology Information

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	18	$299,300	20	$324,600	+2	+$25,300
Other expenses	--	1,152,700	--	1,303,400	--	+150,700
Total	18	1,452,000	20	1,628,000	+2	+176,000

The Toxicology Information Program was established by Presidential Order. Responsibility for its implementation was delegated to the National Library of Medicine by the Secretary, DHEW, in 1966. When operational the toxicology program will: (1) identify, classify, and maintain current descriptions of toxicology information users and significant centers and services which accumulate and analyze toxicology information; (2) propose compatible systems standards and guidelines within Government for storage and retrieval of toxicology information including common vocabulary systems and compatible computer programming, and promote their adoption by the non-Government sector; (3) respond to incoming requests for stored information, directly or by referral, and provide or arrange repackaging of stored information where significantly large user-groups are identified; and, (4) provide a data base for the study of biological effects of chemicals which have a meaning to life systems.

Achievements in the first 18 months of the program include: (1) development of plans, objectives and organization; (2) the development of a Toxicity Bibliography published quarterly beginning in April, 1968; (3) experimental compilation of a bibliography on methodology in analytical toxicology; (4) initiation of a project leading to publication in December, 1968 of a directory through the National Referral Center, Library of Congress, to identify information sources; and, (5) development of project contracts. In 1969, these contracts will: (a) provide information seeking behavior and motivations of users; (b) develop a roster of expert advisors in toxicology; (c) support terminology development in toxicology; and (d) study communication and transfer of information in toxicology.

Program advisory services have been procured from the National Academy of Sciences, National Research Council.

The $176,000 program increase in 1970 will support: two new positions for planning and project management; contractual services for the development of a computer based reference file to available toxicology data on chemical agents; and continued identification of appropriate user needs.

National Medical Audiovisual Center

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	105	$1,193,800	105	$1,194,100	--	+$300
Other expenses	--	768,200	--	1,146,900	--	+378,700
Total	105	1,962,000	105	2,341,000	--	+379,000

Effective FY 1968, The National Medical Audiovisual Center was transferred to the National Library of Medicine as the audiovisual and telecommunication component of that organization. Prior to that time, as the Public Health Service Audiovisual Facility, it was an ancillary program of the National Communicable Disease Center in Atlanta. Concurrent with the transfer, the mission of NMAC was redefined as follows:

(1) operation of the central facility in the Public Health Service for the development, production, distribution, evaluation, and utilization of motion pictures, videotapes, and other audiovisual forms;

(2) coordination of a comprehensive audiovisual program for the Service to assure maximum responsiveness and economy of funds and manpower;

(3) provision for consultation and assistance in the development of specialized audiovisual activities;

(4) promotion of the production, dissemination, and utilization of medical films and other audiovisuals in the schools of health professions and elsewhere;

(5) development and support of a national clearinghouse and archival program; and,

(6) establishment of a national/international film and videotape center for the distribution and exchange of biomedical audiovisuals.

A number of forces are contributing to the dilemna of providing adequate numbers of health personnel to meet urgent global health needs in preventive and curative medicine. Among those most generally recognized are: a population increase coupled with a demand for additional health personnel, a growing shortage of qualified teachers in the health professions, a massive information output, and a rapidly growing communications technology which thus far has outstripped the ability of the health professions to use it. All of these factors have encouraged schools of the health professions and other related medical organizations to seek guidance and assistance from the National Medical Audiovisual Center.

The major objective of the NMAC program is the most efficient dissemination of health information, in an audiovisual format, to the health professions, and relates to the development of prototype audiovisual communications delivery systems. These involve the Center in two critical program areas: (1) manpower and training, and (2) communication of health information. The NMAC will assist schools of the health professions to develop audiovisual capability and prototype classrooms; support regional training conferences and seminars; provide an information clearinghouse on audiovisual technology and expanded audiovisual production; and, strengthen the international exchange program.

In 1970, an increase of $379,000 is requested. Specifically, $212,000 will permit the development, with the cooperation and support of Veterans Administration and private groups, and initial implementation of a Videotape Distribution Center for reproduction, storage and distribution of videotapes to medicine and related professions. The scope of material available on videotapes is constantly expanding. Distribution of tapes will provide practitioners with additional access to material on current techniques, treatment, and therapy.

An increase of $77,000 will support the expansion of the existing collection of motion picture films, audiotapes, and videotapes and other audiovisuals with emphasis on the acquisition and production of materials for innovative programs of health care, training and research.

The 1970 increase includes $62,000 to support four seminars in biomedical communication in order to encourage the use of available biomedical communication resources including audiovisuals and to foster cooperative efforts of mutual benefit to participants.

An increase of $28,000 will provide for maintenance and operation of an automated distribution system to provide more timely access to health audiences of medical audiovisuals and to relate more closely to MEDLARS and the biomedical communication network the reference, cataloging, and bibliographic services of the NMAC.

Lister Hill National Center for Biomedical Communication

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	11	$170,200	15	$214,700	+4	+$44,500
Other expenses	--	664,800	--	1,783,300		+1,118,500
Total	11	835,000	15	1,998,000	+4	+1,163,000

The development of a National Center for Biomedical Communications was undertaken on the recommendation of the House and Senate Appropriations Committees and the House Special Subcommittee on the Investigation of the Department of Health, Education, and Welfare (1966). By Joint Resolution (P.L. 90-456) of Congress, signed by the President on 3 August 1968, the Center was renamed the Lister Hill National Center for Biomedical Communications. The Secretary of Health, Education, and Welfare has established the Center within the organizational framework of the National Library of Medicine.

The Lister Hill National Center for Biomedical Communications is the DHEW focal point for the coordination of biomedical communications systems and network projects, and serves as the Departmental representative in these areas both within DHEW and in the Department's relations with other Federal agencies and private organizations. The Center will apply technology to the development of biomedical communications systems aimed at improving health education, medical research, and the delivery of health services. Specifically, the Center is responsible for the design, development, implementation, and technical management of a Biomedical Communications Network.

The Biomedical Communications Network is an interrelated complex of four service components and one network support component:

The Library Component, the most advanced of present biomedical communications forms, has as its primary functions the acquisition, indexing, cataloging and classifying of reports of new medical scientific knowledge wherever recorded; the storage of this knowledge for use in both present and future time; bibliographic access to and retrieval of this knowledge; and the dissemination of the vehicles, e.g., books, reports, journals, containing knowledge as well as the bibliographic tools for accessing these vehicles. The Component will be a flexible netting of a large number of medical libraries and interconnections with other repositories of scientific information. In its entirety, the Library Component will serve as the guarantor of the organizaticn of medicine's scientific and professional knowledge, and of accessibility to what is already known. This component is essential to and ultimately relates to all biomedical communications facilities.

The Specialized Information Services Component, like the Library Component, is an organizer and a disseminator of medical scientific knowledge; however, this component operates only in relatively narrow, well defined fields and, in response to queries, provides specific, tailored information bearing on a subject. Unlike the Library Component, the Specialized Information Services Component provides information rather than the bibliographic services and books normally associated with a library. This Component will be a sophisticated meeting of existing facilities, e.g., DHEW biomedical information analysis centers, other Federal information analysis centers, and new systems, e.g., toxicology information system, now being developed. The Component will make great use of computer processing, data communications, electronic displays and a wide range of advanced information handling technology.

The Specialized Education Services Component provides the basic services and facilities required for the continuing education of medical professionals, and for

the delivery of basic health information to the medically uninformed. With regard to the medical professionals, the Component is oriented to providing that information which is necessary to guard against technical obsolescence in health services and to improve the overall quality of medical services provided. In addition to providing purely health oriented information and transmitting the results on on-going research, this Component will keep the health professionals informed about relevant, non-medical new technologies that are potentially exploitable for the advancement of medicine. A major portion of the Specialized Education Services Component will be directed toward the undergraduate and graduate programs of medical schools. With regard to the medically uninformed, the Component will make available the facilities for transmitting basic health science information services aimed at increasing health awareness and encouraging people to take advantage of the health services resulting from the Nation's investment in medical research.

The Audio and Audiovisual Component is responsible for the acquisition, creation, maintenance and distribution of audio and audiovisual materials for the Biomedical Communications Network. These materials complement the information and other educational materials provided by other network components. The Audio and Audiovisual Component will create materials where necessary to satisfy user requirements; it will also arrange to acquire such materials from other activities or to have another activity produce such materials for use in the Biomedical Communications Network. The Component may well provide a variety of other services such as serving as a national referral center for biomedical films, and providing a network of audio lecture materials.

The Data Processing and Data Transmission Component is a support component comprising all the data processing and communications facilities of the Biomedical Communications Network; in effect, it is the bond which holds all the other biomedical communications components together in a disciplined network. In the areas of Library Component and Specialized Information Services Component, this component will provide the computer processing and communications facilities to receive requests, search and retrieve responses, and transmit the answer back to the requester. In communications facilities for transmitting alphanumeric educational materials of various kinds to locations wherever medical educational activities are conducted.

Applicable technology exists. A vast reserve of new procedures, techniques, and equipments have been developed over the past ten years. The number of computers in the Federal Government has grown by a factor of sixteen from 1957 to 1967. The computer capability per dollar has increased 50% every year in the same period, amounting to more than a fifty-fold increase in operations per dollar in ten years. Yet in 1966 less than 4% of the Federal Government computers were in DHEW while DHEW spent about 10% of the Federal Budget. The application of communications technology within the DHEW is even more spotty. Analysis has shown that to successfully apply such new technology there must be organized a situation in which the technology "push" can be mated to the need "pull" to begin the evolutionary development of whole new capabilities and services.

Initial activity began in 1967 on the most advanced component centered around the existing NLM MEDLARS system. Work is currently under way on all components. A highly qualified staff of professionals, averaging more than ten years experience in information technology and systems has been recruited. Contractual efforts were initiated with the centers of excellence in information and communication technology. A Remote Information System Center was implemented to connect the Library with computer systems and other libraries throughout the country. Support of the medical professional societies has been mobilized, and imaginative proposals for the use of advanced communication technology, e.g., communication satellites, were developed. In summary, substantial momentum has been developed toward effective utilization of information technology to improve health services delivery, medical education, and biomedical research.

A program increase of $1,163,000 in 1970 will provide the continued impetus necessary to move beyond the design phase to allow engineering development and test applications. Specifically the increase will support four new positions and funds for contractual efforts for planning and project management, engineering development, evaluation of test applications, and implementation planning. The four positions will allow the development of staff to insure the effective management of the Network development.

The increase of $1,163,000 is directed primarily at the Biomedical Communications Network. Of this amount $310,000 is proposed to support the Library Component and allow inter-netting of the Regional Medical Libraries, of the MEDLARS (bibliographic) search centers, and of the three National Libraries. An increase of $508,000 is requested to allow the planning and implementing of test program materials and technical capabilities in continuing medical education. These funds will allow some limited course development and the inter-connection of several regional medical educational television networks. Adequate capabilities for data processing and transmission, timely planning of remote processing support to medical libraries, and effective remote use of the MEDLARS system will require an increase of $300,000. In addition to these increases $100,000 is requested for the application of information sciences technology to other efforts to improve the delivery of health services. Decreases from the 1969 base of $45,000 in the Specialized Information Services component and $10,000 in the Audio and Audio-visual Services component partially offset the increases described above.

Research and Support Contracts

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	--	---	--	---	--	---
Other expenses	--	$585,000	--	---	---	-$585,000
Total	--	585,000	--	---	--	-585,000

No obligational authority is requested in FY 1970. This represents a decrease of $585,000 from the 1969 level. The 1969 figure of $585,000 includes $285,000 in carryover and $300,000 in new obligational authority related to contracts managed by the Research and Development staff. The decrease of $585,000 in 1970 in research and support contracts reflects elimination of this sub-activity in 1970 and incorporation of this amount in the base for the Lister Hill National Center for Biomedical Communications.

Review and Approval of Grants and Contracts

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	33	$426,300	33	$417,600	--	-$8,700
Other expenses	--	237,700	--	176,500	--	-61,300
Total	33	664,000	33	594,000	--	-70,000

Funds and positions for this activity provide administrative staff and program direction for the Medical Library Assistance grant and contract support activity and for international activities of the NLM funded by the Scientific Activities Overseas (Special Foreign Currency) appropriation.

A decrease of $70,000 in 1970 reflects reductions in consultative services and contractual support services due to a lower level of activity in grants review and processing, resulting in part from transfer of the construction grant program to the Bureau of Health Professions Education and Manpower Training.

Program Direction

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	55	$652,500	55	$656,300	--	+$3,800
Other expenses	--	915,500	--	891,700	--	-23,800
Total	55	1,568,000	55	1,548,000	--	-20,000

Funds and positions for this activity support the immediate Office of the Director, the Office of Administrative Management, the Office of Public Information and Publications Management, and reimbursement to the NIH Management Fund for centralized administrative and plant maintenance support services. In April, 1968, the National Library of Medicine became a part of the National Institutes of Health in the reorganization of the Department's health activities. Prior to the reorganization NLM procured some central administrative services from NIH under a reimbursable agreement. Beginning in 1970 NIH will assess the NLM appropriation an amount for transfer to the NIH Management Fund based on pro-rata formulae.

The decrease of $20,000 in 1970 results from decreased reimbursable services of other agencies and non-recurring administrative contract support partially offset by small increases for increased costs of equipment rental, postage, supplies, and central administrative support services.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Library Operations			
(2) Public Health Program Specialist	GS-15		$39,560
Deputy Chief of Office	GS-15		19,780
Chief of Division	GS-15		19,780
(2) Systems Analyst	GS-14		33,892
(3) Systems Analyst	GS-13		43,227
Public Health Program Specialist	GS-12		12,174
(2) Programmer	GS-12		24,348
(2) Programmer	GS-11		20,406
Public Health Program Specialist	GS-9		8,462
Secretary	GS-5		5,732
		(16)	227,361
Toxicology Information			
Chief of Section	GS-15		19,780
Public Health Program Specialist	GS-13		14,409
		(2)	34,189
Lister Hill National Center for Biomedical Communications			
(2) Director of Division	GS-15		39,560
Administrative Officer	GS-13		14,409
Secretary	GS-6		6,321
		(4)	60,290
Total, new positions, all activities		(22)	321,840

WEDNESDAY, APRIL 3, 1969.

WITNESSES

RICHARD L. SEGGEL, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT W. BERLINER, DEPUTY DIRECTOR FOR SCIENCE, NATIONAL INSTITUTES OF HEALTH
DR. MARTIN M. CUMMINGS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE
DR. VIRON LEROY DIEFENBACH, ASSISTANT SURGEON GENERAL AND DIRECTOR, DIVISION OF DENTAL HEALTH, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER
ROSS HOLLIDAY, ASSOCIATE DIRECTOR (ENGINEERING RESOURCES), DIVISION OF RESEARCH SERVICES, NATIONAL INSTITUTES OF HEALTH
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
NATIONAL INSTITUTES OF HEALTH			
Travel and transportation of persons		1	10
Printing and reproduction		2	5
Other services	1,772	1,207	1,915
Supplies and materials	5		
Equipment	44	192	154
Lands and structures	550	2,539	105
Total, National Institutes of Health	2,371	3,941	2,189
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
Travel and transportation of persons	2	7	4
Printing and reproduction	6	51	27
Other services	531	1,703	1,000
Supplies and materials	15		
Equipment			2,000
Lands and structures	1,381	9,093	1,454
Total, General Services Administration	1,935	10,854	4,485
Total obligations	4,306	14,795	6,674

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	Costs to this appropriation					Analysis of 1970 financing			
	Total estimate	To June 30, 1967	1968 actual	1969 estimate	1970 estimate	Deduct selected resources and unobligated balance, start of year	Add selected resources and unobligated balance, end of year	Appropriation required, 1970	Appropriation required to complete
Program by activities:									
1. Animal quarters, NIH	2,606	2,602		4					
2. Biologics standards annex	5,063	4,866	47	150					
3. Cancer-mental health-neurology cafeteria	890	732	50	108					
4. Cancer research facility	10,788	4,762	3,695	2,331					
5. Child health and human development research facility	10,340		94	383		223	223		9,640
6. Combined services facility and warehouse	3,780	22		75	200	883	683		2,800
7. Dental health center addition	5,308	37	35	79	3,543	2,657	614	1,500	1,000
8. Expansion of clinical center facilities	1,550	159	895	300	196	196			
9. Extension of clinical center cafeteria	695	222	466	7					
10. General office building extension	6,800	882	2,892	3,026					
11. Gerontology research facility	8,050	4,606	2,739	655	50	50			
12. Incinerator facility	2,350		21	624	1,705	1,705			
13. Isotope laboratory addition	500		30	470					
14. Lister Hill National Center for Biomedical Communications	12,900				300		600	900	12,000
15. Master utilities extension	10,713	1,896	1,491	1,068	775	470	695	1,000	4,788

16. Multilevel parking facilities:									
(a) Additional facility—General office building	1,510			94	6	6			1,410
(b) Cancer-mental health/neurology buildings	2,110	23	33	675	1,270	1,379	109		
(c) General office building	1,951	21	18	72					1,840
17. National environmental health sciences center	41,392			175	260	1,610	1,350		39,607
18. Neurology-allergy virus research facility	6,575				114		386	500	6,075
19. Neurology-child health facility, Puerto Rico	2,320	26	32	500	1,762	1,762			
20. NIH animal center	15,319	3,855	105	803	916	1,016	100		9,540
21. NIH library relocation	900	855	25	20					
22. Repairs and improvements	6,163	2,773	522	2,052	716	316	100	500	
23. Sabana Seca facility, Puerto Rico	200		9	176	15	15			
24. Service building 12 and 12A	1,800	1,786		14					
Total program costs, funded	162,573	30,125	13,199	13,861	11,828	12,288	4,860	4,400	88,700
Change in selected resources [1]			−8,893	934	−5,154				
Total obligations			4,306	14,795	6,674				
Financing:									
Comparative transfers to other accounts			2,646	13,341					
Unobligated balance available, start of year			−33,878	−37,641	−9,505				
Unobligated balance transferred to other accounts					6,730				
Unobligated balance available, end of year			37,641	9,505	501				
Budget authority (appropriation)			10,715		4,400				
Relation of obligations to outlays:									
Obligations incurred, net			6,952	28,136	6,674				
Obligated balance, start of year			16,130	7,555	24,493				
Obligated balance transferred					−8,782				
Obligated balance, end of year			−7,555	−24,493	−7,914				
Outlays			15,526	11,198	14,471				

[1] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $16,832,000; 1968, $7,939,000; 1969, $8,873,000; 1970, $3,719,000.

Mr. FLOOD. Now we have the National Institutes of Health, Buildings and Facilities. The witness is Mr. Seggel, Associate Director for Administration, National Institutes of Health.

We will insert your biographical sketch in the record at this point.

(The biographical sketch follows:)

Biographical Sketch

Name: Richard L. Seggel.

Position: Associate Director for Administration, NIH.

Birthplace and date: Union City, N.J., January 11, 1914.

Education: Princeton University, A.B., 1936, major in public and international affairs; University of Cincinnati, graduate program in public administration; Princeton University, M.A., 1938, politics (primary field—public administration).

Experience:

1958–present: Executive Officer, NIH (retitled Associate Director for Administration).

1956–58: Director, Office of Management Policy, Office of the Secretary, DHEW.

1954–56: Assistant Executive Officer, Public Health Service, DHEW.

1953–54: Assistant Executive Officer, Bureau of State Services, Public Health Service, DHEW.

1951–53: Chief, Program Planning Branch, Health and Special Weapons Defense Division, Federal Civil Defense Administration.

1945–51: Budget examiner, Bureau of the Budget.

1941–45: Military service—private to captain (AGD); 19 months in European theater.

1940–41: Administrative analyst, Bureau of the Budget.

1939–40: Technical assistant, New Jersey Civil Service Commission.

1938–39: Research assistant, Princeton University.

Association memberships: American Society for Public Administration and chairman of ASPA National Capital Area Chapter's Suburban Forum on Public Administration.

Special awards, citations, or publications: A.B. with honors, 1936; Superior Service Award by DHEW, 1963.

Mr. FLOOD. I see you have a statement. Please proceed.

GENERAL STATEMENT

Mr. SEGGEL. Mr. Chairman and members of the committee, this is a new appropriation to provide funds for the design, construction, and repair and improvement of facilities for the National Institutes of Health. Funds for these purposes were formerly included in a Public Health Service-wide appropriation, but, in accordance with the reorganization of the Department's health functions, are, for fiscal year 1970, being requested in a separate appropriation to NIH.

In summary, we are requesting a total of $4,400,000 in fiscal year 1970 for the following projects:

Equipment for the Dental Health Center addition to be constructed in San Francisco	$1,500,000
Design of an annex to the National Library of Medicine to be named the Lister Hill National Center for Biomedical Communications	900,000
Design of a special virus facility for research in neurological and infectious diseases	500,000
Extension of the NIH master utility system to serve new facilities now in the design and planning stage	1,000,000
Repairs and improvements to the existing NIH plant	500,000

Mr. SEGGEL. I will discuss each of these briefly.

Equipment for the dental health center addition, $1,500,000

Planning and construction funds totaling $2,808,000 were appropriated in 1966 and 1968 for the construction of a wing to the Dental Health Center in San Francisco, Calif. This wing will provide badly needed additional space for laboratory and epidemiological studies and for continuing education of dentists and dental public health workers. The funds requested in 1970 will provide for a portion of the specialized equipment and fixtures required in the dental clinical and laboratory space and television and other audiovisual equipment in experimental teaching areas. The long leadtime for ordering and delivering this equipment makes it necessary to request funds in 1970 to permit installation concurrent with the construction of the building.

Lister Hill National Center for Biomedical Communications, $900,000

It is estimated that the National Library of Medicine will need approximately 149,000 net square feet of additional space to accommodate its new and expanding programs. As you know, Public Law 90–456 refers to a National Center for Biomedical Communications to be constructed and located as part of the National Library of Medicine and specifies that it be named the Lister Hill National Center for Biomedical Communications.

The present facility of the Library was designed for a maximum staff of 250 employees. At present, 341 regular employees work in the building. This excludes 34 employees in rental space in Bethesda. The additional employees have been accommodated by serious crowding of work spaces and by conversion of needed stack space. The problem will become increasingly critical as programs expand to meet the responsibilities which have been placed on the Library.

The Library's rapid growth and expanded mission were not envisioned in 1958 when the present facility was designed. Specifically, the original planning did not anticipate (1) the fully computerized medical literature analysis and retrieval system (Medlars) which has has been in operation since 1964, and which is now under redevelopment as a greatly augmented second generation system and (2) the development of a number of new programs including: the enactment of the Medical Library Assistance Act of 1965 which added an extramural grants and contracts program; the initiation of a toxicology information program in 1967 at the direction of the President; and the establishment of the Lister Hill National Center for Biomedical Communications to apply technology to the development of biomedical communications systems.

The new building will contain specialized space for laboratory research in communications technology and network engineering in addition to office, conference, and support space. Space in the existing NLM building will be returned to its original library use.

The requested sum of $900,000 will provide for the planning and design of this facility.

Virus research facility, $500,000

A new specially designed facility is needed to house research of the National Institute of Neurological Diseases and Stroke and the National Institute of Allergy and Infectious Diseases involving the use of hazardous viral agents. The scientific staffs of both NINDS and NIAID are now working with agents that cause uniformly fatal diseases, and conventional laboratory facilities, which they are now using, are inadequate to protect them from undue exposure to these agents or to contain them in a safe environment. An additional factor is the long latent period of some of these infectious agents, which is measured in months, even years. This new facility, in addition to providing the establishment of maximum safeguards for researchers and their experimental work, will permit the centralization of several widely scattered programs in one location.

This proposed facility will consist of a laboratory building with an estimated gross area of 86,500 square feet and a net area of 41,800 square feet. The net to gross area has been reduced to allow space for isolation of program areas and to allow room for separation of mechanical systems serving these areas. Space will be provided for research laboratories, animal holding facilities, and essential supporting functions, including offices, as required for a staff of 120.

The requested sum of $500,000 will provide for the design of this facility.

Master utilities extension, $1,000,000

The extension of the master utility system on the NIH reservation will be required to serve new facilities already approved by Congress and in the planning stage and those for which planning funds are being requested in 1970. Specifically, these new facilities include the John E. Fogarty International Center for Advanced Study in the Health Sciences, the research building for the National Institute of Child Health and Human Development and the combined services facility and warehouse for which planning funds have been approved by Congress and the special virus research and Library annex facilities, for which planning funds are being requested in 1970.

Utilities needed include an extension of the central air conditioning plant, and steam, water, electric, gas, sewers and similar utility distribution lines. The request of $1 million for 1970 will provide for the design of these added utilities ($500,000) and for the construction costs of installing one additional 3,000-ton machine in the air-conditioning plant ($500,000).

Repairs and improvements, $500,000

As you know, our plant is quite extensive and many of our facilities are now relatively old. The need for repairs and improvements is a continuing one, and in the past 6 years a total of $5,195,000 has been appropriated for this purpose. Examples of projects for which we are requesting $500,000 in 1970 include: renovation of the air-conditioning system in one of our older laboratory buildings, installation of emergency electrical units on our Bethesda reservation, remodeling of electrical switchgear and provision for emergency electrical power at the Rocky Mountain Laboratory, Hamilton, Mont., and repair of the street lighting system on our Bethesda reservation.

I and my associates will, of course, be happy to respond to any questions you may have.

EQUIPMENT FOR DENTAL HEALTH CENTER

Mr. FLOOD. The largest item in the 1970 budget is $1.5 million for partially equipping the addition to the Dental Health Center. The justifications indicate an additional $1 million is going to be needed in 1971.

Mr. SEGGAL. Yes.

Mr. FLOOD. This is not a very large facility. Why is $2.5 million needed to equip it?

Mr. SEGGEL. It is highly specialized equipment involved there; laboratory equipment and equipment for experimental teaching.

I would like Dr. Diefenbach to speak to that, if I may. He is in charge of this project.

Mr. FLOOD. Why $2.5 million for a place the size of that. You are small fry in this league.

Dr. DIEFENBACH. The fundamental reason for the high cost of this equipment, first of all, is that much of the equipment that is now available for use in teaching and clinical research is not regularly adaptable for the types of clinical research and educational technology we have planned for the annex. Consequently, some of this equipment is going to have to be designed especially for this particular purpose. There is a rather long leadtime required for this design work if we are going to utilize the facility when it is built.

Secondly, much of this amount we are speaking to in 1970 is for the installation concurrent with the construction of the building.

Mr. FLOOD. What is the status of the construction?

Dr. DIEFENBACH. The construction award is scheduled to be let in July 1969.

Mr. FLOOD. When do you complete it?

Dr. DIEFENBACH. It will be completed in January of 1971. The walls are actually being built and the heating and cooling system——

Mr. FLOOD. When will it be completed?

Mr. DIEFENBACH. In January 1971.

Mr. FLOOD. Are you going to make it?

Dr. DIEFENBACH. I believe that is a realistic date at this time. We have had several setbacks in the past.

Mr. FLOOD. What is your answer about the $2.5 million? This is long-haired stuff; is that it?

Dr. DIEFENBACH. No; it is not long-haired stuff.

Mr. FLOOD. Have you a bottleneck in the production?

Dr. DIEFENBACH. I think it is not a question of the technology not being available. It is a question the technology has not been applied to clinical dental research.

Mr. FLOOD. Is this especially designed hardware for your shop and nobody else can use it?

Dr. DIEFENBACH. Some of the adaptation of some of the equipment will be for this purpose; that is correct.

LISTER HILL NATIONAL CENTER FOR BIOMEDICAL COMMUNICATIONS

Mr. FLOOD. You have a request for $900,000 for planning the Lister Hill National Center for Biomedical Communications. The total cost for planning and construction is $12.9 million. Tell us something about the facility.

Dr. CUMMINGS. Mr. Chairman, the cost of the basic new structure will be $9.17 million, the estimate for site development is about $218,000, and utilities, $450,000. The additional funds are to restore and rehabilitate the library to its original purposes.

The plans for the building would include the facilities for the technical elements of the communications network that we discussed earlier today.

Mr. FLOOD. The $12.9 million will include what?

Dr. CUMMINGS. Will include the housing for the headquarters and laboratories of the communications network. It will include the housing of the staff now off the campus in rental space, and it will include the library's audio-visual and microfilming operations, all of the technical operations currently used for supplying materials to users. This is the essential elements of the building as it is currently conceived.

Mr. FLOOD. How many square feet?

Dr. CUMMINGS. It will have 149,000 net usable square feet. Its overall dimensions are in the neighborhood of 230,000 gross square feet.

Mr. FLOOD. Do you have any figure for average cost per square foot for new construction or renovation?

Mr. SEGGEL. It depends, if it is a laboratory building it is a higher cost. Part of this facility is laboratory and part office space.

Mr. FLOOD. Do you have a figure?

Mr. SEGGEL. Something in the neighborhood of $45 per square foot for a research facility.

Mr. FLOOD. How does this facility compare with that?

Mr. SEGGEL. This is what would apply to a part of this facility—roughly, $45 per square foot.

Mr. FLOOD. Is that expensive?

Mr. SEGGEL. That is pretty expensive, specialized space. You have to have a lot of utilities in it and this sort of thing, special utilities. Laboratory space is always more costly.

Mr. FLOOD. Of course these are government funds. What do you care about a couple of million one way or the other?

Mr. SEGGEL. We should.

Mr. FLOOD. That is the point.

Mr. SEGGEL. We try to hold these down.

Mr. FLOOD. You do?

Mr. SEGGEL. Yes, sir. But of course GSA is in this. They actually award the contracts and they are responsible for the actual award.

Mr. FLOOD. Is any of the $12.9 million for equipment?

Dr. CUMMINGS. This would include all of the basic installations in terms of conduits and wiring for the equipment that is currently owned by the library, and there is an amount of basic building utilities and equipment to be included. There is no massive equipment project in here. The terminal will be tied to external equipment. We do not project the use of any costly equipment within the facility.

Mr. FLOOD. Under the budget for the National Library of Medicine, there is a request for $1,988,000 for the operation of the Center.

Dr. CUMMINGS. That is correct.

Mr. FLOOD. You have funds in your budget for operations without this facility. Why can you not continue operation without it? Is that not a very obvious question?

Dr. CUMMINGS. We can continue the planning as it is currently underway with a small staff and the use of contractor support, but the implementation of an ongoing network we believe will require facilities from which to operate. We are strictly in the planning phase now.

Mr. FLOOD. When are you going to finish this?

Dr. CUMMINGS. I think this is a 5-year program. If the funds were provided for planning, I would not forecast the building being available in less than 4 or 5 years.

Mr. SEGGEL. About 1974.

VIRUS RESEARCH FACILITY

Mr. FLOOD. You are asking $500,000 to plan a virus research facility. Has there been any infections of laboratory personnel to indicate that the existing facilities are not adequate?

Dr. BERLINER. We have had some laboratory spread infections, but no major serious illnesses.

Mr. FLOOD. Why can you not get along with what you have?

Dr. BERLINER. Because we avoided carrying out some of the work we might well do because we do not have the facilities available to contain these dangerous viruses. The only building we have for working with infectious agents was built about 20 years ago at the time when most of our concentration was on bacterial rather than virus infections, and before tissue culture techniques for the massive multiplication of viruses had been developed.

The building that we do have was built for containment of bacterial infection and is called Memorial Building and dedicated to a number of laboratory people who did catch infections and died. We have not ventured, for instance, to do any work at NIH on kuru for the reason the virus is too dangerous. That work had to be carried out where we could find somebody willing to have animals infected with kuru around. This is a uniformly fatal disease and many of the things we are interested in are of that nature. We would like to learn something about the causes, but we do not have the proper space to do that.

RATIO OF NET TO GROSS SQUARE FEET

Mr. MICHEL. I noted the wide disparity between the gross and net area particularly on the laboratory building. While some of the explanation is plausible, you have over twice as much gross area as you have net space, at least in what you are contemplating here.

You speak of separation of mechanical systems serving the area. Can these areas be serviced with a common powerplant?

Dr. BERLINER. Powerplant, yes, but things like the airflow and so on have to be carefully separated and regulated. You have to have a pattern of flow through the buildings so that contaminated areas and clean areas do not get mixed.

Mr. MICHEL. So I guess it would be expected that in a facility where you are concerned with the thing you are doing there, the ratio has to be worse than any other kind of building?

Dr. BERLINER. This is the lowest ratio of net to gross in any building we have.

Mr. MICHEL. It still has to be under one roof unless you are going to build individual buildings.

Mr. HOLLIDAY. We often locate the mechanical rooms above the laboratories and service areas and provide designs in such a way as to have low ceiling height. This is an access area for the mechanics to serve the lighting and utilities without going into the laboratories. Since they are containment facilities, we need more extensive mechanical areas. They are included in the gross.

Mr. MICHEL. This is a request for only a half million, but that is just for design. What is the projected cost?

Mr. SEGGEL. The construction cost is about $5.5 million. The total would be about $6 million, including the planning funds.

Mr. MICHEL. And you would hope to have that constructed by when?

Mr. SEGGEL. Our projection is 1973. Characteristically that slips a little.

I would say conservatively 1974. It takes about a year or more for the A–E contract and 2 or 3 years for construction of this kind of a facility.

Mr. MICHEL. Then on the Lister Hill Communications Center you have a difference of, I think you said, 230,000 square feet to 149,000 net. Is that normal?

Dr. CUMMINGS. I cannot answer that. I am not enough of the expert in that relationship.

Mr. SEGGEL. As we point out, this building will include specialized space for research in communications technology and so forth. It is not all office space.

Mr. MICHEL. Are you considering only office space in your computations of net?

Mr. SEGGEL. No; the net would be the net usable space but, when you have laboratory facilities in a building, it just means you get less people in and less usable space than you would in an office building.

Mr. FLOOD. How many buildings?

Dr. CUMMINGS. This is to be a tower building project, 14 floors to fit the site that adjoins the library.

Mr. FLOOD. That costs too; does it not? That means an additional cost to build like that instead of a one-story building?

Dr. CUMMINGS. The current site selected for this building is the space between a stream and the National Library, which constrains us in terms of coverage.

Mr. FLOOD. Going up costs, you mean?

Dr. CUMMINGS. I am sure it does, and I guess going down does, too.

The current library was drilled in a granite bed and we are more underground than aboveground, and I think the costs there were quite expensive.

Mr. SEGGEL. Going out is rather difficult. We are beginning to run out of land.

Mr. MICHEL. Here is $900,000 again for design, and the eventual cost of building is going to be what?

Dr. CUMMINGS. $9,170,000 is the preliminary construction estimates.

Mr. MICHEL. I know the Department of Agriculture, when they built their new library, went up too. As I recall, there was something new in design for libraries, particularly, that they thought this was more efficient for some reason or other. It does not come back to me now.

Dr. CUMMINGS. There are people who claim that vertical construction of libraries is more efficient than horizontal construction, and I should point out that this is the judgment of the group making a feasibility study for our site.

PRIORITY ITEMS

Mr. MICHEL. Which of these items is the priority one as far as you are concerned? You have a request here of $4.4 million.

Mr. SEGGEL. Did you say which one or which ones?

Mr. MICHEL. One or ones.

Mr. SEGGEL. The repair and improvements item is important of course to maintain the plant. That is an ongoing item, a recurring thing. If we do not keep the plant up, we are going to be in bad shape later on.

It is difficult to make these kind of choices. That would be the priority item, I guess, if I had to make one but I think these are all very important or they would not be in this budget.

I might say that, of the total program we think we need, we are down to very high priority items, I would say.

Mr. MICHEL. That is all, Mr. Chairman.

Mr. FLOOD. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts available for obligation

	1969	1970
Appropriation	.....	$4,400,000
Unobligated balance brought forward	$37,641,000	9,505,000
Unobligated balance transferred to: "Buildings and facilities", Health Services and Mental Health Administration	.....	-2,953,000
"Buildings and facilities", Consumer Protection and Environmental Health Service	.....	-3,777,000
Comparative transfers to: "Buildings and facilities", Health Services and Mental Health Administration	-4,680,000	.....
"Buildings and facilities", Consumer Protection and Environmental Health Service	-8,661,000	.....
Unobligated balance carried forward	-9,505,000	-501,000
Total obligations	14,795,000	6,674,000

Obligations by Activity

Page Ref.	Description	1969 Estimate	1970 Estimate	Increase or Decrease
	Animal Quarters, NIH	$ 4,000	$ ---	$ -4,000
	Biologics Standards Annex	2,000	---	-2,000
	Cancer-Mental-Neurology Cafeteria	20,000	---	-20,000
	Cancer Research Facility	969,000	---	-969,000
	Child Health and Human Development Research Facility	278,000	---	-278,000
	Combined Services Facility and Warehouse	150,000	150,000	---
143	Dental Health Center Addition	2,671,000	1,500,000	-1,171,000
	Expansion of Clinical Center Facilities	108,000	154,000	+46,000
	Extension of Clinical Center Cafeteria	1,000	---	-1,000
	General Office Building Extension	415,000	---	-415,000
	Gerontology Research Facility	391,000	---	-391,000

Obligations by Activity - Cont.

Page Ref.	Description	1969 Estimate	1970 Estimate	Increase or Decrease
	Incinerator Facility	2,116,000	105,000	-2,011,000
144	Lister Hill National Center for Biomedical Communications	---	900,000	+900,000
146	Master Utilities Extension	330,000	1,300,000	+970,000
	Multilevel Parking - Additional, Bldg. 31	94,000	6,000	-88,000
	Multilevel Parking - Cancer-Mental-Neurology	2,016,000	---	-2,016,000
	Multilevel Parking - General Office Building	52,000	--	-52,000
	National Environmental Health Sciences Center	10,000	1,300,000	+1,290,000
145	Neurology-Allergy Virus Research Facility	---	500,000	+500,000
	Neurology-Child Health Facility, Puerto Rico	2,262,000	---	-2,262,000
	NIH Animal Center	1,545,000	207,000	-1,338,000
	NIH Library Relocation	14,000	---	-14,000
146	Repairs and Improvements	1,152,000	552,000	-600,000
	Sabana Seca Facility, Puerto Rico	184,000	---	-184,000
	Service Buildings 12 and 12A	11,000	---	-11,000
	Total Obligations	14,795,000	6,674,000	-8,121,000

Budget Authority by Activity

Page Ref.	Description	1969 Estimate	1970 Estimate
143	Dental Health Center Addition - equipment	---	$1,500,000
144	Lister Hill National Center for Biomedical Communications	---	900,000
146	Master Utilities Extension	---	1,000,000
145	Neurology-Allergy Virus Research Facility	---	500,000
146	Repairs and Improvements	---	500,000
	Total, budget authority	---	4,400,000

Obligations by Object

Description	1969 Estimate	1970 Estimate	Increase or Decrease
NATIONAL INSTITUTES OF HEALTH			
Travel and transportation of persons	$ 1,000	$ 10,000	$ +9,000
Printing and reproduction	2,000	5,000	+3,000
Other services	1,207,000	1,915,000	+708,000
Equipment	192,000	154,000	-38,000
Lands and structures	2,539,000	105,000	-2,434,000
Total, National Institutes of Health	3,941,000	2,189,000	-1,752,000
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
Travel and transportation of persons	7,000	4,000	-3,000
Printing and reproduction	51,000	27,000	-24,000
Other services	1,703,000	1,500,000	-203,000
Equipment	---	1,500,000	+1,500,000
Lands and structures	9,093,000	1,454,000	-7,639,000
Total, General Services Administration	10,854,000	4,485,000	-6,369,000
Total obligations	14,795,000	6,674,000	-8,121,000

Summary of Changes

1969 Appropriation	$ ---
1970 Appropriation request	4,400,000
Net change	+4,400,000

Increases

1. Dental health center addition - equipment	$1,500,000
2. Lister Hill national center for biomedical communications - planning	900,000
3. Master utilities extension	1,000,000
4. Neurology-allergy virus research facility	500,000
5. Repairs and improvements	500,000
Net change requested	+4,400,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1969 House Report "In view of the rather large unobligated balance in this account, the Committee has not allowed any of the $12,495,000 requested. The Committee will have no objection to the reprogramming of balances in this account to provide for projects included in the 1969 budget request." (p. 31).	Note: This item is in response to all three Reports. In identical letters, dated November 8, 1968, to the Chairman of the House and Senate Subcommittees on the Departments of Labor and Health, Education, and Welfare and Related Agencies of the respective Committees on Appropriations the Department outlined its plans to provide for the construction phase of the Appalachian Health Field Station at Morgantown, W. Va. to proceed on schedule. In summary, the letters stated that the Department has carefully examined the possibilities for redirecting resources within the "Buildings and facilities" account and determined that funds of $5,310,000 can be provided in 1969 for this project without delaying the progress of any other Department project ready for design or construction this year. Restoration of these funds will be requested in subsequent years as required for each project from which the funds are redirected. Construction bids for the Appalachian Health Field Station have been solicited and are due to be submitted for evaluation in February 1969. The Department is examining the current needs and priorities of the direct construction program to determine whether other reprogramming of unobligated balances to provide for projects included in the 1969 budget estimate should be proposed.
1969 Senate Report "So long as it is given advance notice of any such intended action the committee will have no objection to the reprogramming of unobligated balances carried forward in order to provide for projects included in the 1969 budget estimate"... "In order not to delay occupancy of the Appalachian Health Field Station beyond the current target date of May 1970, the committee has included $5,310,000 for the construction of the Appalachian facility and strongly urges the Department.....to continue to afford this project the highest priority." (pgs. 65-66).	
1969 Conference Report "The conferees are agreed that $5,310,000 of funds currently available under the appropriation for 'Buildings and facilities' will be available for the environmental health facility at Morgantown, W. Va. and that this project shall have high priority". (p. 12).	

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Unobligated balance transferred to:			
"Buildings and facilities", Health Services and Mental Health Administration.....	---	$2,953,000	Transfer of unobligated balances as provided for by the proposed appropriation language of the gaining appropriation, as part of the proposed separation in 1970 of the appropriation "Buildings and facilities", Public Health Service.
"Buildings and facilities", Consumer Protection and Environmental Health Service.....	---	3,777,000	
Comparative transfers to:			
"Buildings and facilities", Health Services and Mental Health Administration.....	$4,680,000	---	To reflect the proposed separation in 1970 of the appropriation "Buildings and facilities", Public Health Service into three appropriations. For further explanation see Appropriation Language Changes.
"Buildings and facilities", Consumer Protection and Environmental Health Service.....	8,661,000	---	

Buildings and Facilities

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1961 1/	$3,135,000	$3,135,000	$3,470,000	$3,470,000
1962	21,745,000	18,230,000 2/	18,230,000	18,230,000
1963	29,761,000	31,000,000	33,200,000	33,200,000
1964	19,072,000	13,811,000	16,311,000	16,311,000
1965	21,512,000	21,512,000	23,012,000	22,512,000
1966	7,781,000	9,431,000	8,977,000	8,977,000
1967	18,279,000	18,279,000	18,279,000	18,279,000
1968	10,715,000	10,715,000	15,075,000	10,715,000
1969	12,495,000	---	5,310,000	---
1970 3/	4,400,000			

1/ Prior to 1961 direct construction funds were appropriated on an individual project basis.

2/ Supplemental of $3,515,000 not considered by the House.

3/ Prior to 1970 this appropriation also included direct construction funds for other Public Health Service programs.

Introduction

This appropriation includes all proposed direct construction items of the National Institutes of Health and all continuing projects except the Mental Health-Neurology Research Facility, which was appropriated under "Mental Health Activities" and "Neurology and Blindness Activities" in 1961, and the John E. Fogarty International Center for Advanced Study in the Health Sciences, for which planning funds were appropriated in 1968 under "John E. Fogarty International Center for Advanced Study in the Health Sciences".

Dental Health Center Addition - Equipment

1970 appropriation estimate..... $1,500,000

Planning and construction funds totaling $2,808,000 were appropriated in 1966 and 1968 respectively, for the construction of a wing to the Dental Health Center in San Francisco, California. The funds requested in 1970 of $1,500,000 will provide for a portion of the specialized equipment and fixtures for the dental clinical and laboratory space and for television and other audiovisual equipment for experimental teaching areas. The long lead-time for the ordering and delivery of some of this equipment makes it necessary to request funds in 1970 to permit installation concurrent with the construction of the building. An additional $1,000,000 is estimated to complete the equipping of this addition.

Major programs of the Dental Health Center are in the areas of epidemiological and clinical research and continuing education for dentists and dental public health service workers.

This addition will also provide space for bringing new technology to increased numbers of dental practitioners, educators, and dental workers. Residency, research, and short course training will be offered in a setting where actual clinical and educational research can be demonstrated.

Clinical research performed at the Center includes the assessment of new dental materials, devices, and techniques utilizing patient populations. Epidemiological research has already developed a National Cleft Lip and Cleft Palate Intelligence network. With the addition of the especially equipped research and training wing an expanded intelligence network on periodontal, oral cancer, and other diseases will provide in a single place a national reservoir of dental disease information readily accessible to dental workers throughout the world.

Estimated Progress Schedule (Building)

Design
- Award..... July 1966
- Completion..... April 1969

Construction
- Award..... July 1969
- Completion..... December 1970

Lister Hill National Center for Biomedical Communications - Planning

1970 appropriation estimate..... $900,000

Planning funds in the amount of $900,000 are requested for the Lister Hill National Center for Biomedical Communications, an annex to the present National Library of Medicine facility. Public Law 96-456 refers to a National Center for Biomedical Communications to be constructed and located as part of the National Library of Medicine and specifies that it be named the Lister Hill National Center for Biomedical Communications. The new building will provide 149,000 square feet (net) of space to house new and expanded programs of the National Library of Medicine at an estimated total cost of $12,900,000 for planning and construction.

The Library's rapid growth and expanded mission were not envisioned in 1958 when the present facility was designed. The present facility was designed for a maximum staff of 250 employees. At present, 341 regular employees work in the building and an additional 34 employees must be accommodated in rental space in Bethesda. The additional employees have been accommodated by serious crowding of work spaces and by conversion of needed stack space. The problem will become increasingly critical as programs expand to meet the responsibilities which have been placed on the Library.

Specifically, the original planning did not anticipate the fully computerized Medical Literature Analysis and Retrieval System (MEDLARS) which has been in operation since 1964, and which is now under redevelopment as a greatly augmented second generation system and the development of a number of new programs including: the enactment of the Medical Library Assistance Act of 1965 which added an extramural grants and contracts program; the initiation of a toxicology information program in FY 1967 at the direction of the President; the transfer of the National Medical Audiovisual Center (NMAC) to the Library from the Communicable Disease Center in FY 1968; and the establishment of the Lister Hill National Center for Biomedical Communications to apply technology to the development of biomedical communications systems.

The new building will contain specialized space for laboratory research in communications technology and network engineering in addition to office, conference, and support space. Space in the existing NLM building will be returned to its original library use.

Estimated Progress Schedule

Design
- Award..... October 1969
- Completion..... June 1971

Construction
- Award..... August 1971
- Completion..... August 1973

Neurology - Allergy Virus Research Facility - Planning

1970 appropriation estimate..... $500,000

In 1970, $500,000 is requested for planning of a virus research facility to be used jointly by the National Institute of Neurological Diseases and Stroke and the National Institute of Allergy and Infectious Diseases. This building will provide two essential requirements for research in virus diseases: (1) a facility designed to reduce the hazards involved in the safe handling of viral agents; and (2) space for the expanding programs involving viruses in neurological and infectious diseases.

This facility will consist of a laboratory building with an estimated gross area of 86,500 square feet and a net area of 41,800 square feet. Space will be provided for research laboratories, animal holding facilities, and essential supportive functions, including offices as required for a staff of 120.

The National Institute of Allergy and Infectious Diseases is currently conducting the major portion of their virology research in Building 7 on the NIH Reservation in Bethesda. During the time since viruses were first discovered, viral infections among laboratory personnel have dictated facilities which will reduce these hazards.

One of the major developments in the knowledge of virus infections which was completely unknown at the time Building 7 was designed is the proclivity of viruses to persist in tissue cells and to cause many late effects of infections. Certain adenoviruses cause tumors in animal tissues and may cause similar effects in humans. This type of virus may take a year or longer to cause a tumor when injected subcutaneously in hamsters. Intensive work in the current building at NIH with these viruses originated about 1953, and in the comparative life span of the human and the animal it has to be conjectured that several years might be required for similar tumors to appear in humans who have been exposed. Other tumor-causing viruses such as leukemia, sarcoma viruses of animals, and polyoma viruses are currently being handled without adequate facilities for human safety.

Since 1962, the National Institute of Neurological Diseases and Stroke has devoted increasing attention to the search for a virus etiology of a number of chronic neurological disorders, many of which had previously been considered of toxic, degenerative, or genetic origin. The program has developed along three principal avenues: (1) efforts are being made to transmit these diseases to animals through innoculation of material from affected humans; (2) studies of the serio-epidemiology of infectious diseases during pregnancy, and the effects of infectious diseases on the developing nervous system; and (3) field studies and epidemiological investigations of chronic and neurological disorders.

Planning funds of $500,000 are requested in 1970 with design to be completed in April 1971. Estimated cost of construction is $6,075,000.

Estimated Progress Schedule

Design
- Award..... October 1969
- Completion..... April 1971

Construction
- Award..... August 1971
- Completion..... August 1973

Master Utilities Extension - Design and Construction

1970 appropriation estimate..... $1,000,000

In 1970 $1,000,000 is requested for design costs and a portion of construction costs to extend existing utilities and provide new utilities to serve building projects being designed and proposed for design start in 1970. Previously authorized buildings and buildings proposed in 1970 include the Fogarty International Center; the Child Health and Human Development Research Building; the Mental Health Child Research Building; the Combined Service Facility and Warehouse; the Neurology-Allergy Virus Research Building; and the Lister Hill National Center for Biomedical Communications.

Utilities needed include an extension of the central air conditioning plant, and steam, water, electric, gas, sewer, and similar utility distribution lines. They should be planned concurrently to coordinate the impact on existing utilities and to reduce planning efforts and construction rework. An estimated $4,788,000 additional will be required in subsequent years to complete construction of the utilities systems for the buildings authorized or proposed in 1970.

Estimated Progress Schedule

Design
- Award..... October 1969
- Completion - 1st portion..... December 1969
- 2nd portion..... December 1970

Construction
- Award - 1st portion..... March 1970
- Completion - 1st portion..... June 1971

Repairs and Improvements

1970 appropriation estimate..... $500,000

In 1970 $500,000 is requested for repairs and improvements to the existing NIH plant. The NIH plant is quite extensive and many of the buildings and facilities are now approaching 20 or 30 years of service. The need for repairs and improvements is a continuing one, and in the past six years a total of $5,195,000 has been appropriated for this purpose. Examples of projects which require financing in 1970 include: renovation of the air-conditioning system in one of our old laboratory buildings, installation of emergency electrical units on our Bethesda reservation, remodeling of electrical switchgear and provision for emergency electrical power at the Rocky Mountain Laboratory, Hamilton, Montana, and repair of the street lighting system on the Bethesda reservation.

WEDNESDAY, APRIL 3, 1969.

SALARIES AND EXPENSES, OFFICE OF THE DIRECTOR

WITNESSES

DR. JOHN F. SHERMAN, DEPUTY DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. THOMAS J. KENNEDY, JR., ASSOCIATE DIRECTOR, PROGRAM PLANNING AND EVALUATION, NATIONAL INSTITUTES OF HEALTH
RICHARD L. SEGGEL, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Personnel compensation:			
Permanent positions	4,225	4,812	4,917
Positions other than permanent	106	105	105
Other personnel compensation	85	84	84
Total personnel compensation	4,416	5,001	5,106
Personnel benefits: Civilian employees	343	401	413
Travel and transportation of persons	73	102	102
Transportation of things	6	8	8
Rent, communications, and utilities	76	108	112
Printing and reproduction	132	151	180
Other services	1,006	1,057	1,086
Supplies and materials	44	92	103
Equipment	47	78	88
Quarters and subsistence	−5	−5	−5
Total obligations	6,138	6,993	7,193

PERSONNEL SUMMARY

Total number of permanent positions	488	460	467
Full-time equivalent of other positions	15	15	15
Average number of all employees	443	453	467
Average GS grade	7.8	7.9	8.0
Average GS salary	$9,079	$9,832	$9,955
Average salary of ungraded positions	$6,831	$7,447	$7,466

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
Management and central services (total program costs, funded) [1]	5,812	6,993	7,193
Change in selected resources [2]	326		
Total obligations	6,138	6,993	7,193
Financing: Comparative transfers from other accounts	−6,138	−6,993	
Budget authority (appropriation)			7,193
Relation of obligations to outlays:			
Obligations incurred, net			7,193
Obligated balance, end of year			−755
Outlays			6,438

[1] Includes capital outlays as follows: 1968, $39,000; 1969, $78,000; 1970, $88,000.
[2] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $319,000; 1968, $645,000; 1969, $645,000; 1970, $645,000.

Mr. FLOOD. Now we have salaries and expenses, Office of the Director.

We have Dr. John F. Sherman, the Deputy Director of the National Institutes of Health. You have a brief statement here, Doctor. What do you want to do with it.

Dr. SHERMAN. May I suggest that I read it?

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Mr. FLOOD. All right. We will put your biographical sketch into the record first and then you may proceed.

(Biographical sketch follows:)

BIOGRAPHICAL SKETCH

Name, Sherman, John F.; position, Deputy Director, National Institutes of Health, Bethesda, Md.; birthplace and date, Oneonta, N.Y., September 4, 1919.

Education, February 1946 to June 1949, Union University, College of Pharmacy, Albany, N.Y.; B.S., June 1949 (Cum Laude); September 1949 to January 1963; Yale University, New Haven, Conn. Ph. D. June 1953.

Experience, November 1, 1968, to present, Deputy Director, NIH; January 1, 1964, to October 31, 1968, Associate Director for Extramural Programs, NIH; January 15, 1962, to December 31, 1963, Associate Director for Extramural Programs, NIAMD, NIH; July 1, 1961, to January 14, 1962, Associate Director for Extramural Programs, NINDB, NIH; October 8, 1958, to June 30, 1961, Deputy Chief, Extramural Programs, NIAMD, NIH; August 8, 1957 to October 8, 1958, Assistant Chief, Extramural Programs, NIAMD, NIH; July 1956 to August 1957, Assistant to the Chief, Extramural Programs, NIAMD, NIH; and January 1953 to July 1956, Research Pharmacologist, LTD, NIAID, NIH.

GENERAL STATEMENT

Dr. SHERMAN. Mr. Chairman and Members of the Committee, this is a new appropriation to provide for the central direction and management of the various programs of the National Institutes of Health. In prior years, estimates of these expenses were presented as part of the NIH Management Fund which was authorized by the Congress in the 1958 appropriation act. That act provided for the financing of all the costs of central services at NIH through a distribution of the estimated expenses for these services to the individual appropriation requests of the NIH and a subsequent transfer during the operating year of the specified amounts to the central management fund account.

For 1970, however, the budget estimates for the central program direction and management of each of the Department's health agencies, including NIH, are being presented in the form of a "Salaries and Expenses" appropriation. Accordingly, the estimates of costs for the overall direction of the NIH are included in this appropriation request whereas, those for provision of central services which support the research and other programs of the individual institutes and divisions are continued in the NIH Management Fund. In the latter category are, for example, the estimated expenses of operating the Clinical Center, maintaining our plant, providing animals, instruments, and other equipment and supplies for laboratories, and receiving and referring research grant applications to review panels and the Institutes.

This appropriation request for the Salaries and Expenses of the Office of the Director provides for:

(1) The Director and his immediate staff and the offices responsible for program planning and analysis and informational activities; and

(2) Supporting management functions, involving budget and financial management, personnel management, and management analysis and review.

We would like to stress the point that the NIH has assumed the expanded responsibility given it for health professions education and manpower training and biomedical communications in the Department's reorganization plan of a year ago without any addition to its central resources. There are, however, a few selected areas where we need small increases to strengthen the Director's capability for giving policy direction to our programs. Specificially, we are requesting increases primarily for the addition of seven new positions to strengthen our program planning and evaluation staff and for meeting the added costs of processing and computer services associated with our expanded requirements for program data. The new positions are required to assist us in analyzing the progress of our programs, assessing the availability of resources, and developing recommendations on policy issues. The proposed expansion of this staff capability has been urged by numerous advisors from both within and outside of the Federal structure. It becomes particularly important in the face of our increased responsibilities and the growing complexity of the program and policy decisions which confront the NIH.

SUMMARY OF THE BUDGET

In conclusion, Mr. Chairman, the request for Salaries and Expenses, Office of the Director, is $7,193,000 for 1970, an increase of $200,000 over the comparable 1969 operating level of $6,993,000.

Thank you—I shall be happy to respond to any questions you may have.

Mr. FLOOD. By the way, where have they been hiding you? You have been at N.I.H. for years but we have never had the pleasure of having you sit in that chair before.

Dr. SHERMAN. It is better that way sometimes.

Mr. FLOOD. There is no doubt about that. You may be here under duress, are you?

Dr. SHERMAN. No, sir.

Mr. FLOOD. Well, we are glad you are here.

This office is responsible for the expenditure of $1.5 billion. That is a lot of money, but you are asking for 467 employees and $7,193,000. That is going to look like a lot of employees and a lot of money to some Members who look at this as nothing but overhead.

About how much of this is for what is generally referred to as "executive direction"?

Dr. SHERMAN. I would suggest that all of this is for executive direction. As a matter of fact, it is in this sense we have attempted to describe this particular appropriation and to justify the increases.

REQUEST FOR ADDITIONAL STAFF

Mr. FLOOD. It is an increase of $200,000. Why do you need an increase this year?

Dr. SHERMAN. We would put a great deal of emphasis on the need for the expansion of this planning activity for which seven positions are requested.

Mr. FLOOD. Why?

Dr. SHERMAN. In addition to the sheer expansion alone of the demands on the Office of the Director as a result of the additional responsibilities given us by last year's reorganization—that is, in education and in communications—the complexity of attempting to analyze and to plan for our operation has also increased. And, therefore, the necessity of expanding, as was mentioned in the statement and has been suggested by numerous people, this particular office of Program Planning and Evaluation is the key to Dr. Marston's whole responsibility and its sucessful implementation.

CENTRALIZED ACTIVITIES

Mr. FLOOD. Aren't there things like grant payments that are done under this appropriation that are mighty close to a program operation? In many organizations that I can think of they would be so classified.

Dr. SHERMAN. This is an area where we have attempted in recent years to increase the sophistication of both our capability as well as the capabilities for this type of management in our grantee institutions.

One of the areas which we have been unable to implement, fully but which we are striving toward in this particular context, is to give some degree of technical advice to those institutions so that they are enabled better to manage the funds which go out through our grant process. We feel that we have come a long way, certainly, in our own operations and those of our grantees.

Nevertheless, this particular area, an attempt to conserve the funds to get the most mileage out of those funds, is the responsibility of this activity.

Mr. FLOOD. This is not close to program operations?

Dr. SHERMAN. In the financial sense, certainly, sir.

Mr. FLOOD. The difference is administratively?

Dr. SHERMAN. Yes.

Mr. FLOOD. What about that? Why is it budgeted here?

Mr. SEGGEL. The reason we budget it here is that grant payments are made through our financial management office, which is part of the central structure of the Office of the Director.

I might say we handle payments to educational institutions for the whole Department. It is a centralized operation.

I think, when one looks at the size of this, one should remember that a number of things are done at NIH at a central point rather than various places within other agencies of the department.

Mr. FLOOD. I am in favor of that.

Mr. SEGGEL. We are geographically in one place, whereas in other organizations you might find these activities spread around in various program organizations.

Mr. FLOOD. I am in favor of that.

Mr. SEGGEL. We do consolidated procurement at a central level at NIH because it is more economical.

Mr. FLOOD. You run a good shop.

EFFECT OF A 10-PERCENT REDUCTION IN SALARIES AND EXPENSES

Let's go back to where I started.

What would happen to your operation if Congress in its wisdom decided to cut all of the requests for executive direction and administration 10 percent, take it or leave it?

Give us a statement for the record.

Dr. SHERMAN. Yes, sir, we will provide a statement. I might say here that we certainly would continue to try to do a good job, but it would not be as well done as though we had the necessary resources.

Mr. FLOOD. I believe that.

Mr. SEGGEL. I would say one thing in addition. There are things we have to do, such as getting out these payments to institutions. We simply have to get them out. In other words, backlogs will develop, in my opinion, and serious delays.

Mr. FLOOD. You are the budget man. Dr. Marston is not going to worry about it, you are.

Mr. SEGGEL. That is right. Well, Dr. Marston would be very much concerned too. But so will the outside institutions worry about it and blame us for poor management, and so will the Congress.

In other words, we are asked to do a good job. We have to have resources to run this $1.5 billion operation that you talked about.

Mr. FLOOD. What do you mean by resources?

Mr. SEGGEL. I mean personnel and funds to support them and pay for associated costs. For example we have to handle more than 250,000 vouchers a year.

Mr. FLOOD. I am telling you, and I am not kidding you, the natives are restless up here.

Dr. SHERMAN. Actually, that increase of $200,000 in this particular line is spread over a number of activities in the Office of the Director, and much of it relates simply to increased costs of doing business without any real improvement such as postage, increased use of data facilities, et cetera.

Mr. SEGGEL. This also relates to financing on a full-year basis the costs of positions, which were filled for only part of 1969.

(The additional information requested for the record follows:)

CONSEQUENCES OF A 10 PERCENT CUT IN S. & E. APPROPRIATION

The NIH "Salaries and expenses" appropriation which was established to support the cost of directing and managing the programs of the NIH amounts to less than one-half of 1 percent (0.05 percent) of a total budget of $1.5 billion. Several important points are stressed in this connection:

(1) NIH assumed responsibilities of the programs of the Bureau of Health Manpower and the National Library of Medicine without any addition to its central resorces—that is, to this appropriation.

(2) The complexity of NIH's programs and organization imposes heavy demands on its top management for program and policy review and development and for management coordination, the costs of which are financed through this S. & E. appropriation. There are 15 Institutes and Research Divisions, plus the Bureau of Health Professions Education and Manpower Training, and the National Library of Medicine reporting to the Director, NIH. All together, NIH has more than 140 separately budgeted activities and includes over 45 targeted programs in the research area alone. Many program issues cut across organization lines of the Institutes and the Bureau and may involve major policy questions which require departmental action. The addition of the Bureau of Health Manpower and the National Library of Medicine to the NIH brought with it responsibilities for broad coordination of programs in support of education and the communication process with those in support of research. The need for more intensive studies of program progress and program direction is growing as our programs have become more complex and as increasing emphasis is being placed by the executive branch on analytic and planning techniques.

(3) It should also be added that the Congress has been pressing NIH to do a better job of communicating to the general public, and the central leadership for this effort is financed through this appropriation.

(4) This S. & E. appropriation includes a variety of central services for NIH, which, in many typical organizational structures, are dispersed throughout the program elements and their individual appropriations and accounts and, therefore, are not reflected in their "overhead" appropriation or account. For example, because most of NIH is geographically located in one place, all accounting and voucher auditing (over 250,000 vouchers audited per year) for 23 appropriations and funds encompassing, as mentioned previously, over 140 budget activities (with multiple allowances) and virtually all personnel services for over 11,000 employees are done on a centralized basis and budgeted through the S. & E. appropriation. In addition, this appropriation covers the costs of such central services as: processing payments for over 40,000 grants awarded per year by the Department to approximately 5,500 educational and nonprofit institutions, involving disbursements of over $1.9 billion per annum (and requiring accounting

reports for more than 100 departmental agency appropriations) and financial reviews of more than 2,000 contracts per year.

We have been meeting increasing workloads with the same or decreasing numbers of staff. For example, voucher awards workloads have been increasing at the average rate of more than 15 percent a year, the dollar amount of contracts by more than 15 percent a year, grant payments by 5 percent a year, etc., whereas our total employment for providing these services will have declined by an estimated 8 percent between June 30, 1968, and the same date in 1969. These increasing workloads have up to this time largely been made manageable by installing a number of procedural improvements. However, reductions of employment required by the Revenue and Expenditure Control Act have already begun to result in some backlogs and delays. Further cuts would greatly aggravate the situation and lead to deterioration of service and management controls.

In summary, NIH's resources for central policy direction and management of programs totaling $1.5 billion need to be strengthened, not weakened. Any significant, across-the-board reduction in the fiscal year 1970 estimate for the NIH S. & E. appropriation: would seriously diminish NIH's ability to provide leadership for its programs and effective and responsive policy advice to the Office of the Secretary and the Congress; and would, even with the continuation of our strenuous efforts to effect management improvements, lead to critical backlogs in workload with consequent delays in service, not only to NIH's own programs but to grantee institutions and contractors as well, and/or serious deterioration of management controls. It seems to us that it would be "a pennywise and a pound foolish" policy to reduce NIH's capability for directing its programs and managing its $1.5 billion budget.

Mr. FLOOD. Mr. Michel?

NEED FOR ADDITIONAL POSITIONS FOR POLICY DIRECTION

Mr. MICHEL. Thank you, Mr. Chairman.

Now, Doctor, with respect to the seven new ones, which you say ought to strengthen the Director's capability for giving policy direction to these programs. Now, the new administration takes over. I don't know to what extent they have any influence in the shaping of these programs—we hope eventually they might have some. The first question that comes to mind:

Are we going to have more high-powered policy directors in our administration than in the previous one? Do they cost more or was there no policy direction before and that is something we are going to give it, finally? This is the first thing that comes to mind when I see it explained in that way.

Dr. SHERMAN. I would tend to answer it in a little different vein.

Mr. MICHEL. Choose any way you want.

Dr. SHERMAN. The type of policy that we are concerned about here has to do primarily with science policy and the relationship of scientific programs to the public good. We are coming to an era of scientific activities particularly in the national sense when the capability of designing and carrying out large programs of biomedical research will be much more complicated and therefore require much more sophisticated planning and evaluation than had been true in earlier days when we were building up this scientific capability.

So our need for increased resources in this area deals with such things, for example, as designing our own policy and recommending

to the legislative and executive branches that which will be most appropriate for the support of institutions as institutions, or the relationship between educational activities and research activities in the health area, analyzing our large-scale programs, particularly of an applied type, such as whether we went about the vaccine development program in the most effective way, both managerially and scientifically. A series of policy questions which, as I say, seem to be mostly scientific but which bear very directly on the whole question of national goals and the public good.

Mr. MICHEL. With respect to your request for new positions what attention has been given to reassessing or taking a look at the ones already on board to see if some changes are in prospect among that group. Now, we get some very fine, eminent witnesses coming before this committee. I think we are all in agreement on that. But this is only a very small percentage of that caliber of people in the total figure. Is that being constantly reevaluated?

Dr. SHERMAN. Yes, sir, it is. I think I should point out that that figure of 467, which represents our total budgeted position request for 1970, includes a wide variety of types of people in both professional and supporting roles.

Mr. MICHEL. And sometimes if there is a fattening of supporting roles and two or three of those are not needed, we will give you the resources to put on some very competent professionals.

Dr. SHERMAN. Yes.

Mr. MICHEL. Could we have at this point in the record the number of persons on board at the begining of fiscal year 1969 and those expected to be on board at the close of fiscal 1969?

Dr. SHERMAN. Yes, we will provide those figures for the record.

(The information follows:)

Insofar as the S. & E. appropriation is concerned, there were 466 NIH employees on duty as of Jnne 30, 1968, with a total of 447 expected to be on board on June 30, 1969. In this connection, the President's budget authorizes the establishment in fiscal year 1969 of 460 positions in the S. & E. appropriation which may be occupied, as required by the component organizations, at sometime during the year. However, the Revenue and Expenditure Control Act of 1968 necessitates that actual employment be less than the above-mentioned authorized level on June 30, 1969. As stated previously, we now (April 3, 1969) estimate that June 30 employment will be 447, although this figure is flexible (may be slightly higher or slightly lower) based on actual employee turnover and subsequent application of the provisions of the act.

Mr. MICHEL. Again, was that a reduction?

Dr. SHERMAN. Yes, sir.

Mr. MICHEL. As a result, principally, of the Revenue and Expenditure Control Act; is that right?

Mr. SEGGEL. That is right; by filling only three of four positions vacated, as required by that act.

Mr. MICHEL. I think that will be all, Mr. Chairman.

Mr. FLOOD. Thank you.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

Salaries and Expenses, Office of the Director

Amounts Available for Obligation

	1969	1970
Appropriation	.....	$7,193,000
Comparative transfers from:		
"Biologics standards"	$194,000	.....
"National Cancer Institute"	1,467,000	.....
"National Heart Institute"	919,000	.....
"National Institute of Dental Research"	286,000	.....
"National Institute of Arthritis and Metabolic Diseases"	486,000	.....
"National Institute of Neurological Diseases and Stroke"	615,000	.....
"National Institute of Allergy and Infectious Diseases"	545,000	.....
"National Institute of General Medical Sciences"	391,000	.....
"National Institute of Child Health and Human Development"	536,000	.....
"National Eye Institute"	63,000	.....
"Environmental health sciences"	232,000	.....
"John E. Fogarty International Center for Advanced Study in the Health Sciences"	37,000	.....
"General research and services", NIH	441,000	.....
"National Library of Medicine"	136,000	.....
"Salaries and expenses, Office of the Administrator", HSMHA	51,000	.....
"Regional medical programs"	594,000	.....
Total obligations	6,993,000	7,193,000

Obligations by activity

Page Ref.		1969 Estimate Pos.	1969 Estimate Amount	1970 Estimate Pos.	1970 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
156	Management and central services	460	$6,993,000	467	$7,193,000	+7	+$200,000
	Total obligations	460	6,993,000	467	7,193,000	+7	+200,000

Obligations by object

	1969 Estimate	1970 Estimate	Increase or Decrease
Total number of permanent positions	460	467	+7
Full-time equivalent of all other positions	15	15	...
Average number of all employees	453	467	+14
Personnel compensation:			
Permanent positions	$4,812,000	$4,917,000	+$105,000
Positions other than permanent	105,000	105,000	.....
Other personnel compensation	84,000	84,000	.....
Total personnel compensation	5,001,000	5,106,000	+105,000
Personnel benefits	401,000	413,000	+12,000
Travel and transportation of persons	102,000	102,000	.....
Transportation of things	8,000	8,000	.....
Rent, communications and utilities	108,000	112,000	+4,000
Printing and reproduction	151,000	180,000	+29,000
Other services	1,057,000	1,086,000	+29,000
Supplies and materials	92,000	103,000	+11,000
Equipment	78,000	88,000	+10,000
Subtotal	6,998,000	7,198,000	+200,000
Quarters and subsistence	-5,000	-5,000	.....
Total obligations by object	6,993,000	7,193,000	+200,000

Summary of Changes

1969 estimated obligations	$6,993,000
1970 estimated obligations	7,193,000
Net change	+200,000

Increases	Base Positions	Base Amount	Change from Base Positions	Change from Base Amount
A. Program				
1. Management and central services	460	$6,993,000	+7	+$200,000
Total change requested	...	.....	+7	+200,000

Explanation of Changes

The program increase of $200,000 and seven positions will provide for strengthening the planning and evaluation staff support and for program planning and analysis of NIH programs. Provision is also made for the increased costs and volume of printing and for more extensive utilization of data processing services.

Explanation of Transfers

	1969 Estimate	1970 Estimate	Purpose
Comparative transfers from:			
"Biologics standards"	$194,000	.....	To establish the "Salaries and expenses, Office of the Director", appropriation to fund overall program direction and supporting central management functions.
"National Cancer Institute"	1,467,000	.....	
"National Heart Institute"	919,000	.....	
"National Institute of Dental Research"	286,000	.....	
"National Institute of Arthritis and Metabolic Diseases"	486,000	.....	
"National Institute of Neurological Diseases and Stroke"	615,000	.....	
"National Institute of Allergy and Infectious Diseases"	545,000	.....	
"National Institute of General Medical Sciences"	391,000	.....	
"National Institute of Child Health and Human Development"	536,000	.....	
"National Eye Institute"	63,000	.....	
"Environmental health sciences"	232,000	.....	
"John E. Fogarty International Center for Advanced Study in the Health Sciences"	37,000	.....	
"General research and services", NIH	441,000	.....	
"National Library of Medicine"	136,000	.....	
"Salaries and expenses, Office of the Administrator", HSMHA	51,000	.....	
"Regional medical programs"	594,000	.....	

Salaries and Expenses, Office of the Director

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$7,193,000			

Justification

Salaries and Expenses, Office of the Director

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	460	$5,397,000	467	$5,514,000	+7	+$117,000
Other expenses.....	...	1,596,000	...	1,679,000	...	+83,000
Total.....	460	6,993,000	467	7,193,000	+7	+200,000

General Statement

Introduction

The President's Budget for 1970 includes a new and separate appropriation to provide for the expenses of central direction and management of the various programs of the National Institutes of Health. In previous years, estimates of these expenses were included as part of the NIH Management Fund which was authorized by Congress in the 1958 appropriation act. That act provided for the financing of all the costs of central services at NIH through a distribution of estimated expenses for these services to the individual appropriations of the Institutes and Divisions of the NIH and a subsequent transfer during the operating year of the specified amounts to the central Management Fund account.

For 1970 the funding for central program direction and the management of each of the Department's health agencies, including NIH, is being provided through a Salaries and Expenses appropriation. Accordingly, the estimates attributable to the overall direction and management services of the NIH are included in this Salaries and Expenses appropriation request, whereas, those related to the provision of central services which support the research and other programs of the individual Institutes (such as the operation of the Clinical Center, the provision of animals and instruments, maintenance of the plant, the receipt and referral of grant applications, etc.) are continued in the NIH Management Fund.

Specifically, the estimates included in this Salaries and Expenses appropriation request provide for:

(1) Program direction--the Director, NIH, his immediate staff, and offices responsible for program planning and evaluation and information activities; and

(2) Supporting central management services--financial management, personnel management, and management policy and review activities.

Plans for 1969 and 1970

The National Institutes of Health has assumed the expanded responsibilities given it in the DHEW reorganization plan of April 1, 1968, without any addition to its central resources for providing leadership to its new activities in support of health professions education and manpower training. A small increase is requested in this appropriation to strengthen the Director's capability for analyzing and developing programs and providing overall policy direction. Major emphasis will be placed in the next two years on making our new organization an effective instrument for furthering and coordinating NIH's programs in support of the interrelated fields of biomedical research, health professions education, and biomedical communications.

Management and Central Services

	1969 Estimate		1970 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Direction.....	125	$2,391,000	132	$2,531,000	+7	+$140,000
Supporting Management Services.....	335	4,602,000	335	4,662,000	...	+60,000
Total.....	460	6,993,000	467	7,193,000	+7	+200,000

Program direction: This includes expenses of the Director, his Deputy and Associate Directors and their immediate supporting staffs and offices concerned with program development and analysis, legislative analysis and liaison, resources analysis and informational activities. An increase of seven positions and $57,000 is requested to strengthen the Director's staff for analyzing program progress, developing policy positions, and evaluating trends in the availability of resources to support NIH programs. In addition, $58,000 is required for increased data processing and printing workloads. The remaining increase of $25,000 is for replacement of equipment, supplies and materials, increased communications costs, and furniture, office equipment and supplies for new positions.

Supporting management services: These include: (1) budget formulation and management, financial reporting and analysis, contract and grant financial analysis, accounting, grants payment and settlement, and voucher auditing; (2) personnel services to the Institutes and research divisions, recruitment and placement, training and employee development, classification and salary administration, employee and labor relations; and (3) management policy development, management studies and appraisals, organization and systems analysis and reviews, coordination of policy and procedural issuances, forms and records management, etc.

No increase is requested for these activities, except for $60,000 required to cover costs involved in supporting, on a full year basis in fiscal 1970, positions filled during the course of fiscal year 1969.

New Positions Requested
Fiscal Year 1970

	Grade		Annual Salary
Management and central services			
Scientist administrator.....	GS-15		$19,780
Program analyst.....	GS-13		14,409
Program analyst.....	GS-12		12,174
Program analyst.....	GS-11		10,203
Programmer.....	GS-9		8,462
Secretary.....	GS-6		6,321
Secretary.....	GS-5		5,732
Total new positions.....		(7)	77,081

APRIL 3, 1969.

SCIENTIFIC ACTIVITIES OVERSEAS

(SPECIAL FOREIGN CURRENCY PROGRAM)

WITNESSES

DR. LEO J. GEHRIG, DIRECTOR, OFFICE OF INTERNATIONAL HEALTH
DR. S. PAUL EHRLICH, JR., DEPUTY DIRECTOR, OFFICE OF INTERNATIONAL HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

OBJECT CLASSIFICATION (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
PUBLIC HEALTH SERVICE			
Travel and transportation of persons	575	375	400
Other services	12,684	16,323	14,322
Grants, subsidies, and contributions	131	400	400
Total obligations, Public Health Service	13,390	17,098	15,122
ALLOCATION TO NATIONAL SCIENCE FOUNDATION			
Other services		362	200
Total obligations, National Science Foundation		362	200
Total obligations	13,390	17,460	15,322

PROGRAM AND FINANCING

	1968 actual	1969 estimate	1970 estimate
Program by activities:			
Foreign health research	7,830	17,460	15,322
Total program costs, funded	7,830	17,460	15,322
Change in selected resources[1]	5,560		
Total obligations	13,390	17,460	15,322
Financing:			
Unobligated balance available, start of year	−850	−2,460	
Unobligated balance available, end of year	21,460		
Budget authority (appropriation)	15,000	15,000	15,322
Relation of obligations to outlays:			
Obligations incurred, net	13,390	17,460	15,322
Obligated balance, start of year	13,333	18,833	23,964
Obligated balance, end of year	−18,833	−23,964	−23,926
Outlays	7,890	12,329	15,360

[1] Selected resources as of June 30 are as follows: Unpaid undelivered orders, 1967, $13,197,000; 1968, $18,757,000; 1969, $18,757,000; 1970, $18,757,000.

Mr. FLOOD. Now we have the budget for "Scientific activities overseas" (special foreign currency program). The witness is Dr. Leo J. Gehrig, Director of the Office of International Health. I see you have a statement, Doctor.

Dr. GEHRIG. Yes, sir.

Mr. FLOOD. What do you want to do with it?

Dr. GEHRIG. I would appreciate the opportunity of reading it, if I may.

Mr. FLOOD. All right. Suppose you do.

First, we will put your biographical sketch into the record at this point.

(The biographical sketch follows:)

BIOGRAPHICAL SKETCH OF PRINCIPAL WITNESS

Name: Leo J. Gehrig, M.D.

Position: Assistant Surgeon General.

Birthplace and date: Mapleton, Minn. April 25, 1918.

Education: University of Minnesota, B.S., B.M., M.D. Internship; Salt Lake County General Hospital, University of Utah Medical School, 1944–45. Residency; thoracic surgery, Overhold Thoracic Clinic 1947–50. General surgery, U.S. Public Health Service Hospital, Staten Island, N.Y., 1952–55. PHS executive career development program, 1960–61.

Experience: Director, Office of International Health, April 1968 to present: Deputy Surgeon General, November 1965 to April 1968; Chief, Bureau of Medical Services, April 1964 to November 1965; Deputy Chief, Bureau of Medical Services, U.S. Public Health Service, Washington, D.C., 1962 to April 1964; Medical Director, U.S. Peace Corps, 1961–62; Program Officer, Bureau of Medical Services, 1960–61; Deputy Chief, Division of Hospitals, Bureau of Medical Services, U.S. Public Health Service, 1959–60; Assistant Chief, Division of Hospitals, Bureau of Medical Services, U.S. Public Health Service, 1957–59; Deputy Chief, Surgery, U.S. Public Health Service Hospital, Seattle, Wash., 1955–57; Chief Thoracic Surgery, U.S. Public Health Service Hospital, Staten Island, N.Y. 1950–52; Acting Director, Tuberculosis Control, Territorial Department of Health, Juneau, Alaska, 1946–47.

Association memberships: Diplomate, American Board of Surgery; diplomate, American Board of Thoracic Surgery; Fellow, American College of Surgeons; Alpha Omega Alpha Honorary Medical Society.

GENERAL STATEMENT

Dr. GEHRIG. Mr. Chairman and members of the committee, I am Leo J. Gehrig, Director of the Office of International Health which is a staff office of the Assistant Secretary for Health and Scientific Affairs.

The Office of International Health is responsible for the development of Public Health Service policies concerning international health activities; participation with the State Department in formulating U.S. technical positions relating to the World Health Organization and on other international health matters; guidance to the Administrations of the Public Health Service in their international health programs; and for administering and coordinating activities of the special foreign currency program. It is with this latter program that we are concerned today.

Funds were first appropriated in 1961 for the special foreign currency program under which local foreign currencies derived principally from the sale of U.S. agricultural commodities may be used to support scientific activities overseas in countries where these funds are declared to be in excess of operating needs of the United States. These scientific activities assist us in achieving goals within the mission of our domestic programs, and promote U.S. foreign policy through assistance in the health efforts of participating countries.

As of mid-February 1969, there were approximately 200 active projects. Projects are developed and supervised by many operating programs of the three Administrations of the Public Health Service. Activities encompassed have ranged from basic biomedical research, through applied research studies on communicable diseases, occupa-

tional and environmental health problems, to translations of foreign medical literature for the benefit of U.S. scientists and practitioners alike.

The program is based on collaboration and mutual benefit between the United States and participating countries. Of advantage to the U.S. health concern is the potential to utilize foreign resources which are frequently unique. Uniqueness may derive from a variety of circumstances, such as the increased frequency or occurrence of a disease condition for study, the existence of unusual research talent and interest or availability of language expertise.

The unfortunate circumstance of malnutrition in India, for example, has allowed for the conduct of important studies aimed at determining more effective means of combating this condition. Reasearch has included studies to understand better the fundamental deficiencies in malnourished infants and methods for development of food supplements from available local materials. In addition, it has been possible to study the relative effectiveness of such food supplements through controlled feeding programs.

A population research program, which complements research efforts in the United States and elsewhere in the world, has been developed during the past year. New studies include the testing of special methods for estimating population growth in developing countries, determining the extent to which certain factors such as the availability of health services and economic circumstances contribute to infant mortality, and more basic investigations of the hormonal regulation of fertility in animals. Eight new population research projects have been funded so far this year, and several more are currently undergoing review.

During the next fiscal year it is planned to expand these efforts and increase activities in the area of contraceptive development, studies on the medical effects of currently used contraceptive methods, and research and evaluation of the manpower, facilities, and operational requirements for population and family planning programs.

The biomedical communication efforts supported under this program assist in bringing to American health practitioners, scientists, and educators significant foreign literature in health sciences research and practice. These efforts include the translation of foreign medical literature, the development of critical reviews on specific topics of interest, and the preparation of abstracts and bibliographies.

Since the first availability of excess foreign currencies to the Public Health Service for scientific activities overseas this program has grown and matured. It is a significant resource for supplementing the research efforts of the Administrations of the Public Health Service. For this purpose we are requesting for 1970 appropriation authority to use excess foreign currencies equivalent to $15,322,000.

I would be pleased to answer any questions you may have.

TUBERCULOSIS IN ALASKA

Mr. FLOOD. Now, while this has nothing to do with the matters before us, I see that you were involved in tuberculosis control in Alaska. You were up there some 20 years ago. Why were you interested in this program?

Dr. GEHRIG. Mr. Flood, at that time, in 1946, tuberculosis was the first killer in Alaska.

Mr. FLOOD. Among the Eskimo?

Dr. GEHRIG. It occurred much more frequently among the native populations which included the Eskimo, the Indian, and the Aleut.

Mr. FLOOD. Why, in that kind of weather and temperature, tuberculosis?

Dr. GEHRIG. Interestingly enough, one of the things we learned through the years of attempting to freeze, was that it really had no effect on the tuberculosis patient. So I think the climatic conditions in Alaska did not contribute to the prevention of the disease but in many instances contributed to its occurrence.

Mr. FLOOD. That surprises me. I thought at one time people were sent to areas with a cold climate as a treatment for tuburculosis.

Dr. GEHRIG. It was important. As a matter of fact, Dr. Trudeau in Saranac Lake had many patients exposed to subzero temperatures.

Mr. FLOOD. I played in a stock company in Saranac Lake back in the twenties.

Now, did you ask for this job, your present job?

Dr. GEHRIG. Yes; as a matter of fact, I did.

Mr. FLOOD. You are a thoracic surgeon. What is that?

Dr. GEHRIG. This encompasses the surgical area that runs—I think it is best described—from the neck to the abdomen. Of course, now it has, in contrast to the days when I was trained, taken on an increasing role in cardiovascular surgery itself. We were just beginning then to do mitral valve repairs but now with open cardiac work it is a much bigger field. At that time we carried out surgery of the lung, the esophagus, some cardiac procedures and that of the diaphragm and chest wall. That about encompassed what we knew then.

REDUCTION IN FUNDS AVAILABLE

Mr. FLOOD. Now, you are asking for a small increase in the appropriation. You are actually budgeting a decrease of $2,138,000 when you take into account these unobligated funds carried forward from 1968. Taking that into consideration, what is the reason for requesting a net reduction? Isn't this program working out as well as you expected?

Dr. GEHRIG. Mr. Flood, I guess, as they say, "I am awfully glad you asked that question" because we, in fact, are very enthusiastic about the potential of this program which, in fact, is a very modest program.

Mr. FLOOD. What about the figures?

Dr. GEHRIG. The presentation of this request, I think, represents a consideration by the administration of what could appropriately be considered within the budget. With these funds we will remain essentially at last year's level. As you indicated, it really is in fact about $2 million less. We attempt to use these excess currencies as we have other funds in the most effective manner possible. It does not, in my honest opinion, represent the total amount of resource that can be effectively used, but the considerations that led to this final figure were, of course, beyond our role and were in consideration of other health needs in the national budget.

ORIGINAL REQUEST FOR FUNDS

Mr. FLOOD. As a thoracic surgeon, if there is too much fat in the area in which you operate, you have a problem. Did you actually cut the fat out of this, or did you ask for more, and your request was cut?

Dr. GEHRIG. The request that we made was larger than this. It was cut.

Mr. FLOOD. To the Secretary?

Dr. GEHRIG. We presented to the Secretary a budget which was higher than this.

Mr. FLOOD. How much higher?

Dr. GEHRIG. The original estimate and request was $41,645,000.

Mr. FLOOD. What did the Secretary ask for of the Bureau of the Budget?

Dr. GEHRIG. He presented this same figure to the Budget Bureau.

FUNDS AVAILABLE IN ISRAEL

Mr. FLOOD. Why has Israel been dropped from the program? Is it because they lack sufficient counterpart funds?

Dr. GEHRIG. We have been advised by the Bureau of the Budget and the Department of Treasury that there are not sufficient funds for new projects in Israel. Israel has not, however, been formally taken off the excess currency list.

Mr. FLOOD. That is what I thought.

Dr. GEHRIG. The excess currencies which do exist in that country are aparently closely approaching the needs of this Government and consequently we have been advised that no new funds would be provided to us. This matter has not been finally settled. It continues to be under consideration. But this year to date we have not been able to secure any Israeli pounds.

Mr. FLOOD. Well, this is not a decision you make. It is beyond your control.

FAMILY PLANNING RESEARCH

While the total program here is going down, take a look at page 195. There you have $2.4 million for family planning research in 1969. You are increasing the amount to $3,500,000 for 1970. What are some of the projects that you are funding now and what are your plans for this 40-percent increase?

Dr. GEHRIG. The increase here is very significant, particularly in light of, as you have indicated, a budget which overall does not increase. It, however, has been a very deliberate move because of the importance and priority which has been established for obtaining more research information on the family planning problem. At the present time I might indicate in a general way some of the areas within which we are working. There has been a very real effort made in the development of vital statistical information with regard to population dynamics. This, for example, has been important in many of the countries that have been most realistically faced with expanding and exploding populations. The vital data on births and deaths is rather inadequate.

Mr. FLOOD. What new projects do you plan to fund with this increase?

Dr. GEHRIG. You asked me first as to the areas we are working in. These happen to be some areas already funded not relating to the 1970 increase.

Mr. FLOOD. Let's talk about the 1970 increase.

Dr. GEHRIG. In the 1970 increase, projects that are planned include the following areas: The medical effects of currently used methods and materials for contraception and birth control. This encompases the area of risk of thromboembolic disease in users, the occurrence of congenital malformation in children born to users of oral contraceptives, and the comparison of suction curettage versus classical curettage in abortion. These are some of the areas relating to the medical effects. In contraceptive developmeent we have a second major area that we would plan to move ahead in.

Mr. FLOOD. You mean the things?

Dr. GEHRIG. That is right. The efficacy and acceptability of new techniques and products and also selected studies in reproductive biology itself.

Mr. FLOOD. You are not getting into the pill area?

Dr. GEHRIG. As I mentioned, in connection with the medical effects, the thromboembolic disease occurrence in users of oral contraceptives does specifically refer to the pill area. Other areas we will be concerned with are the knowledge, attitudes, and practices regarding family planning. In other words, this encompasses the social behavioral aspects of acceptance and the conduct of family planning methods.

Mr. FLOOD. How would you find that out? Would you knock on the door and say "good morning, Mrs. Jones. Do you use so-and-so? Why, you would get a punch in the mouth, wouldn't you?

Dr. GEHRIG. Yes, I must agree that that sort of social behavioral research, while exceedingly important, is also very difficult to approach because of the sensitivity of the entire area.

Mr. FLOOD. Do you talk to the family doctors? Will the medics help you on this.

Dr. GEHRIG. I think the physician would participate in this. Another methodology, however, would be to take two communities in which you have, what appears to be very diverse effects insofar as increase in family size and study, what is in fact affecting one community versus the other.

FERTILITY PATTERNS IN YUGOSLAVIA

There have been identified some areas overseas which show relatively slow family increases.

Mr. FLOOD. Where?

Dr. GEHRIG. Yugoslavia.

Mr. FLOOD. Do you know enough about Yugoslavia to know whether it would be the Croats, the Slovenes or the Serbs? And would you know how it may differ with regard to religion?

Dr. GEHRIG. I don't believe I can speak directly to this. I do believe I can provide the information, however.

Mr. FLOOD. Those would be very interesting observations. If you had not thought about looking at that, you should.

(The information follows:)

STUDY OF FERTILITY PATTERNS IN YUGOSLAVIA

Yugoslavia has within its relatively small area the full range of demographic experience exhibiting strong contrasts in fertility patterns. The country includes areas with one of the highest and one of the lowest birth rates in the world. (See table below.) These reflect the nationality-religious-geographic differences in the country: The Roman Catholic, Croatian-Slovene peoples are located in the more industrialized areas in the north and are European oriented; the Muslim remnants of the Turkish empire are located in poverty-stricken agricultural areas in the south of the country. Between the low birth rates of the former and the high rates of the latter, are members of the Serbian Orthodox Church and others. Yugoslavia is experiencing large migrations from the agricultural areas to the urban centers—which was typical of Western Europe in the last century when the demographic transition from high mortality and fertility rates changed to the current low rates for mortality and fertility. Data are not available to fully document demographic theories concerning this transition. Opportunity to study it in Yugoslavia while it is in the process of change will give a basis to determine what are the economic, social or cultural conditions which affect and are affected by the demographic change.

In addition to obtaining an understanding of the socioeconomic and cultural factors influencing fertility patterns, we are interested in studying the effect of migration from agricultural areas to urban environments on birth rates. Also, we are supporting family planning programs in many countries with Muslim cultures. If there is anything to be learned from the experience of Muslim-oriented Yugoslavs in relation to the reaction to population policies or as a result of their emigration to industrial areas, it may prove useful to all the Muslim-oriented cultures of the world, and to the establishment of policy in the operation of U.S.-supported family planning programs.

	Infants per 1,000 women		
	All areas	Urban	Rural
Yugoslavia	137	106	144
Low fertility region	113	91	119
Slovenia	105	89	108
Croatia	109	88	114
Voivodina	110	93	116
Serbia proper	121	93	127
High fertility region	198	160	205
Montenegro	174	134	178
Bosnia and Hercegovina	185	135	191
Macedonia	202	179	208
Kosmet	264	227	269

Source: The population of Yugoslavia: Paul F. Myers and Arthur A. Campbell; Bureau of the Census, Washington, D.C., 1954.

Dr. GEHRIG. As a matter of fact, in the development of this project it was pointed out that here you had three different religious groups. There is also apparently a differentiation on the basis of urban and rural populations which enters into it.

Mr. FLOOD. Yes, just like Czechoslovakia.

Dr. GEHRIG. These are some of the factors in the methodology of attempting to assess social and behavioral impacts on family planning which may be important. This is one of the uses planned within the 1970 program.

Mr. FLOOD. Pick another one.

Dr. GEHRIG. Another broad area includes studies of manpower and facilities for research and services in population and family planning. In other words, this represents the organizational review of how you deliver this service to a community.

VALUE OF RESEARCH TO UNITED STATES OF AMERICA

Mr. FLOOD. All right. Now, suppose for the record, you describe a few projects that have been completed under this appropriation during the past few years. I want a few projects that have yielded valuable results to this country, for the record. And right now you can pick one, a prize one if you like, which has been completed under this appropriation which has been of benefit to the United States of America.

Dr. GEHRIG. Yes, sir. I would like to point out two. I would request your permission to speak about projects that really are complete to the point where we are able to point to accomplishments, but which are continuing.

Mr. FLOOD. Now, you know what "completed" means; in this scientific context, I don't. Now you tell me.

Dr. GEHRIG. What I am saying is that these are completed so that I can point to results, but they are projects which are actively going on because of their continuing contributions.

TRANSLATION AND DOCUMENTATION OF SCIENTIFIC LITERATURE

First, I would like to refer to the efforts that have been developed in the translation and documentation of scientific literature overseas. This has occurred in a number of countries. In Israel, for example, we have been able to train and utilize through the National Library of Medicine some medical abstracters and indexers who continue to work in that country and have provided over a period of time to the——

Mr. FLOOD. That is no trick there. They are bilingual and multilingual anyhow.

Dr. GEHRIG. It is exceedingly valuable to us in this program. I would agree that it is not as unusual there as it would be here to find not only bilingual but multilingual people.

Mr. FLOOD. Sure.

Dr. GEHRIG. This has been helpful in the indexing and abstracting field. It has also been helpful in the engagement of highly qualified scientific people. For example, in Poland an individual who is probably one of the world's most renowned scientists in the problem of amputation and rehabilitation has developed a monograph which brings together not only the surgical problem of amputation but also the latest in the rehabilitation and early application of prostheses for amputees. This is of great value to our people and of importance to the scientific community around the world.

Mr. FLOOD. That is a good example.

Dr. GEURIG. The opportunity for translation, again as a further example, has provided the continuing availability in English of a major environmental health journal from Russia which makes the information accessible to our interested people and to the National Library of Medicine.

Mr. FLOOD. Now, that is Russia, Poland, and Israel.

Dr. GEHRIG. Another example happens to be from Germany. It is a German periodical important in the field of air pollution which is translated and inserted into our literature banks. These are not the totality, but some examples in this matter of translation.

NUTRITION

A second area, which I personally feel keenly about, is the area of nutrition. In India there have been dovetailed two separate projects, one at Mysore, India in what is known as the Central Food Technological Research Institute and, second, at the Christian Medical College in Vellore. The studies have encompassed three major areas.

Mr. FLOOD. You certainly have picked two tough sections.

Dr. GEHRIG. Of course, one of the advantages of this program and the application in India is that the existence of malnutrition to the degree that it is seen there makes this work not only pertinent to their needs and of interest to them, but provides a unique resource for study that is so badly needed in this problem. They have looked at some of the fundamental problems of nutrition and they have proceeded to develop from local materials dietary supplements which in two instances are now being produced commercially in India. They have been able to proceed with additional feeding experiments on children to test the end product of this work.

I need not point out that this does not solve the problem of malnutrition, but through this excess currency program utilizing these surplus funds it has been possible to further our knowledge of it. This is a second example of important accomplishments and there are others.

STUDIES IN AFRICA AND ASIA

Mr. FLOOD. You might add two more; one in Africa and one in Asia if you have them.

Dr. GEHRIG. We would be pleased to.

(The information follows:)

A STUDY OF GENETIC ANOMALIES IN EGYPT

(Principal Investigator: Dr. Nemat Hashem)

Egypt provides an unusual opportunity to study genetic influences upon neurological diseases because of the high consanguinity rate, represented by a high incidence of first cousin marriages, of about 40 percent. In a childrens neurological clinic established by the principal investigator in 1957 in Cairo, 25 percent of 11,000 children seen in a 5-year period had cerebral palsy and mental deficiency, 23 percent had infections of the nervous system (poliomyelitis, encephalitis), and 20 percent had epilepsy. Fifty percent of the patients were classified as probable genetic anomalies. This project is attempting to identify these anomalies further.

Two highly unusual associations between chromosomal anomalies and clinical syndromes have been observed; (a) a patient with XYY pattern with the clinical syndrome of rocker bottom heels, arthyrogryposis multiplex, ptosis, and low-set ears; and (b) a patient with a nonhomologous chromosome of the 16 to 18 groups associated with a peculiar clinical syndrome: a combination of lipaemia, micrognathia, microcornia, cataract and bifid chin.

In view of difficulties experienced in getting synthetic media and certain chemicals for chromosome studies, Dr. Hashem has developed a simplified technique for culture of human leukocytes for cytogenetic studies which represents an important contribution to the field.

The importance of Dr. Hashem's findings in this field in the United States is indicated by the fact that of 1,142 requests for her 14 published reports, 737 or 66 percent were from American investigators or practitioners.

SEATO Cholera Research Laboratory

Dacca, East Pakistan

The special foreign currency program under collaborative research agreement No. 08–002–1 supports a major research effort at the SEATO Cholera Research Laboratory, Dacca, East Pakistan, directed to a determination of the pathogenesis of cholera and development, improvement and demonstration of measures for the prevention and eventual eradication of cholera. This laboratory is a unique facility. It was developed as an autonomous international laboratory at the Institute of Public Health in Dacca as the result of an agreement between the United States and Pakistan. Clinical investigators from the United Kingdom and Australia in addition to those from Pakistan and the United States participate in the research activities of the laboratory. The laboratory was located in this area because cholera is present at all times in East Pakistan and the neighboring Indian province of West Bengal. This area is generally regarded as the historic seedbed of the disease from which great epidemics have arisen and spread to other parts of the world. The research of the laboratory has three major aspects: (1) Studies of environmental factors of the disease, (2) clinical studies of differences in susceptibility and physiological changes caused by the disease, and (3) evaluation of vaccines. The value of the facilities and research and training activities to the United States and the contributions of this project to medical science in the United States will be apparent from a few of the items reviewed in the following summary.

This laboratory and geographical area provide the only site in the world where field studies for testing vaccines can be conducted and for this reason alone represent an invaluable resource to the Division of Biologics Standards of NIH, which has responsibility for evaluating U.S. vaccines.

This laboratory has enabled NIH researchers and their university associates in the United States and elsewhere to study cholera in other parts of Asia such as Hong Kong, the Philippines, Thailand, and other SEATO countries. It provides the only source of material for teaching about cholera available to the United States. Through the facilities of this laboratory the Jefferson Medical College group in Philadelphia stockpiled special diagnostic antisera from a cholera outbreak in Hong Kong and prepared a teaching manual describing new and quick methods for isolating and identifying *vibrio cholerae*. A training film on cholera treatment was completed based on the work of the Cholera Research Laboratory in Dacca. It is available for showing in the United States and abroad, and numerous copies have been sent to organizations to assist in the training of physicians.

The second international symposium on cholera sponsored by the laboratory included nearly all of the principal cholera researchers in the world. The proceedings of this conference represent the latest information available at that time on many aspects of cholera and have been widely quoted by the World Health Organization authorities in its anticholera activities. Numerous subsequent scientific publications from the laboratory resulting from research supported by this project have served to provide an up-to-date addendum on a continuing basis.

Studies on the rate of exchange of the sodium ion between plasma and gut lumen were conducted during the acute phase of the disease as well as later, indicate that a major physiological defect in cholera is a diminished transport of the sodium ion out of the gut lumen.

Another important development has been the demonstration that the adult rat can serve as a suitable experimental animal contrary to past belief. It has been further demonstrated that *succus entericus* in rats contains a substance which neutralizes the cholera toxin. This provides an entirely new approach to the study of cholera in man and animals.

Preliminary studies indicate that a promising new approach to serological evaluation of cholera may have been developed. Such a test is necessary to provide objective evidence of the effectiveness of a toxin or toxoid in protecting man against cholera. Such an evaluation procedure will make it possible to undertake field testing of a toxoid as a means of immunizing against cholera sooner than was anticipated.

Three major advances in the epidemiological program have been achieved. These are:

(1) The demonstration of the effectiveness of a U.S.-manufactured vaccine in reducing cases of cholera in both adults and children heavily exposed to the disease.

(2) The demonstration that vibriocidal antibody is positively correlated with the effectiveness of vaccines and a person's immunity to cholera and that it can thus serve as a measure in vaccine evaluation.

(3) The identification of important factors in the spread of epidemic infection which may be susceptible to other preventive measures.

A further significant therapeutic advance is the development of a single formula electrolyte solution which, in combination with tetracline therapy, reduced mortality to below 1 percent. Recent development of an oral solution for therapy has far-reaching promise in the restoration of fluid in the field where intravenous fluid in the patient cannot be supplied.

An important result of this research activity supported at the laboratory has been the sharp upsurge in interest among U.S. researchers in the problems of cholera. This interest is yielding some promising work on vaccines and toxoids which may change the whole approach to cholera prevention.

The research of this laboratory has been reported in 63 publications in the biomedical research literature.

Mr. FLOOD. Mr. Michel.

NUTRITION

Mr. MICHEL. On this latter item, you know that that is getting to be a household word in the bureaucracy. Every other witness comes up here doing something on malnutrition. When I see here that we are going to conduct important studies aimed at determining more effective means of combating this condition, how long does it take to find out what malnutrition is? How many years can you beat this thing over the head and still keep pouring money into it and say we have to investigate and research malnutrition? It just cannot be that difficult a subject matter to explore, can it? The body requires certain things and other things are injurious to it. I guess what we are all looking for is: What do we need to properly sustain life? Is that so darned difficult to come up with?

Dr. GEHRIG. Mr. Michel, I would say that it is not a simple problem. I quite agree with you. Tremendous efforts have gone into this area not only by our country, but by multilateral agencies and other governments. There is a great deal yet we do not know, even though there have been great additions to our knowledge. I would only indicate as an example of the complexity of this problem, how under this program it has been possible to study an important compound known as Co-Enzyme Q which appears to be an important element related to vitamins.

Mr. FLOOD. What is the value of it to the body?

Dr. GEHRIG. It appears to be important in the treatment of certain forms of anemia, particularly megaloblastic anemia.

Mr. FLOOD. What is megaloblastic anemia?

Dr. GEHRIG. It is a deficiency within our circulating blood and has a variety of components. It usually represents a diminution and abnormality in the circulating red blood corpuscles. It has been felt that in this form of anemia the teratment of it can be effectively handled with the use of vitamin E in selected cases.

Mr. FLOOD. Can you get a pill or a capsule or a shot in the arm, or what?

Dr. GEHRIG. This is a part of it.

Mr. FLOOD. What do you mean "yes"? Is it a pill, or both, or what?

Dr. GEHRIG. This is a substance and its form of medication is a pill. But the point I wish to make here is if you go behind vitamin E which appears to have some value, Co-Enzyme Q appears to be the substance made in the body that is important.

Mr. FLOOD. What is Co-Enzyme Q?

Dr. GEHRIG. I wish I could describe it beyond that.

Mr. FLOOD. Try. I haven't the faintest idea what you are talking about.

Dr. GEHRIG. Co-Enzyme Q is an enzymatic substance important to the production of hemaglobin and other metabolic reactions in the body.

Mr. FLOOD. An enzyme?

Dr. GEHRIG. Yes, and closely related to several vitamins. It appears to be the active ingredient that is of therapeutic value in some forms of anemia.

Mr. FLOOD. That is good enough.

Dr. GEHRIG. I use this example only as one of the multitude of areas in which malnutrition presents problems for research and one that has been carried out under this program.

Many less basic efforts are being carried out in the efforts I described of attempting to develop substances from locally grown materials that are effective. In the feeding experiments, for example, it has been found that kwashiorkor, which is one of the more common severe forms of malnutrition, the feeding of certain basic proteins alone such as fish is not really adequate to solve the problem. Additional nutrients are necessary, and this information further indicates that the area of exploration that is necessary in malnutrition is very broad. I think the efforts that we can support through this program will be an important addition to the totality of effort which is necessary.

USE OF CHEAP AND NOURISHING FOOD COMPOUNDS

Mr. MICHEL. I made mention earlier in the year before this subcommittee and my other Subcommittee on Agriculture that I personally have been conducting a little experiment in eating some of this corn-soymeal-dried milk compound that we are producing in this country, and can produce for 7.5 cents per pound, and shipping it over to India, particularly. It is supposed to be a very nutritious food.

Now, you are not eating a New York sirloin when you are eating this gruel, obviously, but with a little bit of sugar it is not bad. If I were hungry enough, as I have been, it has satisfied me. Now, there are a lot of hungry people in India where this research is going on. We have a lot of hungry people—well, I don't know if they are altogether hungry people, but a lot of people in this country are suffering from some nutrition deficiency. Now, what I would like to know, is any research going to determining how to make this more palatable, this type of food, so that it gets utilized. Here we are talking about a very cheap food, 7.5 cents per pound. I am still on about the third or fourth little package of this material and it is amazing how far it will go. What do we do to really put what we know that much

about onto the market? What are we doing to put it to good use, put it to work?

Dr. GEHRIG. I think this is very pertinent to the effort that I referred to in India because they have pioneered a mixture of wheat, peanut oil, and Bengal gram, all available locally. They are now having it made by five different manufacturers for use in the famine State of Bihar. It is available there at a price of 2.5 rupees per kilogram which makes it economically feasible. The point you further made is that while one may develop a nutritious application or mixture, the next secret is how to make it acceptable to an individual so that he can eat it over a period of time. The feeding experiments have been the next step in testing it out.

Mr. MICHEL. I realize that a taste peculiar to a U.S. citizen might not be completely acceptable to countries such as India.

Dr. GEHRIG. That is right.

Mr. MICHEL. I recall some years ago going into research on a different kind of soybean here because Japan had such a good market of $100 million per year for soybeans if we could only produce the kind that tasted, to them, the same as the ones that they got from China. Now, through research we developed that kind of bean and we got a darned good market out of it.

FISH FLOUR

Mr. FLOOD. What about the same question with respect to fishmeal or flour made from fish?

Dr. GEHRIG. They have developed additional plain flours from raw material which have included such things as fish flours.

Mr. FLOOD. Wasn't Paul Douglas carrying the spear for that?

Mr. CARDWELL. Yes, sir; he was.

Mr. FLOOD. What is the situation now?

Mr. CARDWELL. It is now being marketed. The Food and Drug Administration has reached agreement wherein it will be labeled and can be marketed in this country. I think it is marketed only in bulk, though. I don't think it is marketed in small retail lots.

Mr. FLOOD. What about the oversea food programs?

Dr. GEHRIG. Insofar as the research area in this program, and really I can't speak beyond that, they have looked into fish flours.

Mr. FLOOD. Will you at this point in the record put in a paragraph or two on fishmeal?

Dr. GEHRIG. Yes, sir.

(The information follows:)

FISHMEAL

Fish flour, more commonly known as fish protein concentrate (FPC) is a high protein (80 percent) food supplement made by removing most of the oil and water from good grade whole fish. Its use as a protein supplement is especially attractive since it can be made from extensive ocean resources which are not now used as food. It is a light tan-colored stable powder with very little odor and flavor, which can be added to familiar foods such as bread, pasta, soups, tortillas, and chappatis, without changing their characteristics. When used at a 5 to 10 percent level, it not only increases the protein content of the food substantially, but improves the quality of the cereal protein already present. Such foods have been found to be highly acceptable.

FPC has been approved by the Food and Drug Administration (FDA) when made from hake. Further work is being carried out by the Bureau of Commercial Fisheries (BCF) to enable a number of other common species to be use. So far, no widespread market has developed. One commercial company has a plant completed to make FPC and is scheduled to supply nearly 1,000 tons to the Agency for International Development (AID) in 1969. Under the authority of Public Law 90-549, BCF has signed a contract with a commercial company to design, construct, and operate a demonstration plant in Gray's Harbor, Aberdeen, Wash., capable of processing 50 tons of hake a day into FPC. This will demonstrate the large-scale feasibility of the process, provide the technical and economic data needed by potential investors, and provide sizable quantities of the product for industry development and for use by AID.

BCF is also investigating new processes for making FPC by offering a potential for lower cost and more versitile products.

In a food supplement trial conducted under the special foreign currency program in India, fish flour was found to be not entirely satisfactory when used alone in the treatment of children with protein-calorie malnutrition. Normal preschool children fed fish flour had no greater increases in height than children fed an equal quantity of vegetable protein. However, as fish flour could form an important source of protein, a second trial of the product was decided on.

Thirty-four children of preschool age, attending a village day-creche, were allocated to two groups. The basal diet given to both groups provides 1 gram vegetable protein and 100 calories/kilogram/day. The experimental group is given, in addition, 1 gram of fish protein/kilogram/day and the control group 1 gram vegetable protein/kilogram/day. Heights and weights are recorded at frequent intervals. The trial is in progress.

MALNUTRITION

Mr. CARDWELL. Could I say something on your basic question about the use of the term "malnutrition"? You have heard a whole host of witnesses, as you say, who describe what they are doing in the field of malnutrition and you extend this to your experience on the Agriculture Committee. Now, in the case of HEW, I don't know whether Dr. Gehrig would agree with me but I would hope that he would. I think when we use the term "malnutrition", we are not talking about that word in a very literal and narrow sense, we are talking about it broadly. Often we are talking about the subject of nutrition, the subject of the cause and effect of diet and its relationship to health, the capacity of young people to learn and assimilate. We are talking about a whole host of things. We have bureaucratically latched on to this now popular term "malnutrition". I don't think we really mean it in that sense of the word every time we use it. I would defer to Dr. Gehrig on that subject.

Mr. MICHEL. I think that is a good point.

Dr. GEHRIG. An excellent point.

Mr. FLOOD. These fellows surprise me regularly with things like that.

COORDINATION OF FAMILY PLANNING RESEARCH

Mr. MICHEL. Of course, there is another area we hear a lot about, family planning.

Yesterday we had witnesses testifying as to what we were doing about developing what you say some of this research money has gone for developing over in India. Now, are these two research centers going to be coordinating their information or are we just trying to find out the best contraceptive for Indians over there? They probably need it a lot more than we do.

Dr. GEHRIG. In our population program which has had real emphasis, the National Institute for Child Health and Human Development has been asked and does function as a coordinating point for all of the development of these projects. Even though the projects may be primarily of interest and managed by other programs in the Public Health Service, they are all coordinated at this one point. So I think we have attempted to establish a good way of insuring that the communciation is as one program rather than a diverse group of efforts.

Mr. MICHEL. I will tell you frankly I am not at all opposed to it if it could be done over in India with these counterpart funds, where we have a big reservoir of them. I would just as soon, or rather, do it there as with appropriated dollars here at home, but I don't like to see us doing it in both areas, or in competition as between the two programs.

Dr. GEHRIG. In this connection the use of these excess currencies has provided a mechanism of not only extending but in some situations utilizing areas which we cannot replicate in this country for study. So I don't think it is doing the same thing, but it is providing opportunities to extend areas of domestic interest.

Mr. MICHEL. How many countries are we doing family planning research in, in this currency program? Put that in the record, and the amounts.

Dr. GEHRIG. I will.

(The information follows:)

SCIENTIFIC ACTIVITIES OVERSEAS—FAMILY PLANNING PROJECTS FISCAL YEAR 1969

Country	Number	Dollar equivalents
India	10	$811,299
Yugoslavia	3	1,050,583
Total, ongoing projects	13	1,861,882
India	4	726,191
Pakistan	1	24,096
Yugoslavia	1	200,000
Total, pending projects	6	950,287
Number of countries	3	
Number of projects	19	
Total cost		2,812,169

Mr. MICHEL. Thank you.

Mr. FLOOD. Mr. Shriver.

COUNTRIES IN WHICH FOREIGN CURRENCIES ARE AVAILABLE

Mr. SHRIVER. In that connection, would you put into the record a chart showing the amount of excess currencies we have in the countries and where it is? Maybe it has already been asked for.

Dr. GEHRIG. We have a listing. Now, if it has not been supplied it will be available. The currency figures we have are the total of the U.S. currencies available in each of these countries. Of course, you understand these amounts would be available to all governmental departments. So, while you will get a figure, it is the total U.S. availability.

Mr. SHRIVER. Yes; that is what I want. Is it in the justifications?

Dr. GEHRIG. It is not presented in the justifications but, if I recall correctly, the printed President's budget does include it. We will be glad to provide it for this hearing record.

(The information follows:)

(ANALYSIS OF FOREIGN CURRENCIES, DEC. 31, 1968 (IN THOUSANDS OF DOLLARS)

Excess currency countries	Available for U.S. use				Available for country use			
	Nonrestricted Public Law 480 money [1]	Nonrestricted sales only	Restricted	Total available for U.S. use	AID accounts	Other Government agency accounts	Total available for country use	Cash balance on hand
Burma	1,131	10,132	3	11,266	8,114	0	8,114	19,380
Ceylon	2,384	2,486	104	4,974	3,108	0	3,108	8,082
Guinea	5,488	120	1	5,609	23,102	(2)	23,102	28,711
India	315,783	388,963	13,115	717,861	341,277	8,892	350,169	1,068,030
Israel	4,296	0	6,150	10,446	11,719	29	11,748	22,194
Morocco	1,221	9,580	2,005	12,806	16,480	89	16,569	29,375
Pakistan	38,180	91,103	2,845	132,128	78,170	23,934	102,104	234,232
Poland	436,189	0	16,957	453,146	0	0	0	453,146
Tunisia	3,518	12,368	1	15,887	7,981	133	8,114	24,001
United Arab Republic	144,690	10,135	823	155,648	101,782	0	101,782	257,430
Yugoslavia	19,960	38,526	5	58,491	9,484	0	9,484	67,975
Total excess currency countries	972,840	563,413	42,009	1,578,262	601,217	33,077	634,294	2,212,556

[1] Public Law 480 money subject to waivers and sales.
[2] Less than $500 not shown.

Mr. SHRIVER. For instance, how much is available in Israel?

Dr. GEHRIG. As of December 31, 1968, the latest figures available from the Treasury Department, there was $10,446,000 worth of Israeli pounds available for United States use.

Mr. SHRIVER. Do you have plans to use any of that for research in Israel?

Dr. GEHRIG. We had originally planned to, as I indicated a little earlier, but these funds have not been made available this year because

the level of funds apparently has dropped to the point where new projects cannot be initiated.

Mr. SHRIVER. The reason I am asking is that I am the ranking member of the committee that appropriates for AID and we have this question. Among other things, we have included funds the past 2 years for some special schools in Israel. I noted that the funds the last time were pretty well depleted.

Dr. GEHRIG. That is correct. This year we have not utilized any funds for new obligations in Israel.

AIR POLLUTION STUDIES

Mr. SHRIVER. On page 203 of the justifications you say that the Consumer Protection and Environmental Health Service portion of this program will investigate the problems of air pollution in countries where we have excess currencies, such as India, Pakistan, and United Arab Republic. Do they have air pollution problems in those countries that you can investigate?

Dr. GEHRIG. Yes.

Mr. SHRIVER. Can you use those funds in those countries that are not industrial countries?

Dr. GEHRIG. There are among the excess currency countries, particularly, two in which there is sufficient industrial development to provide some of the same problems. These I believe would be primarily Yugoslavia and Poland.

Mr. SHRIVER. But not Indian, Pakistan, or United Arab Republic?

Dr. GEHRIG. There is another aspect to this, Mr. Shriver. In India, for example, there is available one opportunity for doing studies with regard to the cleaning of coal, and some of the other things that we are concerned with in attempting to develop an air pollution program for the Nation. Even though the environment need not necessarily be similar to ours, some of the processes that are required to prevent pollution could be attacked in India.

Mr. FLOOD. Of course, India and Poland, account for over two-thirds of all the excess currency.

Mr. SHRIVER. I think that is all I need to ask.

Mr. FLOOD. Thank you, Doctor.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Scientific Activities Overseas (Special Foreign Currency Program)

Amounts Available for Obligation

	1969 Estimate	1970 Estimate
Appropriation	$15,000,000	$15,322,000
Unobligated balance brought forward	2,460,000	...
Total obligations	17,460,000	15,322,000

Obligations by Activity

Page Ref.		1969 Estimate	1970 Estimate	Increase or Decrease
195	Foreign health research	$17,460,000	$15,322,000	$-2,138,000

Obligations by Object

	1969 Estimate	1970 Estimate	Increase or Decrease
Travel and transportation of persons	$375,000	$400,000	$+25,000
Other services:			
Project contracts	16,685,000	14,522,000	-2,163,000
Grants, subsidies and contributions	400,000	400,000	...
Total obligations by object	17,460,000	15,322,000	-2,138,000

Summary of Changes

1969 estimated obligations	$17,460,000
1970 estimated obligations	15,322,000
Net change	-2,138,000

A. Increases:	1969 Base	1970 Estimate
1. Program		
(a) National Institutes of Health	...	$ 7,200,000
(b) Health Services and Mental Health Administration	...	6,741,000
(c) Consumer Protection and Environmental Health Service	...	1,376,000
(d) Office of International Health	...	5,000
Total program increases	...	15,322,000
B. Decreases:		
1. Nonrecurring program cost prior year	...	-17,460,000
Net change	...	-2,138,000

Explanation of Changes

In fiscal 1969 there was a large unobligated balance brought forward from the prior year. This is not expected to occur in 1970. The net change in FY 1970 is therefore a decrease in the amount of funds available for obligation.

Scientific Activities Overseas (Special Foreign Currency Program)

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$3,707,000	N.C.	0	0
1961	3,707,000	$3,707,000	$3,707,000	$3,707,000
1962	10,084,000	8,000,000	10,084,000	9,000,000
1963	2,800,000	2,800,000	2,800,000	2,800,000
1964	6,647,000	4,000,000	4,000,000	4,000,000
1965	1,000,000	1,000,000	1,000,000	1,000,000
1966	6,000,000	6,000,000	5,000,000	5,000,000
1967	19,217,000	19,217,000	10,000,000	10,000,000
1968	18,685,000	15,000,000	15,000,000	15,000,000
1969	30,000,000	15,000,000	15,000,000	15,000,000
1970	15,322,000			

Scientific Activities Overseas (Special Foreign Currency Program)

Introduction

The Scientific Activities Overseas appropriation permits the use of U.S.-owned excess foreign currencies to enhance the achievement of the domestic health objectives of the Public Health Service and to promote U.S. foreign policy. International objectives are directed toward the development of techniques for the prevention and treatment of serious disease problems and the development of mechanisms for the promotion of health in underdeveloped countries with resulting improvement of health, social, and economic conditions for all mankind.

Specifically, these foreign currencies, declared in excess of normal U.S. needs by the Department of the Treasury, are used to fund agreements for high-quality research projects by competent foreign health scientists. Actual costs for comparable research performed in the United States would be considerably higher.

Projects are conducted on a collaborative basis assuring the mutual interest of the U.S. and the host country, its institutions, and medical and health-related personnel. In carrying out research of importance to U.S. interests, benefits accrue which contribute to the attainment of the host countries' national and community health goals; the strengthening of institutional and organizational structures capable of dealing effectively with priority health problems; the dissemination of the latest information regarding modern health techniques; and the demonstration and application of contemporary health practices for the prevention, control, and treatment of disease.

Emphasis is placed on biomedical and health services research and development. Priority areas of endeavor include: nutrition, disease control, environmental health, health manpower development and population and family planning.

Two million four hundred thousand dollars is specifically designated for family planning and population projects in 1969, and $3,500,000 is proposed for 1970. The Center for Population Research in the National Institute of Child Health and Human Development, NIH, will continue to serve as a focal point for the development, stimulation, and support of these studies throughout the Public Health Service.

A variety of important and unique research opportunities of high potential usefulness exists in excess currency countries, allowing the special foreign currency program to develop new knowledge and insights that would not otherwise be so readily attainable. Proposals are reviewed by technical experts to assure that projects will contribute significant new information to aid in meeting health projects at home and abroad and be relevant to U.S. international health priorities and objectives. These reviews assess the soundness of approach, capability of the foreign researcher, and the significance and priority of the work within the technical area concerned. Evaluation includes the availability of scientific manpower and research facilities, as well as the uniqueness and relevancy of the cultural, ecological, and clinical material.

There follows a discussion of the goals and objectives of the respective agencies of the Public Health Service participating in the Scientific Activities Overseas Program, as well, as examples of specific projects aimed at meeting these goals.

A summary of estimated obligations by country follows:

	1969 Estimate	1970 Estimate
Ceylon	75,500	125,000
Guinea	75,500	439,000
India	7,655,730	4,086,400
Israel	---	---
Morocco	89,000	431,000
Pakistan	1,834,988	2,941,000
Poland	1,369,155	2,251,400
Tunisia	800,900	536,000
U.A.R. (Egypt)	393,936	471,000
Yugoslavia	5,165,102	4,041,200
Total	17,459,811	15,322,000

National Institutes of Health

The National Institutes of Health Special Foreign Currency Program is designed and operated with the objective of extending NIH activities into the international medical, biomedical, and health sciences community. The purpose of this activity is to utilize resources indigenous to "excess currency" countries which will contribute to the attainment of the domestic missions of the individual operating units of the Institute in the areas of biomedical research, health manpower, and medical literature documentation and dissemination.

The NIH attempts to achieve this objective through the instrument of collaborative research and information exchange agreements. Support is provided for projects involving U.S. biomedical scientists, both within NIH intramural laboratories as well as at U.S. academic institutions, and foreign research institutions on problems of mutual interest and importance to the U.S. and the host country and within the responsibility of the NIH. The involvement of U.S. scientists, in the role of collaborators and project officers for projects in the areas of their professional interests and competence, provides technical guidance and current first-hand information about the status of projects and the foreign scientific environment. This is important to informed and responsible program management to assure that benefits accrue to the U.S.

The selection of programs of merit, relevance to domestic objectives, promise of productivity, and the provision of continuing technical surveillance are always primary considerations in the administration of this program. Careful review assures that the individual research projects supported by this program are an integral part of the research programs of the separate Insitutes and operating units.

At the present time, NIH supports projects in India, Israel, Pakistan, Poland, U.A.R. (Egypt), and Yugoslavia. The program is based on utilization of unique resources of these host countries as represented by trained scientific manpower, multilingual competence, literature of contemporary and historical importance, research institutions and laboratory facilities, cultural and anthropological patterns, ecology, high incidence of diseases, or clinical materials of interest not found in the U.S. The research program is progressively involved in two of the major contemporary world problems, nutrition and population.

Nutrition has long been a concern of NIH. Projects concerned with nutritional research were among the first projects funded in 1961 when the Special Foreign Currency Program was developed. Research in this field continues to be a significant element of the NIH program. Unique opportunities have been utilized over the years in Egypt, India, and Pakistan.

The traditional concern of NIH with problems of growth and development, human genetics, congenital abnormalities, and endocrine disturbances serves as a logical basis for extending its programs to population studies, the other great world problem. The NIH, in addition to serving a coordinating function for projects concerned with population studies supported by all agencies of the PHS, has an active research program of its own. It is anticipated that development efforts during the past two years will culminate in activation of projects in most of the major areas of concern in population studies, namely, demography, reproductive physiology, behavioral studies, and contraceptive agent development and evaluation.

There is a preoccupation in the U.S. with electrophysiological studies of physiological function because of the modern electronic instrumentation provided by the industrial sector. This has resulted in a lapse of interest and activity in supporting investigations of anatomical structure, which are essential if the ultimate objective of physiology is to be attained. Through this program the unexcelled resources of Poland in the fields of neuroanatomy and pathology have been brought to bear on current neurophysiological problems at NIH. Efforts are also being made to integrate neurophysiological studies in Yugoslavia with those

in the U.S. through this program. Studies in the fields of immunology, bacteriology, mycology, parasitology, virology, and rickettsiology are planned for 1970. The metabolism program will be extended to include projects in India and Yugoslavia. Investigations into cardiovascular disease and cancer will be undertaken in India.

An unanticipated aspect of this program which promises future intangible benefits is becoming increasingly apparent. Some scientists from the lesser-developed excess-currency countries, after a period of training at the NIH or elsewhere in the U.S., are able to establish research programs at home under the support of this appropriation. Upon return to their homelands, they maintain active collaboration with their U.S. preceptors and thus remain a part of the U.S. medical science community. In some instances, by virtue of research support, these young men are able to reestablish themselves in the medical hierarchy and exercise influence beyond their years by introducing modern concepts of medical training, clinical investigation, and patient care which will have long-term effects within their countries as well as beyond their borders. Thus, the immediate contribution to biomedical research from these countries is only one of the benefits from this program.

Through cooperative efforts with other countries in expanding and improving biomedical communication, NIH is drawing upon unique scientific resources outside the United States and strengthening its domestic mission to collect, preserve, and disseminate information in the health sciences for maximally-effective utilization by American practitioners, scientists, and educators. Various media are employed to tap the rich resources of foreign scientific literature and professional skills, among them: the selective translation and publication of significant monographic studies, special reports, and conference proceedings in priority areas of health research; cover-to-cover translation of Eastern European biomedical publications of broad health relevance; abstracting from foreign language periodicals for English-language users; the acquisition, microfilming, and cataloging of both current and historic biomedical literature; support of the preparation and publication of analytic, critical reviews of recent developments and emerging trends in health science fields; sponsoring of collaborative programs for indexing biomedical literature for use in Index Medicus and MEDLARS, the NIH computer based information storage and retrieval system; assistance for scholarly research projects in the history of medicine; and the development of biomedical audiovisual demonstration and exchange programs. This program will be operated in Poland, Yugoslavia, India, and Pakistan during 1970. While the diversification of program channels giving access to international biomedical communication will be continued and expanded, emphasis will be given to the preparation of reports on subjects of core importance to public and personal health services, including: studies of drug efficacy and toxicity, environmental health, family planning, and regional and national disease patterns.

National Institutes of Health

Estimated obligations by Country

	1969 Estimate	1970 Estimate
India	4,205,248	1,850,400
Israel	---	---
Pakistan	1,129,288	2,340,000
Poland	638,655	1,022,400
U.A.R. (Egypt)	343,370	288,000
Yugoslavia	1,475,932	1,699,200
Total	7,792,493	7,200,000

Health Services and Mental Health Administration

The Scientific Activities Overseas Program of the Health Services and Mental Health Administration (HSMHA) shares the primary research goals of the domestic program: development of the most effective methods of preventing, diagnosing, and treating serious communicable disease, mental disease, heart disease, stroke, cancer, malnutrition and other important organic disease; testing the development of comprehensive medical care systems in the light of their provision of adequate care and effective utilization of health manpower; and development of workable emergency medical methods most adaptable to all types of medical emergencies.

Available excess foreign currencies allow HSMHA to extend its program to meet these objectives in several important and unique ways. In the recognized priority area of population and family planning, the Agency is concerned with the collection of quantitative information on natality, fertility, family planning, and related demographic variables. The Scientific Activities Overseas appropriation contributes to the progress of this objective by offering unusual opportunities for the testing of data collection techniques of competent foreign research personnel under a wide variety of conditions. In particular, India is an unusual country for developing techniques to evaluate the effectiveness of population policies. Qualified personnel trained in probability statistics and demography are available, and techniques developed can be adapted to the United States and other countries.

In 1970 increased activity is planned for international vital registration programs, objective evaluation of population policies, assessment of causes of infant mortality and of the health needs of children, and study of the relationship of environment to health. Special emphasis will be placed on development of new approaches to maternity care programs and their influence on fetal development in an effort to combat causes of infant mortality. Domestically this information would have particular relevancy to the objective of raising the health level of American Indians, Alaskan natives, and other lower socio-economic groups in the U.S.

Unusual disease and social conditions in the excess foreign currency countries provide a unique setting for the carrying on of significant clinical studies in such priority areas as malnutrition, cardiovascular disease, cancer, endocrine disorders, renal disease and radiation hazards. For example, the cause of rheumatic heart disease, rheumatic fever, remains a problem in the U.S. because the lack of sufficient numbers of cases in any one area makes extensive study of the problem difficult. Concentrations of rheumatic fever in India and Yugoslavia, however, permit studies of the natural history of the disease, the relationship to it of various strains of streptococci, and the value of prophylactic treatment.

In the important area of nutrition research, it is planned during 1970 to carry out in Pakistan a project to reduce infant mortality by introducing specific nutrition and public health measures in experimental villages and then to compare the acceptability of family planning programs with other control villages.

During 1970 HSMHA nutrition research programs will also attempt to measure scientifically the benefits accruing from the controlled distribution of special nutrient-rich food supplements in East Pakistan and to explore the role of Coenzyme Q in the production of red cells in the blood in relation to the role of Vitamin E in India.

Communicable diseases are responsible for most of the sickness and death throughout the world. To find better ways of eradicating, preventing, diagnosing, and treating these conditions, projects are developed overseas in locations where the environment and patterns of the disease to be studied are most favorable for research. In coordination with domestic objectives, major programming efforts in 1970 will be devoted to high priority projects such as controlled studies of attenuated live measles vaccine and studies of infectious hepatitis, rabies and other

diseases which are a serious threat to U.S. citizens at home or abroad. Of great promise is a study being initiated collaboratively with the World Health Organization and the Government of India to test the feasibility of eradicating certain disease-carrying mosquitos by means of genetic modification. Success in this effort will open new horizons in man's effort to control such diseases as malaria and yellow fever.

Similarly excess-currency countries provide excellent opportunities for the study of mental disorders. Since the determining factors in the etiology and outcome of mental illnesses may be biological, psychological or cultural, there is a real advantage in performing comparative and parallel studies on individuals from different ethnic groups, living in varying cultural environments. Excess foreign currency countries also provide an excellent spectrum of linguistic and pharmacologic resources for the International Reference Center for Information on Psychotropic Drugs administered by the National Institute of Mental Health.

Methods for the organization and delivery of health services and health manpower development represent other areas of high priority in domestic programs as well as in the international health field. Of particular importance are methods for improving health services to the disadvantaged and other special population groups. Similarly there is need for developing new categories of health manpower and new methods for health education in order to increase the effectiveness of available resources. Projects to be undertaken during 1970 toward the achievement of these priority objectives include: 1) Studies of different approaches to organizing and delivering health services to low-income and other groups in countries possessing unusual variances both in rural and growing urban areas (Morocco, Tunisia, Pakistan); 2) Studies of hospital patient education services designed to develop and test new educational methodologies leading to the possibility that more effective methods of educating patients and their families in respect to particular disease conditions, necessary personal hygiene, and home-care programs will decrease patient time in hospitals, permit greater utilization of professional health personnel, and thus provide an effective means for reducing the rising costs of medical care in the U.S. today; and 3) Extension of the Public Health Service International Fellowship Program to India and Pakistan for junior and senior medical students under which those who participate gain understanding and research experience with diseases and health needs not readily obtainable in this country.

In summary, the HSMHA is continuing to develop a foreign program interrelated with its domestic objectives and designed to provide answers to high priority health problems of maximum interest to the U.S.A.

Health Services and Mental Health Administration

Estimated obligations by Country

	1969 Estimate	1970 Estimate
Ceylon	75,000	125,000
Guinea	75,000	225,000
India	3,200,000	1,925,000
Israel	---	---
Morocco	89,000	431,000
Pakistan	604,700	600,000
Poland	550,000	570,000
Tunisia	800,000	535,000
U.A.R. (Egypt)	50,000	180,000
Yugoslavia	3,202,670	2,150,000
Total	8,646,370	6,741,000

Consumer Protection and Environmental Health Service

The objective of the Consumer Protection and Environmental Health Service (CPEHS) is to assure that our growing knowledge of both ecology and technology is vigorously applied to man's environment and the products he consumes so that he will be afforded the greatest possible protection from hazards to his health and economic and social well-being. CPEHS supports studies in excess currency countries which will enhance our knowledge and capabilities in these areas and ultimately advance the health of all mankind.

One of the primary goals of the CPEHS is to promote the implementation of measures and standards which will insure a high level of protection for man against environmental insults. Accordingly, CPEHS has the responsibility for the investigation of causes of air pollution, the determination of its effect upon life and property, and the development of air-quality criteria and emission standards. Available excess currencies have allowed research to be conducted on improving established control techniques and processes for air pollutants. Further studies are planned to identify additional pollutants, to investigate the fate of atmospheric carbon monoxide, to control sulfur oxide in boiler performance, and to do quantitative analyses of metals in standard smoke samples. In addition, suspended air particulate matter will be sampled and measured for lead and mercury content, and the resulting measurements will then be related to human body levels of these metals in various population groups. Essential technical and scientific literature will be translated abroad and distributed to academic institutions and to the air pollution technical audience.

The CPEHS also has the responsibility for safeguarding consumers from products exposed to potentially hazardous radiation, upgrading the quality of drinking water supplies, and improving solid waste management. Present radiation studies overseas include the relation to brain damage of x-ray treatment of tinea capitis, effects of radioactive phosphorus in fetal development, and the effects of unusually high levels of natural background radiation on certain population groups.

To promote the development and improvement of techniques and procedures necessary to meet existing and emerging needs for consumer protection, CPEHS is carrying out an intensified drug inspection program, is determining the safety of drugs, and is investigating the therapeutic equivalency of drugs. Comparable studies in excess foreign currency countries would increase, intensify, and solidify hypotheses developed and being tested domestically. For example, projects have been proposed to assess the risk of thrombosis, carcinoma, abnormalities of carbohydrate metabolism, and congenital malformations, resulting from oral contraceptives.

To increase social and technical knowledge about the broad influence of all factors upon positive consumer protection and environmental control, man's ecology is examined and evaluated. Extensive surveillance techniques and methods are developed to measure the impact of environment on man's health and welfare, and to ensure that measures are taken to minimize or avert current or potential hazards. Studies on optimal individual space, noise, privacy, ventilation, and recreational needs will provide information useful in establishing housing hygiene criteria and standards. A study is proposed of the effects of environmental stress on physical, mental, and social health of population groups. The establishment of a primate colony in India has been suggested to study the toxicity and the pharmacological action of drugs, combined with the development of a research training program, to provide a capability not available elsewhere in the world at a similar cost.

There are other unique features and outstanding resources available in some countries that provide unusual opportunities. Yugoslavia's occupational health problems are similar to many in the U.S. and can be cooperatively investigated; proposed studies will emphasize problems of acute and chronic lead poisoning, and

industrial and urban noise. High residues of pesticides in Guinea afford opportunity to study their effects at levels higher than those found in the U.S.

As environmental health is one of the major priority program areas of the PHS, emphasis in 1970 will be concentrated on those most compelling controllable hazards and those areas most seriously affecting man's environment.

Estimated obligations by Country

	1969 Estimate	1970 Estimate
Guinea	---	214,000
India	248,482	309,000
Israel	---	---
Poland	180,000	659,000
Pakistan	100,000	---
U.A.R. (Egypt)	---	3,000
Yugoslavia	485,500	191,000
Total	1,013,982	1,376,000

Office of International Health

Travel funds are requested by the Office of International Health to enable the PHS program coordinator and members of the professional staff to visit countries in which excess currencies are available. Travel will be performed for the purpose of developing policy and program objectives consistent with both United States and host country interests. Working relationships with the Ministries of Health will be developed and potential project areas explored. Looking toward U.S. interest in providing leadership in the search for solutions to important international health problems in fields such as nutrition, population, and environmental health, the staff will attempt to assure maximum utilization of P.L. 480 research toward progress in these areas.

Estimated obligations by Country

	1969 Estimate	1970 Estimate
Ceylon	500	---
Guinea	500	---
India	2,000	2,000
Israel	---	---
Pakistan	1,000	1,000
Poland	500	---
Tunisia	900	1,000
U.A.R. (Egypt)	566	---
Yugoslavia	1,000	1,000
Total	6,966	5,000

General Research Support Grants

WITNESSES

DR. THOMAS G. BOWERY, ACTING DIRECTOR, DIVISION OF RESEARCH FACILITIES AND RESOURCES
DR. ROBERT Q. MARSTON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LEONARD D. FENNINGER, DIRECTOR, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
JOHN W. HAMBLETON, FINANCIAL MANAGEMENT OFFICER, BUREAU OF HEALTH PROFESSIONS EDUCATION AND MANPOWER TRAINING
KENT A. SMITH, EXECUTIVE OFFICER, DIVISION OF RESEARCH FACILITIES AND RESOURCES
BERTIL G. BERGQUIST, BUDGET OFFICER, DIVISION OF RESEARCH FACILITIES AND RESOURCES
JOHN E. SHARKEY, DIRECTOR OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JAMES B. CARDWELL, DEPUTY ASSISTANT SECRETARY, BUDGET

PROGRAM AND FINANCING (IN THOUSANDS OF DOLLARS)

	1968 actual	1969 estimate	1970 estimate
Program by activities: General research support grants (obligations) (object class 41.0)	59,674	60,700	61,500
Financing:			
Receipts and reimbursements from: Federal funds	−59,700	−60,700	−61,500
Unobligated balance lapsing	26		
Budget authority			
Relation of obligations to outlays:			
Obligations incurred, net	−26		
Obligated balance, start of year	47,816	60,948	60,948
Obligated balance, end of year	−60,948	−60,948	−60,948
Adjustments in expired accounts	−428		
Outlays	−13,586		

Mr. Flood. Now we have the request for general research support grants. Dr. Thomas G. Bowery, Acting Director, Division of Research Facilities and Resources will be the witness.

I see you have a statement, Dr. Bowery. How do you want to proceed?

Dr. Bowery. I would like to read it into the record, sir.

Mr. Flood. All right. Suppose you do that. We will also put your biographical sketch into the record at this point.

(The biographical sketch follows:)

Biographical Sketch of Principal Witness

Name: Thomas Glenn Bowery.
Position: Acting Director, Division of Research Facilities and Resources.
Birthplace and date: Bellevue, Pennsylvania, December 17, 1921.
Education: B.S., 1943, Michigan State University, East Lansing, Mich., Ph. D., 1951—Rutgers University, New Brunswick, N.J.
Experience:
1968—Present—Acting Director, Division of Research Facilities and Resources, National Institutes of Health, Bethesda, Md.

1967–68—Associate Director for Operations, Office of the Director, Division of Research Facilities and Resources, National Institutes of Health, Bethesda, Md.

1965–67—Assistant Chief for Operations, Office of the Chief, Division of Research Facilities and Resources, National Institutes of Health, Bethesda, Md.

1964–65—Extramural Operations and Procedures Officer, Office of the Director, Office of the Associate Director for Extramural Programs, National Institutes of Health, Bethesda, Md.

1963–64—Special Assistant to the Associate Director for Research Grants, Office of the Director, National Institutes of Health, Bethesda, Md.

1962–63—Grants Associate, Grants Associates Program, Division of Research Grants, National Institutes of Health, Bethesda, Md.

1959–62—Research professor, Department of Entomology, North Carolina State College, Raleigh, N.C.

1953–59—Research associate professor, Department of Chemistry, North Carolina State College, Raleigh, N.C.

1951–52—Research assistant professor, Petsicide Residue Laboratory, Everglades Experiment Station, University of Florida, Belle Glade, Fla.

1948–51—Research associate in chemistry, office of the State Chemist, New Jersey Agricultural Experiment Station, New Brunswick, N.J.

1946–48—Research fellow, Entomology Department, Rutgers University, New Brunswick, N.J.

Association memberships: American Associate for the Advancement of Science; American Chemical Society; American Society for Public Administration, and, Sigma Xi.

Publications: Author of some 23 publications in seven journals.

GENERAL STATEMENT

Dr. BOWERY. Mr. Chairman and members of the committee.

It is a pleasure for me to appear before you to report the status of the National Institutes of Health's efforts to strengthen the Nation's biomedical research and research training programs through the mechanism of institutional support.

Our approach has been through the use of what we term the general research support program. The basic intent of this program is to strengthen the overall institutional capacity for medical and health-related research and research training and, thereby, to increase both the short-term and long-term effectiveness of the research efforts of scientists within institutions.

The general research support program has encouraged institutional responsibility, flexibility, and freedom in the support of research, and research training, in the health sciences. These grants have furnished institutions with an almost unparalleled opportunity to exercise their mature judgment and creativity in achieving their own long-range research objectives.

Two basic approaches involving three program elements are currently in operation—the broad support mechanisms of the general research support grant and the biomedical sciences support grant; and the competitive program of the Health Sciences Advancement Award.

GENERAL RESEARCH SUPPORT AND BIOMEDICAL SCIENCES SUPPORT GRANTS

With the increasing emphasis on the goal of better health for the American people through expanded appropriations for biomedical research came a demand from Congress, under Public Law 86–798, dated September 15, 1960, for financial support to institutions for planning and executing their own research and research training programs.

In 1962, 153 schools of medicine, dentistry, osteopathy, and public health were the first recipients of general research support grants. One year later, the general research support grant program was extended to include other health professional schools. Awards were given to schools of veterinary medicine and pharmacy; to hospitals and research institutes engaged in biomedical research; and to State and municipal health departments. In 1966, the program was extended to include nonhealth professional components of graduate academic institutions, and 91 universities received biomedical sciences support grants.

During 1968, 413 institutions were given awards under the general research support grant and the biomedical sciences support grant. Of these, 288 were academic institutions. One hundred and twenty-five were nonacademic organizations such as research-oriented hospitals and biomedical research institutes. Of the 288 academic institutions that received the grant, 186 schools were engaged in training health professionals in medicine, dentistry, public health, veterinary medicine, pharmacy, and osteopathy. In 1969, four new medical schools and one new dental school will receive general research support grants.

A few examples may illustrate more specifically how these flexible funds have been used by institutions to further their own research goals.

CREATION OF NEW ACADEMIC PROGRAMS AND DEPARTMENTS

During the last few years, many interdisciplinary categories of medical science have attained status sufficient that separate research and training enterprises have coalesced to form new and more powerful organizational entities better able to attack major health problems. A recent example of this can be seen at the University of Utah. A few years ago the university's department of surgery was reorganized in order to undertake a major research effort in the areas of organ transplantation and artificial organs. Although the surgical skills for such an undertaking were available, a research team was needed. The availbility of the general research support grant quickly allowed the institution to undertake a major recruitment effort which culminated in the employment of an excellent research group in transplantation and the staffing of a well-qualified pathology department. The new staffing combination brought nearly $800,000 in research support to the school, attracted new industry to the research park adjacent to the campus, and led to the creation of a new bioengineering institute which has become involved with additional segments of the university's biomedical research program.

PROVISION OF CENTRALIZED RESOURCES AND SERVICES

Instruments needed for research in today's complex world of science are often too expensive, or too complicated for assignment to a single research project or to an individual investigator. To assure optimum use of this equipment, many research institutes have established centralized instrumentation resources for their community of scientists.

To illustrate, during the past year, the University of California School of Pharmacy acquired its first mass spectrometer, largely due to a general research support grant. In the initial months of its operation, it has been used to solve problems of chemical structure of a variety of biologically important materials, including steroids, peptides, and opium alkaloids, among other materials.

In addition to meeting service requirements of research workers, administrators have discovered a secondary benefit of such resources: the existence of modern centralized instrumentation facilities is extremely helpful in recruiting top-flight scientific talent and in retaining key members of the research faculty.

SUPPORT OF PILOT OR EXPLORATORY PROJECTS

Flexible and prompt funding by general research support can readily initiate pilot or exploratory projects in their early, developmental stages.

For instance, an investigator at the University of Wisconsin developed a new tissue typing technique to match donor and recipient for organ and bone marrow transplants under general research support funding. As a result, a 2-year-old boy with a rare genetic defect is surviving without major symptoms nearly 5 months after receiving bone marrow transplants from his 9-year-old sister. As with transplants of other organs, bone marrow transfusion raises the possibility of major graft-versus-host reactions. The University of Wisconsin team working with the boy reasoned that this could be avoided if donor and recipient were closely matched. Research with animals, funded by general research support, had shown that the new tissue typing technique was valid. Later, the test was used successfully with renal transplants. Finally, it was used in the bone marrow transplant.

These are but three examples of how the general research support programs have served as a powerful instrument to help institutions throughout the Nation strengthen and expand their health-related research capabilities.

Mr. FLOOD. Would a bone graft or any graft from a twin be more likely to be successful than from a younger or an older brother or sister?

Dr. BOWERY. I think from the twin it would be much more likely to be successful.

Dr. BERLINER. If it is an identical twin.

Mr. FLOOD. If it is an identical twin?

Dr. BERLINER. Yes.

Mr. FLOOD. What is the difference between an identical and any other sort of twin?

Dr. BERLINER. Identical twins are the product of the same fertilized ovum and therefore are genetically identical, whereas sibling twins, that is, twins not identical but born at the same time, bear the same relationship as other siblings do whether they are born earlier or later.

Mr. FLOOD. Two ova fertilized at the same time; is that it?

Dr. BERLINER. Yes.

Mr. FLOOD. And the other situation is one ovum?

Dr. BERLINER. That is right.

Dr. BOWERY. These two programs continue to fill important research needs, and to justify congressional expectations of the early 1960's that they would contribute significantly to institutional improvement.

HEALTH SCIENCES ADVANCEMENT AWARD

Three years ago, the National Institutes of Health established a program to support an institution's self-developed plan for attaining a new level of achievement in the health sciences through a time-limited award. The amount of this award was to be determined by the intrinsic scientific merit of the proposal, and by its expected benefit to the institution and the Nation. Prior to the establishment of this program, it had become evident that increasing the number of biomedical research institutions of first-rank capability was vitally important to expand the Nation's capacity to conduct medical research. A broad base of scientifically excellent academic institutions was indispensable to the individual scientist's endeavors to improve our citizens' health and to enhance the quality of their lives.

The Health Sciences Advancement Award, as the new program was called, is designed to strengthen broad areas of institutional biomedical research through grants to carefully selected colleges and institutions that cannot yet be considered preeminent in the health sciences; that possess adequate biomedical research and research training strength for future growth; that offer high po'ential for achieving program goals; and that can provide assurance that they can sustain new levels of excellence beyond the award period.

Although the Health Sciences Advancement Award is only in its third year, there is already growing evidence that new outstanding health science research centers will be emerging in the future.

For example, the University of Virginia, an early Health Sciences Advancement Award grantee, is building an excellent research and research training program with a number of highly qualified professors that have been recruited or retained in five major departments in the school of medicine—anatomy, biochemistry, microbiology, pathology, and physiology. The number and quality of graduate students have markedly increased thus permitting a fuller realization of the departments' scientific capabilities.

The impact of the HSAA on the University of Virginia has been wide-ranging, with budgetary support for the basic science departments from the Commonwealth of Virginia markedly increased and with the general climate for improvement in the area of medical research and education very favorable. Thus, the total science program of the university has moved forward at a gratifying and exciting pace.

Purdue University, a more recent Health Science Advancement Award grantee, has moved vigorously in its research and research training program in neurobiology. The faculty and students from five departments are cooperating in these studies. The simplifying concept and flexibility of these institutional funds have permitted a much more coordinated attack on problems in this area than has ever been achieved before in the university's history. Acquisition of key new faculty; rapid selection and appointment of graduate students; more sophisticated approaches to equipment acquisition by teams of specialists; and

more deliberate planning of scientific strategies on a comprehensive basis all attest to the value of this form of Federal support for institutional advancement.

BUDGET REQUEST

The General Research Support Programs described previously are funded by a transfer of funds from the appropriations of the several institutes of the National Institutes of Health and of the National Institute of Mental Health. Therefore, the appropriation for these programs is not a separate proposal for funds from the President's fiscal year 1970 budget; rather it appears as a line item in the budget submissions of the various categorical institutes, from which the funds are transferred and aggregated into an account administered by the Division of Research Facilities and Resources.

For fiscal year 1970, the President's budget requests, through the budgets of the several institutes, $61,500,000, $800,000 above the operating level for fiscal year 1969, for the three General Research Support Programs as follows: $49 million for the General Research Support Grant Program; $7,500,000 for the Biomedical Sciences Support Grant Program; and $5 million for support of the Health Sciences Advancement Award.

I would be pleased to answer any questions, sir.

DETERMINATION OF BUDGET PRIORITIES

Mr. FLOOD. These funds are derived by transfer from other appropriations. If—and this is very likely; it is more probable than possible—if these other appropriations were cut 2, 3, 5, or 10 percent, selectively or even more probably, across the board, should the subcommittee reduce the amount of general research support grants in the same proportion, or would you give this a higher priority?

Dr. BOWERY. I think the judgment as to whether the funds should remain in the individual categorical institute or be transferred to this program would be basically the judgment of the Office of the Director. I would tend to have my own personal preference.

Mr. FLOOD. Dr. Berliner, this is really more your responsibility. You are the safety man.

This man's money comes from someplace else. He has to get it from other appropriations. You have been sitting here for some time, and you have reasonable cause to believe that these other appropriations, the source of this man's funds, may be cut 2, 3, 5, or even 10 percent.

Should we, if this happens, reduce the amount of general research support grants in the same proportion, or would you give this a higher priority?

Dr. BERLINER. I am not entirely sure. I think we would have to see what the effect of such a cut in the appropriations would be. We would prefer, if this question were to arise, to make the judgment at the time it became necessary.

Dr. SHERMAN. May I add a word to that, Mr. Flood. It seems to me, considering what has happened during the last year with respect to money going into these grantee institutions by several routes, par-

ticularly the project route and this type, that Dr. Berliner's answer becomes particularly important because we appear to be on the knife edge.

Mr. FLOOD. Did you hear his answer to my question?

Dr. SHERMAN. Yes, sir.

The problem here is to discern what is going to be best for these institutions under these circumstances. Depending on the extent of cut or increase, we might choose administratively to put that same over-all amount of money out by different devices, each of which contributes to the stability.

Mr. FLOOD. Suppose you were Mr. Michel, would you propose that we apply the same cut to this activity or would you give it a higher priority?

Dr. SHERMAN. I would hope he would find some way to give us the flexibility, sir.

ELIGIBILITY FOR HEALTH SCIENCES ADVANCEMENT AWARDS

Mr. FLOOD. Doctor, how do you determine eligibility for health science advancement awards?

What is your benchmark? How do you determine eligibility? Be sure you say this properly; and when you read the transcript of your answer, if you want to add to it, for heaven's sake don't hesitate to embellish it or add to it so it is good. You will do us a great favor.

Dr. BOWERY. Eligibility is determined on how we think the plan as developed by the institution will substantially increase the institution's capacity for carrying out better research and research training. Thus we have not yet established any specific upper or lower limits of eligibility as far as those schools that have achieved great——

Mr. FLOOD. Who do you mean by "we"?

Dr. BOWERY. The "we" are basically non-Federal consultants who come from the academic and scientific community who sit with us and review these applications.

Mr. FLOOD. Do they just knock on the door and walk in and sit down, or what?

Dr. BOWERY. No. They are involved in project site visits of the applicants and take a look onsite at the nature of what the institution wants to do. They go behind the written word and ask direct questions of individual scientists, the comptrollers, the presidents of the universities, better to determine and ascertain the nature of what the institution feels it wants to do.

Mr. FLOOD. Do they belong to an exclusive club, a special society? Are they handpicked? Must they be born to the purple?

Dr. BOWERY. As all NIH advisory committee members, they are selected based on our knowledge of their capacity to analyze situations, and they are nominated essentially by my office through the

channel of the Office of Director to the Secretary, and the Secretary invites these people to participate.

Mr. FLOOD. How do you select them? From record? From repute? Is there internal politics? Does somebody say, "Call Dr. So-and-So. I know him. He was a classmate of mine. We belong to the same club."

Dr. BOWERY. We try to bring a balance as to the type of institution they represent—major universities, smaller universities. We try to pick a balance as far as the disciplines they represent. We try to pick a balance as far as the geography of the country they represent.

Mr. FLOOD. Put in the record a little more detail on this subject.

(The requested statement follows:)

Health Sciences Advancement Awards are available on a competitive basis to academic institutions, within the United States and its territories, that grant graduate degrees in the biomedical sciences. In a multiple campus university, each campus having a separate academic administration and offering graduate programs in the biomedical sciences is considered an "institution" and may submit a separate application. With the exception of a multiple campus university, only one application, whether on behalf of a health professional school, of an entire medical center, or of several schoools or colleges within the university, can be submitted by an academic institution for review at one time.

The primary criterion for the evaluation of an Health Sciences Award application from an institution will be the impact that the proposed program will have on improving the health science program of the applicant. The impact will be measured in terms of the total anticipated institutional improvement relative to the present state of the proposed program.

It is expected that distinguished institutions will readily meet the usual eligibility criteria but will, in addition, be expected to present an unusually superior or creative program to insure the necessary relative increase in excellence. In general, this will not be achieved by a proposal to improve an isolated or deficient component but by presenting a plan organized to capitalize on the unique strengths of the institution.

The awards are not primarily designed for the development of an institution that presently is able to qualify for only limited amounts of Federal research and research training support in the health sciences. Institutions whose present research and research training activities are relatively small and narrow in scope are advised to defer applications until such time as their existing competence has been expanded, in order that the impact and relative improvement resulting from an award can be foreseen with a greater degree of confidence.

Funding preference is accorded to applicant institutions that (1) fall within the limits of the probable impact discussed above; (2) offer the greatest potential for achieving their proposed goals; and (3) provide the greatest assurance that the new levels of achievement will be sustained beyond the period of the award.

Mr. FLOOD. What institutions are getting the awards this year?

Dr. BOWERY. We are currently in the process of making nine awards, and we would anticipate, hopefully, by the start of fiscal year 1970 that we would make awards to an additional one or two institutions.

Mr. FLOOD. Will you list them for the record?

(The information follows:)

Institutions receiving health sciences advancement awards in fiscal year 1969

Institution	*Program title*
Cornell University, Ithaca, N.Y.	Proposal for developing biological sciences at Cornell
University of Virginia, Charlottesville, Va.	Developmental grant for research and support of basic science departments, school of medicine
Purdue University, Lafayette, Ind.	Development of neurobiology program
Vanderbilt University, Nashville, Tenn.	A proposal for health sciences achievement program at Vanderbilt University
University of Colorado, Denver and Boulder, Colo.	University of Colorado program for advancing the health sciences
Washington University, St. Louis, Mo.	Advancement of the sciences fundamental to research and training in the health professions
Rice University, Houston, Tex.	Integrated program in the sciences basic to health
University of California, Davis, Calif.	Comparative medicine
University of Oregon, Eugene, Oreg.	Development of programs in macromolecular chemistry, developmental biology, and neurobiology at the University of Oregon

Mr. FLOOD. Will the same schools continue next year?

Dr. BOWERY. Yes. These awards are for 5 years. The nine will be continuing. We hope to add to that.

CRITICISMS OF HEALTH SCIENCES ADVANCEMENT AWARDS

Mr. FLOOD. As of course you know, there was considerable opposition to this program in the beginning. First of all, were you legitimate? Under the law could you exist?

Dr. BOWERY. That is correct.

Mr. FLOOD. Apparently it was decided that you were.

Dr. BOWERY. The Comptroller General issued an opinion in June of 1967 that the program was legal under the law.

Mr. FLOOD. Mr. Smith of this committee was concerned about this.

In addition to that, you have this business of the caste system, the sacred cows. That bothered some people. You are concentrating in a very limited, narrow area, only nine schools up to now. The criticism that you should reach out and bring in more of the less-developed

institutions and bring them up to a higher level, instead of taking these Brahmins and forgetting everybody else.

What is your current assessment of this critique? Is there still this kind of opposition? Do you feel it any more?

Dr. BOWERY. I think it is lessening, although there is certainly a recognition on our part and on the part of our advisers that something in the nomenclature of a health science development award to try to reach down to some of the lesser-endowed institutions and to help them move forward is something that we should develop.

However, budgetary constraints have forced us not to seek funds for that type of program. I think a recognition that there are other areas besides the "Brahmins" that you have mentioned, that do need help, does exist.

Mr. FLOOD. You do? So do they. I still get it. You do not get much of it?

Dr. BOWERY. In our verbal discussions when we are out in the field, we get some concern raised by individuals. As far as direct mail to us, we have not had a great deal of such concern expressed. I think they recognize, at least within the fiscal constraints of the last several years, that to mount a new developmental type program would cost reasonably large sums of money which do not appear to be available at this time.

NEW ACTIVITIES

Mr. FLOOD. Is there any significant change proposed in any of the activities funded under this account?

Dr. BOWERY. There is an increase of $800,000 which would go into the general research support grant program to accommodate newly eligible institutions.

Mr. FLOOD. That is not a new activity funded under this account.

Dr. BOWERY. No; it is a continuation and extension of the same activity.

Mr. FLOOD. You are emphasizing it a bit. You are emphasizing this particular activity.

Dr. BOWERY. Yes. And as some of the newer medical schools are coming into eligibility requirements for this program, we would hope to be able to make such awards to them as we have in the past to other medical schools and professional schools.

Mr. FLOOD. Mr. Michel.

Mr. MICHEL. No questions.

Mr. FLOOD. Thank you very much, gentlemen.

Dr. BOWERY. Thank you, sir.

JUSTIFICATION MATERIAL

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

General Research Support Grants

Amounts Available for Obligation

	1969	1970
Appropriation (total obligations).....	$60,700,000	$61,500,000

Obligations by Activity

Page Ref.		1969 Estimate	1970 Estimate	Increase or Decrease
176	Grants:			
	(a) Traditional general research support....	$48,200,000	$49,000,000	+$800,000
	(b) Biomedical sciences support.....	7,500,000	7,500,000	---
	(c) Health sciences advancement awards..	5,000,000	5,000,000	---
	Total obligations....	60,700,000	61,500,000	+800,000

Obligations by Object

		1969 Estimate	1970 Estimate	Increase or Decrease
176	Grants, subsidies, and contributions (total obligations).....	$60,700,000	$61,500,000	+$800,000

Summary of Changes

1969 estimated obligations.....	$60,700,000
1970 estimated obligations.....	61,500,000
Net change.....	+800,000

Increase

Program

Traditional general research support.....	800,000

Explanation of Change

The program increase of $800,000 will provide general research support awards to some 14 newly eligible institutions including five new medical schools and one dental school with little or no change in awards to the presently eligible grantees.

Authorizing Legislation

Legislation	1970 Authorization
Public Health Service Act Section 301(d)--Make....grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs.....	Indefinite

PUBLIC HEALTH SERVICE ACT

Title III--General Powers and Duties of Public Health Service

Part A--Research and Investigation

Appropriation

Section 301(d). Make----grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs: Provided, that such uniform percentage, not to exceed 15 per centum, as the Surgeon General may determine, of the amounts provided for grants for research or research training projects for any fiscal year through the appropriations for the National Institutes of Health may be transferred from such appropriations to a separate account to be available for such research and research training program grant-in-aid for such fiscal year.

Significant Items in House and Senate Appropriations Committee Reports

Item	Action Taken or to be Taken
1969 Senate Report	
(1) The Committee suggests that, in connection with the rearrangement of program responsibility, consideration be given to the method of funding general research support including the possible desirability of direct funding for this program which is becoming increasingly important to the maintenance of the institutional stability of the recipients. (Page 59)	(1) A specific recommendation regarding the funding of General Research Support has been deferred as there is currently under evaluation the effect of both a major revision in the formula for the allocation of funds and the assimilation of the responsibility for the support of educational institutions as a result of the reorganization of the health functions within the Department.

General Research Support Grants

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1962	$14,500,000	$16,000,000	$20,000,000	$20,000,000
1963	30,000,000	30,000,000	30,000,000	30,000,000
1964	30,000,000	30,000,000	30,000,000	30,000,000
1965	40,000,000	40,000,000	45,000,000	45,000,000
1966	45,200,000	45,200,000	50,000,000	45,200,000
1967	51,700,000	51,700,000	51,700,000	51,700,000
1968	61,700,000	61,700,000	75,000,000	61,700,000
1969	60,700,000	60,700,000	60,700,000	60,700,000
1970	61,500,000			

General Research Support Grants

Introduction

Strong and effective academic and research institutions are indispensable to the betterment of health care and to the improvement of fundamental conditions of human life. Such institutions are an essential national resource dedicated to the education and training of scientific manpower. Through these institutions concepts vital to medical knowledge and necessary for application to the health of man are shaped and practiced.

The General Research Support Program provides grants to public and nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs. The basic intent of this Program is to strengthen the overall institutional capacity for medical and health-related research and research training and, thereby, to increase both the short-term and long-term effectiveness of the research projects of individual scientists within institutions.

The Program encourages institutional responsibility, flexibility, and freedom in the support of research and research training in the health sciences. The grants furnish institutions with an almost unparalleled opportunity to exercise their mature judgment and creativity in achieving their own long-range research objectives.

The success of the National Institutes of Health programs depends upon their coupling with the goals of the Nation's academic and other research institutions. Therefore, the goals of the General Research Support Program are to bring about a vigorous and fruitful national health research program which will undergird the development of the highest quality health care in the future. This is accomplished by three grant support mechanisms: the traditional General Research Support Grants; the Biomedical Sciences Support Grants which serve to enhance the effectiveness of project research at the institutions and allow the institution to redress imbalance and cultivate excellence in their research programs; and the Health Sciences Advancement Awards which serve to expand the national base for research in the health sciences by strengthening an increased number of institutions in their advancement toward greater capability in this field.

Program Plans

Traditional General Research Support Program: This program will provide continued support to encourage health professional academic and other health-related institutions to meet emerging opportunities in research. These funds will also contribute to long-range institutional development and to the improvement of health research and the research environment by giving the institution general, rather than project support. Under this program approximately 344 separate awards will be made to schools of medicine, dentistry, public health, osteopathy, pharmacy, and veterinary medicine, and to hospitals, research institutes, research foundations, and state and municipal health departments in 1970.

Biomedical Sciences Support Grants Program: This program extends the concept of general research support to non-health professional components of universities which have demonstrated a major engagement in biomedical research and research training. The National Institutes of Health has long recognized the importance to the Nation of the contributions to research in the health sciences made by investigators and teachers in academic components not covered by the traditional General Research Support Program, as demonstrated by the fact that a significant proportion of research project grants, graduate training grants, center grants, etc., go to these components. It is essential that flexible general research support funds be provided in order that the project-oriented funds may be utilized most effectively in these components, and that they may have the same benefits

that now accrue to the health professional and health-related schools. Approximately 115 institutions will be funded under this program in 1970.

Health Sciences Advancement Award Program: In 1966 funds were provided to institutions to accelerate the advancement of existing capabilities in health research and related graduate research training activities. These funds support institutional self-developed plans for attaining a new level of achievement in the health sciences through a time-limited award. The amount of the awards were determined by the intrinsic scientific merit of the proposal, and by its expected benefit to the institution and the Nation. Prior to the establishment of this program, it had become evident that upgrading the biomedical research activities of institutions not considered currently in the front rank was increasingly important if the Nation was to continue to make significant contributions to the medical sciences. Approximately 12 Health Sciences Advancement Awards will be sustained in 1970.

Distribution of Funds by Program Area in 1970

The requested amount of $61,500,000 would be distributed as follows: $49,000,000 for the General Research Support to approximately 344 institutions; $7,500,000 for Biomedical Sciences Support Grants to approximately 115 institutions; and $5,000,000 for Health Sciences Advancement Awards to approximately 12 institutions.

The following table illustrates the planned 1969 and 1970 distribution of general research support grants:

	1969 Estimate		1970 Estimate	
	No.	Amount	No.	Amount
Traditional General Research Support				
Educational Institutions:				
Dentistry	50	$2,400,000	51	$1,619,000
Medical	99	26,170,000	102	26,800,000
Osteopathy	5	132,000	5	66,000
Public Health	12	2,078,000	12	2,160,000
Pharmacy	12	640,000	13	700,000
Veterinary Medicine	16	1,900,000	17	2,150,000
Noneducational Institutions:				
Hospitals	76	8,300,000	80	8,670,000
Research Foundations, Institutes and Others	57	6,120,000	61	6,360,000
Health Departments	3	460,000	3	475,000
Subtotal	330	48,200,000	344	49,000,000
Biomedical Sciences Support Grants	108	7,500,000	115	7,500,000
Health Sciences Advancement Awards	12	5,000,000	12	5,000,000
Total	450	60,700,000	471	61,500,000

The general research support grants program is administered by the staff and funds of the Division of Research Facilities and Resources. Grant funds are provided by applying a uniform percentage to the amounts provided for research grants in the appropriations of the several institutes and one division of the National Institutes of Health, and the National Institute of Mental Health of the Health Services and Mental Health Administration.

The following table shows the estimated amounts to be provided by each of the contributing appropriations:

	1969 Estimate	1970 Estimate
National Institutes of Health		
National Cancer Institute	$6,838,000	$6,831,000
National Heart Institute	9,425,000	9,425,000
National Institute of Dental Research	1,194,000	1,215,000
National Institute of Arthritis and Metabolic Diseases	9,409,000	9,409,000
National Institute of Neurological Diseases and Stroke	5,818,000	5,818,000
National Institute of Allergy and Infectious Diseases	5,889,000	5,871,000
National Institute of General Medical Sciences	8,127,000	8,120,000
National Institute of Child Health and Human Development	4,082,000	4,469,000
National Eye Institute	1,612,000	1,912,000
Division of Environmental Health Sciences	551,000	567,000
Subtotal, NIH	52,945,000	53,637,000
Health Services and Mental Health Admin.		
National Institute of Mental Health	7,755,000	7,863,000
Total	60,700,000	61,500,000

APPENDIX

On May 5, 1969 the President submitted amendments to the budget which affected most of the appropriations on which hearings contained in this volume had already been held. These revisions are contained in H. Doc. No. 91–113. Following is a listing of those items covered in this volume which were changed and those which were not:

CHANGED

Biologics standards (p. 1242)
National Cancer Institute (p. 1245)
National Heart Institute (p. 1256)
National Institute of Dental Research (p. 1263)
National Institute of Arthritis and Metabolic Diseases (p. 1271)
National Institute of Neurological Diseases and Stroke (p. 1280)
National Institute of Allergy and Infectious Diseases (p. 1288)
National Institute of General Medical Sciences (p. 1296)
National Institute of Child Health and Human Development (p. 1303)
National Eye Institute (p. 1313)
Environmental health sciences (p. 1319)
General research and services (p. 1324)
John E. Fogarty International Center for Advanced Study in the Health Sciences (p. 1332)
Health manpower (p. 1339)
Dental health (p. 1348)
National Library of Medicine (p. 1353)
Buildings and facilities (p. 1366)
Salaries and expenses, Office of the Director (p. 1371)
Scientific activities overseas (special foreign currency program) (p. 1383)
General research support grants (p. 1378)

NOT CHANGED

Construction of health educational, research, and library facilities
Payment of sales insufficiencies and interest losses

Following is the Department's explanation of each of the changes in in the budget beginning, for each, on the page indicated in parentheses in the above listing.

Appropriation Estimate

BIOLOGICS STANDARDS

To carry out sections 351 and 352 of the Public Health Service Act pertaining to regulation and preparation of biological products, and conduct of research related thereto, [$8,338,000] $8,225,000.

NATIONAL INSTITUTES OF HEALTH

Biologics Standards

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (total obligations)	$8,338,000	-$113,000	$8,225,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Biologics standards (Total obligations).	285	$8,338,000	-5	-$113,000	280	$8,225,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions....	285	-5	280
Full-time equivalent of all other positions.....	5	--	5
Average number of all employees.....	280	-5	275
Personnel compensation:			
Permanent positions.....	$2,574,000	-$76,000	$2,498,000
Positions other than permanent.....	30,000	--	30,000
Other personnel compensation.....	49,000	--	49,000
Total personnel compensation....	2,653,000	-76,000	2,577,000
Personnel benefits.....	255,000	-5,000	250,000
Travel and transportation of persons...	112,000	--	112,000
Transportation of things.....	15,000	--	15,000
Rent, communications, and utilities....	51,000	--	51,000
Printing and reproduction.....	10,000	--	10,000
Other services.....	4,050,000	-19,000	4,031,000
Supplies and materials.....	1,015,000	-8,000	1,007,000
Equipment.....	180,000	-5,000	175,000
Subtotal.....	8,341,000	-113,000	8,228,000
Quarters and subsistence charges.....	-3,000	--	-3,000
Total obligations by object.....	8,338,000	-113,000	8,225,000

Summary of Changes

1970 obligations:

Original estimate	$8,338,000
Revised estimate	8,225,000
Net change	-113,000

	Original estimate Pos.	Original estimate Amount	Amendment Pos.	Amendment Amount
Decreases:				
1. Immunology	36	$555,000	-5	-$94,000
Payment to "National Institutes of Health management fund" for centrally furnished services	--	1,576,000	--	-19,000
Net change	xxx	xxx	-5	-113,000

Explanation of Changes

Direct operations--This $94,000 decrease will delay acceleration of the research program concerned with viral and tissue immunology, which will be operating at a level approximately $44,000 higher than 1969.

Biologics Standards

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	$4,817,000	$4,787,000	$4,787,000	$4,787,000
1965	4,969,000	4,969,000	4,969,000	4,969,000
1966	6,406,000	6,406,000	7,206,000	6,806,000
1967	7,905,000	7,904,000	7,904,000	7,904,000
1968	8,649,000	8,649,000	8,649,000	8,649,000
1969	8,499,000	8,499,000	8,499,000	8,499,000
1970	8,225,000			

Biologics Standards

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	285	$2,905,000	-5	-$81,000	280	$2,824,000
Other expenses.....	--	5,433,000	--	-32,000	--	5,401,000
Total.....	285	8,338,000	-5	-113,000	280	8,225,000

The Division, as the result of the decrease of $94,000 and 5 positions will have available $44,000 over the 1969 level to gather information, particularly through laboratory research directed towards the eventual adoption of standards, for reagents to be used in tissue and organ transplants, and for enzymes such as asparaginase. Both of these fields are developing at an extremely rapid rate and it is incumbent on the Division to keep abreast of the "state of the art."

The estimates reflect a decrease of $19,000 in the management fund for centrally provided services.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Biologics Standards						
Medical Officer.....	1	GS-15	$21,098	---	---	---
Medical Officer.....	1	GS-14	19,771	---	---	---
Medical Officer.....	1	GS-13	18,249	---	---	---
Scientist.....	1	GS-12	12,174	---	---	---
Scientist.....	1	GS-11	10,203	---	---	---
Total new positions, all activities.....	5		81,495	---		---

Appropriation Estimate

NATIONAL CANCER INSTITUTE

For expenses necessary to carry out title IV, part A, of the Public Health Service Act; [$184,402,000] $180,725,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (total obligations)	$184,402,000	-$3,677,000	$180,725,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research		$80,488,000		+$7,000		$80,495,000
General research support grants		(6,831,000)		(+7,000)		(6,838,000)
Scientific evaluation grants		(151,000)		(--)		(151,000)
Specialized research centers		(12,950,000)		(--)		(12,950,000)
Leukemia research support centers		(1,500,000)		(--)		(1,500,000)
Fellowships		4,201,000		-591,000		3,610,000
Training		11,186,000		-412,000		10,774,000
Direct operations:						
Laboratory and clinical research	478	17,178,000	-5	-133,000	473	17,045,000
Collaborative research and development	749	66,102,000	-20	-2,396,000	729	63,706,000
Biometry, epidemiology, and field studies	97	1,565,000	-8	-89,000	89	1,476,000
Review and approval of grants	119	2,598,000	-3	-46,000	116	2,552,000
Program direction	58	1,084,000	-1	-17,000	57	1,067,000
Total obligations	1501	184,402,000	-37	-3,677,000	1464	180,725,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
NATIONAL INSTITUTES OF HEALTH			
Total number of permanent positions...	1,427	-37	1,390
Full-time equivalent of all other positions.....	35	--	35
Average number of all employees.....	1,409	-8	1,401
Personnel compensation:			
Permanent positions.....	$14,650,000	-$85,000	$14,565,000
Positions other than permanent.....	278,000	--	278,000
Other personnel compensation.....	149,000	--	149,000
Total personnel compensation.....	15,077,000	-85,000	14,992,000
Personnel benefits.....	1,667,000	-10,000	1,657,000
Travel and transportation of persons.	690,000	-29,000	661,000
Transportation of things.....	128,000	--	128,000
Rent, communications, and utilities..	501,000	--	501,000
Printing and reproduction.....	467,000	--	467,000
Other services.....	63,071,000	-2,552,000	60,519,000
Supplies and materials.....	3,486,000	-5,000	3,481,000
Equipment.....	2,550,000	--	2,550,000
Grants, subsidies and contributions..	95,875,000	-996,000	94,879,000
Subtotal.....	183,512,000	-3,677,000	179,835,000
Deduct quarters and subsistence charges	-10,000	--	-10,000
Total, National Institutes of Health.....	183,502,000	-3,677,000	179,825,000

Obligations by Object--continued

	1970 Original Estimate	Amendment	1970 Revised Estimate
ALLOCATION TO VETERANS ADMINISTRATION			
Total number of permanent positions...	74	--	74
Full-time equivalent of all other positions.....	10	--	10
Average number of all employees.....	82	--	82
Personnel compensation:			
Permanent positions.....	$574,000	--	$574,000
Positions other than permanent.....	137,000	--	137,000
Other personnel compensation.....	1,000	--	1,000
Total personnel compensation.....	712,000	--	712,000
Personnel benefits.....	52,000	--	52,000
Travel and transportation of persons	60,000	--	60,000
Transportation of things.....	1,000	--	1,000
Rent, communication, and utilities..	2,000	--	2,000
Printing and reproduction.....	1,000	--	1,000
Supplies and materials.....	30,000	--	30,000
Equipment.....	42,000	--	42,000
Total, Veterans Administration.	900,000	--	900,000
Total obligations by object....	184,402,000	-3,677,000	180,725,000

Summary of Changes

1970 obligations:

Original estimate	$184,402,000
Revised estimate	180,725,000
Net change	-3,677,000

	Original estimate		Amendment	
	Pos.	Amount	Pos.	Amount
A. Increases:				
1. Program:				
(a) Research grants...	---	$80,488,000	---	+$7,000
Subtotal, increases....	xxx	xxx	---	+7,000
B. Decreases:				
1. Program:				
(a) Fellowships.....	---	4,201,000	---	-591,000
(b) Training.....	---	11,186,000	---	-412,000
(c) Laboratory and clinical research.....	478	9,455,000	-5	-65,000
(d) Collaborative research and development.....	749	65,672,000	-20	-2,379,000
(e) Biometry, epidemiology, and field studies....	97	1,474,000	-8	-85,000
(f) Review and approval of grants.....	119	1,576,000	-3	-35,000
(g) Program direction..	58	1,034,000	-1	-15,000
Subtotal, program decreases.....	xxx	xxx	-37	-3,582,000
2. Payment to "National Institutes of Health Management Fund" for centrally furnished services:.....	---	9,280,000	---	-102,000
Subtotal, decreases.....	xxx	xxx	-37	-3,684,000
Net Change.....	xxx	xxx	-37	-3,677,000

Explanation of Changes

Research grants--This revised estimate will provide an additional $7,000 for general research support grants. A reapplication of the formula based on the latest available information resulted in small increases and decreases in individual institutes, however, the overall NIH total for general research support grants will remain at the 1969 level ($52,945,000) a reduction of $692,000 below the original 1970 estimate of $53,637,000.

Fellowships-- This revised estimate will provide for support of 167 postdoctoral and special fellowships and 80 career award and career development fellowships.

Training--This revised estimate will provide for support of 75 graduate training and 98 cancer clinical training grants.

Laboratory and clinical research--This revised estimate will allow the National Cancer Institute to perform research within this budget activity at approximately the same level as in 1969.

Collaborative research and development--This revised estimate will require reductions below the original estimate in research relating to virus causation of cancer, cancer therapy, demography, and in chemical causation of cancer. The programs will operate at a level which is $600,000 below that for 1969.

Biometry, epidemiology, and field studies--This revised estimate will allow expansion of $100,000 over the 1969 level and will be used for data handling and analysis of the information collected under the Third National Cancer Survey.

Review and approval of grants--This revised estimate will allow the National Cancer Institute to operate within this budget activity at approximately the same level as in 1969.

Program direction--This revised estimate will allow the National Cancer Institute to operate within this budget activity at approximately the same level as in 1969.

National Cancer Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$75,218,000	$83,308,000	$110,203,000	$91,257,000
1961	88,869,000	102,469,000	126,375,000	111,000,000
1962	117,167,000	125,672,000	160,000,000	142,836,000
1963	139,109,000	150,409,000	158,409,000	155,742,000
1964	145,114,000	144,340,000	145,114,000	144,340,000
1965	139,714,000	138,970,000	148,970,000	148,970,000
1966	153,968,000	157,618,000	163,768,000	163,768,000
1967	163,957,000	170,656,000	175,656,000	175,656,000
1968	183,356,000	183,356,000	192,356,000	183,356,000
1969	187,707,000	182,592,000	191,592,000	185,149,500
1970	180,725,000			

Justification

National Cancer Institute

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	1501	$17,498,000	-37	-$95,000	1464	$17,403,000
Other expenses.....	---	166,904,000	---	-3,582,000	---	163,322,000
Total.....	1501	184,402,000	-37	-3,677,000	1464	180,725,000

General Statement

The National Cancer Institute conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling cancer in man. These objectives are pursued directly through universities, non-profit research organizations and commercial concerns supported with grants and contracts and include both laboratory and clinical studies.

The revised estimate is 37 positions and $3,677,000 below the original estimate. There is a net decrease of $996,000 in grants and $2,681,000 in direct operations. The decrease in direct operations consists of $2,579,000 in program decreases and $102,000 in centrally furnished services from the National Institutes of Health Management Fund.

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research Projects.....	$59,056,000	---	$59,056,000
Special Programs.....	21,432,000	+$7,000	21,439,000
Total Research Grants.....	80,488,000	+7,000	80,495,000

There is an increase in Research Grants of $7,000 which will allow the National Cancer Institute to award General Research Support Grants at the same level as in 1969.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total fellowships.....	$4,201,000	-$591,000	$3,610,000

The Fellowships program will operate at a level which is $764,000 below that for 1969. This program will continue to support training for young scientists with outstanding potential for careers of independent research in disciplines related to cancer research. Continued emphasis will be given to the shortage areas of radiation therapy, surgery, hematology, and clinical pharmacology.

Funds requested for the 1970 revised estimate will provide for 247 awards, compared to 285 in the 1970 original estimate, a decrease of 38.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total training grants.....	$11,186,000	-$412,000	$10,774,000

The Training Grants program will operate at a level which is $867,000 below that for 1969. In Graduate Training, emphasis will continue to be placed in disciplines where cancer researchers are in short supply, such as radiation therapy, clinical pharmacology, and chemical carcinogenesis. The Cancer Clinical Training Program will continue to make awards to raise the quality of clinical cancer institutions, to broaden the scope and content of the cancer training in the prevention, diagnosis, treatment, rehabilitation, and public health aspects of cancer, and to coordinate and cooperate with regional medical program activities in cancer.

Funds requested for the 1970 revised estimate will provide for 173 awards, compared to 182 in the 1970 original estimate, a decrease of 9.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	478	$5,672,000	-5	-$13,000	473	$5,659,000
Other expenses.....	---	11,506,000	---	-120,000	---	11,386,000
Total.....	478	17,178,000	-5	-133,000	473	17,045,000

This program will operate at approximately the same level as in 1969. Research will continue within this budget activity to add to our knowledge about the basic processes of cancer and to improve methods of therapy.

This revised estimate represents a program decrease of 5 positions and $65,000, and a decrease of $68,000 for centrally furnished services for the National Institutes of Health Management Fund.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	749	$8,648,000	-20	-$51,000	729	$8,597,000
Other expenses.....	---	57,454,000	---	-2,345,000	---	55,109,000
Total.....	749	66,102,000	-20	-2,396,000	729	63,706,000

It will be necessary to effect reductions totalling $2,396,000 below the 1970 original estimate in research relating to virus causation of cancer, cancer therapy, demography, and in chemical causation of cancer. Included in the reduction is $1,040,000 for the Third National Cancer Survey. However, this program is so vital that the National Cancer Institute intends to carry this activity on at a slightly reduced level than originally proposed by paring down other programs as the year progresses in a fashion which would do the least damage to the NCI efforts.

The programs under Collaborative Research and Development will operate at a program level which is $600,000 below that for 1969. These reductions will be equally divided between Cancer Therapy, Special Virus Cancer and the Breast Cancer Task Force. Based on the revised estimate, it is planned to continue all programs within Collaborative Research and Development although at a slightly reduced level than now being conducted during 1969.

This revised estimate represents a program decrease of 20 positions and $2,379,000, and a decrease of $17,000 for centrally furnished services for the National Institutes of Health Management Fund.

Biometry, Epidemiology, and Field Studies

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	97	$1,146,000	-8	-$21,000	89	$1,125,000
Other expenses.....	---	419,000	---	-68,000	---	351,000
Total.....	97	1,565,000	-8	-89,000	89	1,476,000

This program will operate at a level of $100,000 above that for 1969. These funds will be used for data handling and analysis of the information collected under the Third National Cancer Survey.

This revised estimate represents a program decrease of eight positions and $85,000, and a decrease of $4,000 for centrally furnished services for the National Institutes of Health Management Fund.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	119	$1,270,000	-3	-$8,000	116	$1,262,000
Other expenses.....	---	1,328,000	---	-38,000	---	1,290,000
Total.....	119	2,598,000	-3	-46,000	116	2,552,000

This program will operate at approximately the same level as in 1969.

This revised estimate represents a program decrease of three positions and $35,000, and a decrease of $11,000 for centrally furnished services for the National Institutes of Health Management Fund.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	58	$762,000	-1	-$2,000	57	$760,000
Other expenses.....	---	322,000	---	-15,000	---	307,000
Total.....	58	1,084,000	-1	-17,000	57	1,067,000

This program will operate at approximately the same level as in 1969.

This revised estimate represents a program decrease of one position and $15,000, and a decrease of $2,000 for centrally furnished services for the National Institutes of Health Management Fund.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Laboratory and Clinical Research:						
Scientist	1	GS-14	$16,946	--	---	---
Chemist	1	GS-13	14,409	--	---	---
Biologist	1	GS-9	8,462	--	---	---
Biologist	1	GS-7	6,981	--	---	---
Chemist	1	GS-7	6,981	--	---	---
	5		53,779	--		---
Collaborative Research and Development:						
Medical Officer	2	GS-15	39,560	--	---	---
Scientist	1	GS-15	19,780	--	---	---
Biologist	1	GS-14	16,946	--	---	---
Scientist	1	GS-14	16,946	--	---	---
Scientist	1	GS-13	14,409	--	---	---
Medical Officer	1	GS-12	12,174	--	---	---
Biologist	1	GS-11	10,203	--	---	---
Biologist	1	GS-9	8,462	--	---	---
Chemist	1	GS-9	8,462	--	---	---
Contract Specialist	1	GS-9	8,462	--	---	---
Statistical Assistant	1	GS-9	8,462	--	---	---
Biologist	3	GS-7	20,943	--	---	---
Chemist	3	GS-7	20,943	--	---	---
Biologist	1	GS-5	5,732	--	---	---
Secretary	1	GS-5	5,732	--	---	---
	20		217,216	--		---
Biometry, Epidemiology, and Field Studies:						
Mathematician	1	GS-15	19,780	--	---	---
Medical Officer	1	GS-14	16,946	--	---	---
Medical Officer	2	GS-13	28,818	--	---	---
Mathematician	1	GS-11	10,203	--	---	---
Statistician	1	GS-11	10,203	--	---	---
Statistician	1	GS-9	8,462	--	---	---
Clerk-Stenographer	1	GS-5	5,732	--	---	---
	8		100,144	--		---
Review and Approval of Grants:						
Scientist	1	GS-15	19,780	--	---	---
Scientist	1	GS-13	14,409	--	---	---
Secretary	1	GS-7	6,981	--	---	---
	3		41,170	---		---
Program Direction:						
Public Health Program Specialist	1	GS-13	14,409	--	---	---
	1		14,409	--		---
Total new positions, all activities	37		426,718	--		---

Appropriation Estimate

NATIONAL HEART INSTITUTE

For expenses, not otherwise provided for, necessary to carry out title IV, Part B, of the Public Health Service Act, [$163,141,000] $160,513,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Heart Institute

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)...	$163,141,000	-$2,628,000	$160,513,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research.....		$101,307,000		---		$101,307,000
General research support grants.....		(9,425,000)		---		(9,425,000)
Scientific evaluation and planning.....		(163,000)		---		(163,000)
Categorical clinical research centers.....		(4,500,000)		---		(4,500,000)
Heart cooperative drug study.....		(4,820,000)		---		(4,820,000)
Specialized research centers.....		(925,000)		---		(925,000)
Fellowships.....		7,309,000		-746,000		6,563,000
Training.....		17,442,000		-499,000		16,943,000
Direct operations:						
Laboratory and clinical research.....	387	13,641,000	-12	-137,000	375	13,504,000
Collaborative research and development.....	35	18,148,000	-4	-1,179,000	31	16,969,000
Biometry, epidemiology, and field studies.....	64	1,724,000	0	-3,000	64	1,721,000
Training activities.....	4	204,000	0	0	4	204,000
Review and approval of grants.....	99	2,723,000	0	-13,000	99	2,710,000
Program direction.....	31	643,000	-4	-51,000	27	592,000
Total obligations.....	620	163,141,000	-20	-2,628,000	600	160,513,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions.....	620	-20	600
Full time equivalent of other positions..	30	-2	28
Average number of all employees.....	626	-16	610
Personnel compensation: Permanent positions.....	$6,481,000	-$161,000	$6,320,000
Positions other than permanent.....	242,000	-19,000	223,000
Other personnel compensation.....	52,000	---	52,000
Total personnel compensation.....	6,775,000	-180,000	6,595,000
Personnel benefits.....	715,000	-12,000	703,000
Travel and transportation of persons..	285,000	-4,000	281,000
Transportation of things.....	109,000	-9,000	100,000
Rent, communications, and utilities...	242,000	---	242,000
Printing and reproduction.....	118,000	---	118,000
Other services.....	26,169,000	-1,145,000	25,024,000
Supplies and materials.....	1,706,000	-15,000	1,691,000
Equipment.....	964,000	-18,000	946,000
Grants, subsidies, and contributions..	126,058,000	-1,245,000	124,813,000
Total obligations by object.....	163,141,000	-2,628,000	160,513,000

Summary of Changes

1970 obligations:

Original estimate	$163,141,000
Revised estimate	160,513,000
Net change	-2,628,000

Decreases	Original Estimate Pos.	Original Estimate Amount	Amendment Pos.	Amendment Amount
A. Program				
1. Fellowships	---	$7,309,000	---	-$746,000
2. Training grants	---	17,442,000	---	-499,000
3. Laboratory and clinical research	387	8,376,000	-12	-100,000
4. Collaborative research and development	35	18,112,000	-4	-1,178,000
5. Program direction	31	619,000	-4	-50,000
Total program decrease	xxx	xxx	-20	-2,573,000
B. Payment to "National Institutes of Health management fund" for centrally-furnished services	---	6,776,000	---	-55,000
Total net changes requested	xxx	xxx	-20	-2,628,000

Explanation of Changes

Fellowships--The decrease of $746,000 will result in an estimated 301 awards in 1970 compared with 365 in the 1970 original estimate.

Training grants--The decrease of $499,000 will result in an estimated support of 256 graduate research and clinical training programs in 1970 as compared with 266 in the 1970 original estimate.

Laboratory and clinical research--The program decrease of $100,000 and 12 positions will postpone expansion into laboratory space to be newly assigned to this Institute.

Collaborative research and development--The program decrease of $1,178,000 and 4 positions in this activity will result in a revised 1970 support level $400,000 below 1969. The decrease will reduce support for further systematic biological testing and evaluation of circulatory assist devices currently under development by the Artificial Heart Program. The existing Myocardial Infarction Research Units will be supported at a reduced level, and the initiation of new units will be postponed.

Program direction--The program decrease of $50,000 and 4 positions will maintain staffing support for the Office of the Director, National Heart Institute at the 1969 level.

National Heart Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$45,594,000	$52,744,000	$89,500,000	$62,237,000
1961	63,162,000	71,762,000	125,166,000	86,900,000
1962	97,073,000	105,723,000	160,100,000	132,912,000
1963	126,898,000	143,398,000	149,398,000	147,398,000
1964	130,108,000	129,325,000	130,545,000	129,325,000
1965	125,640,000	124,521,000	125,171,000	125,171,000
1966	141,412,000	146,212,000	143,462,000	141,462,000
1967	148,407,000	154,770,000	164,770,000	164,770,000
1968	167,954,000	167,954,000	177,954,000	167,954,000
1969	169,735,000	164,120,000	172,120,000	166,927,500
1970	160,513,000			

Justification

National Heart Institute

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	620	$7,490,000	-20	-$192,000	600	$7,298,000
Other expenses	---	155,651,000	---	-2,436,000	---	153,215,000
Total	620	163,141,000	-20	-2,628,000	600	160,513,000

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research projects	$81,474,000	---	$81,474,000
Special programs	19,833,000	---	19,833,000
Total research grants	101,307,000	---	101,307,000

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total fellowships	$7,309,000	-$746,000	$6,563,000

Funds requested for the 1970 revised estimate will provide for 301 awards, compared to 365 in the 1970 original estimate, a decrease of 64.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total training grants	$17,442,000	-$499,000	$16,943,000

Funds requested for the 1970 revised estimate will provide for 368 awards, compared to 378 in the 1970 original estimate, a decrease of 10. The decrease will curtail a planned expansion of the clinical training effort in such program areas as cardiology, cardiovascular surgery, and pulmonary diseases.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	387	$4,562,000	-12	-$75,000	375	$4,487,000
Other expenses		9,079,000		-62,000		9,017,000
Total	387	13,641,000	-12	-137,000	375	13,504,000

The decrease for Laboratory and Clinical Research foreseen in the revised 1970 estimate eliminates 12 additional positions and corresponding funds which were intended for utilization of additional laboratory space assigned to the Institute and to provide supportive staff to research teams working in such areas as new approaches to molecular biology and in delineating lipid-protein patterns for eventual application in the community.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	35	$463,000	-4	-$74,000	31	$389,000
Other expenses		17,685,000		-1,105,000		16,580,000
Total	35	18,148,000	-4	-1,179,000	31	16,969,000

The decrease in the revised 1970 estimate will result in a reduced level of support for the following programs: (1) systematic biological testing and evaluation of artificial heart and circulatory assist devices in animals, the next phase of the Artificial Heart Program's mission to develop a family of devices to meet clinical needs for mechanical circulatory assistance; and (2) studies in the Myocardial Infarction Program on the problem of sudden pre-hospital cardiac death. The initiation of new Myocardial Research Units will also be postponed.

Biometry, Epidemiology, and Field Studies

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	64	$876,000	---	---	64	$876,000
Other expenses		848,000		-$3,000		845,000
Total	64	1,724,000	---	-3,000	64	1,721,000

The decrease in the revised 1970 estimate affects payment to the "NIH management fund" for centrally-furnished services.

Direct Training

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	4	$46,000	---	---	4	$46,000
Other expenses		158,000		---		158,000
Total	4	204,000	---	---	4	204,000

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	99	$1,124,000	---	---	99	$1,124,000
Other expenses		1,599,000		-$13,000		1,586,000
Total	99	2,723,000	---	-13,000	99	2,710,000

The decrease in the revised 1970 estimate affects payment to the "NIH management fund" for centrally-furnished services.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	31	$419,000	-4	-$43,000	27	$376,000
Other expenses		224,000		-8,000		216,000
Total	31	643,000	-4	-51,000	27	592,000

The decrease will eliminate 4 additional positions in the Office of the Director, NHI, which had been requested for the development of planning functions.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
LABORATORY AND CLINICAL RESEARCH						
Scientist	2	GS-13	$28,818	---	---	---
Scientist	2	GS-12	24,348	---	---	---
Research technician	2	GS-9	16,924	---	---	---
Research technician	2	GS-7	13,962	---	---	---
Laboratory technician	2	GS-5	11,464	---	---	---
Laboratory technician	2	GS-3	9,200	---	---	---
	12		104,716			
COLLABORATIVE RESEARCH AND DEVELOPMENT						
Scientist	1	GS-15	19,780	---	---	---
Scientist	1	GS-14	16,946	---	---	---
Administrative staff assistant	2	GS-11	20,406	---	---	---
	4		57,132			
PROGRAM DIRECTION						
Deputy director of office	1	GS-17	26,264	---	---	---
Administrative staff assistant	1	GS-15	19,780	---	---	---
Administrative staff assistant	1	GS-14	16,946	---	---	---
Clerical assistant	1	GS-5	5,732	---	---	---
	4		68,722			
Total new positions, all activities.	20		230,570	---		---

Appropriation Estimate

NATIONAL INSTITUTE OF DENTAL RESEARCH

For expenses, not otherwise provided for, to carry out title IV, part C of the Public Health Service Act [$30,062,000] $29,289,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Dental Research

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$30,062,000	$-773,000	$29,289,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research.....		$15,559,000		-$21,000		$15,538,000
General research support grants.....		(1,215,000)		(-21,000)		(1,194,000)
Scientific evaluation grants.....		(42,000)		.....		(42,000)
Categorical clinical research centers.....		(400,000)		.....		(400,000)
Dental research institutes.....		(3,400,000)		.....		(3,400,000)
Fellowships.....		1,694,000		-165,000		1,529,000
Training.....		5,390,000		-184,000		5,206,000
Direct operations:						
Laboratory and clinical research.....	221	4,947,000	-4	-235,000	217	4,712,000
Collaborative research and development.....	4	942,000	...	-100,000	4	842,000
Biometry, epidemiology and field studies.....	22	436,000	...	.....	22	436,000
Review and approval of grants.....	36	763,000	-1	-67,000	35	696,000
Program direction.....	23	331,000	...	-1,000	23	330,000
Total obligations.....	306	30,062,000	-5	-773,000	301	29,289,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions..	306	-5	301
Full-time equivalent of all other positions.....	14	...	14
Average number of all employees.....	309	...	309
Personnel compensation:			
Permanent positions.....	$3,236,000	-$55,000	$3,181,000
Positions other than permanent.....	116,000	.....	116,000
Other personnel compensation.....	22,000	.....	22,000
Total personnel compensation.....	3,374,000	-55,000	3,319,000
Personnel benefits.....	365,000	-5,000	360,000
Travel and transportation of persons.	158,000	-17,000	141,000
Travel and transportation of things..	38,000	-5,000	33,000
Rent, communications & utilities.....	106,000	-5,000	101,000
Printing and reproduction.....	47,000	-5,000	42,000
Other services.....	2,661,000	-293,000	2,368,000
Supplies and materials.....	460,000	-7,000	453,000
Equipment.....	213,000	-11,000	202,000
Grants, subsidies & contributions....	22,643,000	-370,000	22,273,000
Subtotal.....	30,065,000	-773,000	29,292,000
Deduct quarters and subsistence charges.....	-3,000	.....	-3,000
Total obligations by object.....	30,062,000	-773,000	29,289,000

Summary of Changes

1970 Obligations

Original estimate	$30,062,000
Revised estimate	29,289,000
Net change	-773,000

	Original Estimate		Amendment	
	Positions	Amount	Positions	Amount
Decreases:				
1. Research grants	...	$15,559,000	...	-$21,000
2. Fellowships	...	1,694,000	...	-165,000
3. Training	...	5,390,000	...	-184,000
4. Laboratory and clinical research	221	3,844,000	-4	-210,000
5. Collaborative research and development	4	939,000	...	-100,000
6. Review and approval of grants	36	555,000	-1	-65,000
7. Payment to "National Institutes of Health management fund" for centrally furnished services	...	1,354,000	...	-28,000
Total change requested	xxx	xxx	-5	-773,000

Explanation of Changes

Research grants--The decrease of $21,000 is in the general research support grant program.

Fellowships--The decrease of $165,000 represents a reduction of twelve fellowship awards to a 1970 level of 101 awards.

Training--The decrease of $184,000 represents a reduction of three training grants to a 1970 level of 88 awards.

Laboratory and clinical research--The decrease of $210,000 and 4 positions will impede expansion of research in dental caries and oral and related diseases.

Collaborative research and development--The decrease of $100,000 will prevent expansion of the contract program related to the cause and prevention of dental caries.

Review and approval of grants--The decrease of $65,000 will eliminate one additional position for management of the extramural programs.

National Institute of Dental Research

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$7,420,000	$9,725,000	$10,164,000	$10,019,000
1961	11,204,000	12,604,000	16,710,000	15,500,000
1962	13,933,000	14,681,000	20,000,000	17,340,000
1963	17,199,000	19,199,000	22,199,000	21,199,000
1964	19,809,000	19,689,000	19,809,000	19,689,000
1965	20,209,000	20,090,000	20,190,000	20,190,000
1966	22,177,000	22,177,000	23,677,000	23,677,000
1967	24,884,000	28,308,000	28,308,000	28,308,000
1968	30,307,000	30,307,000	32,307,000	30,307,000
1969	30,414,000	29,553,000	30,414,000	29,983,500
1970	29,289,000			

Justification

National Institute of Dental Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	306	$3,739,000	-5	-$60,000	301	$3.679.000
Other expenses	...	26,323,000	...	-713,000	...	25,610,000
Total	306	30,062,000	-5	-773,000	301	29,289,000

The 1970 revised estimate of $29,289,000 and 301 positions represents a reduction of $773,000 and 5 positions below the 1970 original estimates.

The funds available in fellowships and training will support 101 and 88 awards, respectively, as compared to 113 and 91 in the original estimate. The reduction in these areas will curtail to some extent, the development of dental scientist-teachers.

The cut in direct operations of 5 positions and $375,000 will reduce the intramural activities to the 1969 level of support.

The revised estimate reflects a decrease of $28,000 in the management fund for centrally furnished services.

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research projects.....	$10,502,000	.....	$10,502,000
Special programs.....	4,636,000	-$21,000	4,615,000
Total research grants.....	15,559,000	-21,000	15,538,000

The 1970 revised estimate reflects a decrease of $21,000 in the general research support grant program which reduces this program to the 1969 level of support.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total fellowships.....	$1,694,000	-$165,000	$1,529,000

Funds requested for the 1970 revised estimate will provide for 101 awards, compared to 113 in the 1970 original estimate, a decrease of 12 awards.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total training grants.....	$5,390,000	-$184,000	$5,206,000

Funds requested for the 1970 revised estimate will provide for 88 awards as compared to 91 in the 1970 original estimate, a decrease of 3 awards.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	221	$2,673,000	-4	-$46,000	217	$2,627,000
Other expenses	...	2,274,000	...	-189,000	...	2,085,000
Total	221	4,947,000	-4	-235,000	217	4,712,000

Funds requested for the 1970 revised estimate will provide $4,712,000 for 217 positions, compared to $4,947,000 for 221 in the original request, a decrease of 4 positions and $235,000, of which four positions and $210,000 were to support research on dental caries and other related areas defined by the Caries Task Force and $25,000 for centrally furnished services from the National Institutes of Health management fund.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	4	$64,000	...	.....	4	$64,000
Other expenses	...	878,000	...	-$100,000	...	778,000
Total	4	942,000	...	-100,000	4	842,000

Funds requested for the 1970 revised estimate reflect a decrease of $100,000 for contract research related to dental caries.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	36	$423,000	-1	-$14,000	35	$409,000
Other expenses	..	340,000	..	-53,000	..	287,000
Total	36	763,000	-1	-67,000	35	696,000

Funds requested for the 1970 revised estimate will provide $696,000 for 35 positions as compared to $763,000 for 36 positions in the original request, a decrease of one position and $67,000.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	23	$287,000	..	.....	23	$287,000
Other expenses	..	44,000	..	-$1,000	..	43,000
Total	23	331,000	..	-1,000	23	330,000

Funds requested for the 1970 revised estimate will provide $330,000 for 23 positions as compared to $331,000 for 23 positions, a decrease of $1,000. This decrease is related to centrally furnished services from the National Institutes of Health management fund.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Laboratory and clinical research						
Chemist	2	GS-9	$20,308	--	---	---
Dental director	2	C.O.	35,134	--	---	---
	4		55,442			
Review and approval of grants						
Scientist administrator	1	GS-13	14,409	--	---	---
	1		14,409			
Total new positions, all activities	5		60,851	--	---	---

Appropriation Estimate

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES

For expenses necessary to carry title IV, part D, of the Public Health Service Act with respect to arthritis, rheumatism, and metabolic diseases, [$139,968,000] $137,668,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and Metabolic Diseases

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$139,968,000	$-2,300,000	$137,668,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research		$92,289,000		0		$92,289,000
General research support grants		(9,409,000)		0		(9,409,000)
Scientific evaluation and planning		(20,000)		0		(20,000)
Categorical clinical research centers		(1,500,000)		0		(1,500,000)
Fellowships		6,475,000		$-993,000		5,482,000
Training		15,480,000		-408,000		15,072,000
Direct Operations:						
Laboratory and clinical research	499	15,664,000	-12	-273,000	487	15,391,000
Collaborative research and development	28	6,670,000	-3	-579,000	25	6,091,000
Biometry, epidemiology and field studies	26	712,000	0	-1,000	26	711,000
Review and approval of grants	74	2,373,000	-2	-44,000	72	2,329,000
Program direction	20	305,000	0	-2,000	20	303,000
Total obligations	647	139,968,000	-17	-2,300,000	630	137,668,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions.....	647	-17	630
Full-time equivalent of other positions...	38	0	38
Average number of all employees.....	623	+22	645
Personnel compensation:			
Permanent positions.....	$7,216,000	$-153,000	$7,063,000
Positions other than permanent.....	266,000	-7,000	259,000
Other personnel compensation.....	36,000	0	36,000
Total personnel compensation.....	7,518,000	-160,000	7,358,000
Personnel benefits.....	714,000	-15,000	699,000
Travel and transportation of persons..	260,000	-11,000	249,000
Transportation of things.....	74,000	-4,000	70,000
Rent, communications, and utilities...	195,000	-2,000	193,000
Printing and reproduction.....	160,000	0	160,000
Other services.....	14,361,000	-623,000	13,738,000
Supplies and materials.....	1,580,000	-84,000	1,496,000
Equipment.....	880,000	0	880,000
Grants, subsidies and contributions...	114,244,000	-1,401,000	112,843,000
Subtotal.....	139,986,000	-2,300,000	137,686,000
Deduct quarters and subsistance charges...	-18,000	0	-18,000
Total obligations by object.....	139,968,000	-2,300,000	137,668,000

Summary of Changes

1970 obligations:

Original estimate	$139,968,000
Revised estimate	137,668,000
Net change	-2,300,000

	Original Estimate		Amendment	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Program				
1. Fellowships	--	$6,475,000	--	-$993,000
2. Training	--	15,480,000	--	-408,000
3. Laboratory and clinical research	499	10,261,000	-12	-218,000
4. Collaborative research and development	28	6,648,000	-3	-579,000
5. Review and approval of grants	74	1,031,000	-2	-35,000
6. Program direction	20	288,000	--	-1,000
Subtotal, program decreases	xxx	xxx	-17	-2,234,000
B. Centrally furnished services from the "National Institutes of Health management fund"	--	6,812,000	--	-66,000
Net change	xxx	xxx	-17	-2,300,000

Explanation of Changes

Fellowships--The decrease of $993,000 will fund 74 fewer awards than the original 1970 estimate of 383 for a total of 309.

Training grants--The decrease of $408,000 will fund 9 fewer awards than the original 1970 estimate of 275 for a total of 266.

Laboratory and clinical research--The decrease of $218,000 will eliminate plans for 12 new positions and related research support costs in the laboratories and clinics.

Collaborative research and development--The decrease of $579,000 will eliminate the original increase requested of $79,000 in the Artificial Kidney Program and will reduce it $400,000 below the 1969 level. The decrease will also eliminate 3 positions and $100,000 in the Diabetes and Endocrine Hormone Development Program which will be maintained at the 1969 level.

Review and approval of grants--The decrease of 2 positions and $35,000 will eliminate the increase originally requested to strengthen this activity which will remain the same as 1969.

Program direction--The decrease of $1,000 maintains at the 1969 level, the overall administrative management activities in the office of the Institute Director.

National Institute of Arthritis and Metabolic Diseases

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	31,215,000	37,790,000	51,200,000	46,862,000
1961	47,541,000	52,841,000	70,760,000	61,200,000
1962	68,740,000	73,661,000	90,000,000	81,831,000
1963	91,921,000	98,721,000	105,721,000	103,388,000
1964	114,717,000	113,679,000	114,717,000	113,679,000
1965	113,369,000	113,344,000	113,544,000	113,344,000
1966	119,203,000	121,203,000	123,203,000	123,203,000
1967	129,908,000	133,687,000	135,687,000	135,687,000
1968	143,954,000	143,954,000	147,204,000	143,954,000
1969	151,718,000	141,287,000	147,287,000	143,888,000
1970	137,668,000			

Justification

National Institute of Arthritis and Metabolic Diseases

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation & benefits..	647	$8,232,000	-17	$-175,000	630	$8,057,000
Other expenses.....	--	131,736,000	---	-2,125,000	---	129,611,000
Total.....	647	139,968,000	-17	-2,300,000	630	137,668,000

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research projects.....	$81,360,000	0	$81,360,000
Special programs.....	10,929,000	0	10,929,000
Total research grants.....	92,289,000	0	92,289,000

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Fellowships.....	$6,475,000	-$993,000	$5,482,000

The funds provided in the 1970 revised estimate will support 309 fellowships which is 74 fewer than the 1970 original estimate. This decrease will primarily effect the postdoctoral and special fellowship programs which are designed to increase the number of individuals trained for research and teaching.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Training Grants.....	$15,480,000	-$408,000	$15,072,000

The funds provided in the 1970 revised estimate will support 266 training grants which is 9 fewer than the 1970 original estimate.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	499	$6,637,000	-12	-123,000	487	$6,514,000
Other expenses.....	---	9,027,000	---	-150,000	---	8,877,000
Total.....	499	15,664,000	-12	-273,000	487	15,391,000

The 1970 revised estimate will eliminate the increase of $218,000 to provide for 12 new positions and related research costs in new and continuing laboratory and clinical investigations which had been planned in the 1970 original estimate. The revised estimate will also decrease by $95,000, the funds available to the National Institutes of Health management fund for centrally furnished services.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	28	$347,000	-3	-$37,000	25	$310,000
Other expenses	--	6,323,000	--	-542,000	--	5,781,000
Total	28	6,670,000	-3	579,000	25	6,091,000

The 1970 revised estimates will eliminate the increase of $79,000 provided in the original estimate for the Artificial Kidney Program and will reduce it $400,000 below the 1969 level. The revised estimate will also eliminate a planned increase of 3 positions and $700,000 for the Diabetes and Endocrine Hormone Development Program.

Biometry, Epidemiology, and Field Studies

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	26	$239,000	--	-----	26	$239,000
Other expenses	--	473,000	--	1,000	--	472,000
Total	26	712,000	--	1,000	26	711,000

The 1970 revised estimate will decrease by $1,000, the funds available to the National Institutes of Health management fund for centrally furnished services.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	74	$781,000	-2	-$23,000	72	$758,000
Other expenses	--	1,592,000	--	- 21,000	--	1,571,000
Total	74	2,373,000	-2	- 44,000	72	2,329,000

The 1970 revised estimate will eliminate the 2 positions and $35,000 provided in the original estimate to strengthen the grants management and professional staff. The revised estimate will also decrease by $9,000, the funds available to the National Institutes of Health management fund for centrally furnished services.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	20	$228,000	--	-$1,000	20	$227,000
Other expenses	--	77,000	--	- 1,000	--	76,000
Total	20	305,000	--	- 2,000	20	303,000

The 1970 revised estimate maintains at the 1969 level, the overall administrative management activities in the office of the Institute Director and decreases by $1,000 the funds available to the National Institutes of Health management fund for centrally furnished services.

New Positions Requested Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
Laboratory and Clinical Research	No.	Grade	Salary	No.	Grade	Salary
Medical Officer	2	GS-14	$39,542	...	...	...
Medical Officer	1	GS-13	18,249	...	...	...
Scientist	2	GS-13	28,818	...	...	...
Scientist	2	GS-12	24,348	...	...	...
Research technician	2	GS-6	12,642	...	...	...
Secretary	2	GS-5	11,464	...	...	...
Clerk-typist	1	GS-4	5,145	...	...	...
	12		140,208	...	...	...
Collaborative Research and Development						
Medical Officer	1	GS-14	19,771	...	...	...
Secretary	1	GS-6	6,321	...	...	...
Clerk-steno	1	GS-4	5,145	...	...	...
	3		31,237	...	...	...
Review and Approval						
Grants Management Specialist	1	GS-9	8,462	...	...	...
Grants Management Specialist Assistant	1	GS-7	6,981	...	...	...
	2		15,443	...	...	...
Total, new positions, all activities	17		186,888	...	...	...

Appropriation Estimate

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

For expenses necessary to carry out title IV, part D of the Public Health Service Act with respect to neurology and stroke, [$103,485,000] $101,256,000.

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND STROKE

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$103,485,000	$-2,229,000	$101,256,000

Obligations by Activity

	1970 Original Estimate		Amendments		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research		59,506,000		---		59,506,000
General research support grants		(5,818,000)		---		(5,818,000)
Scientific evaluation and planning		(130,000)		---		(130,000)
Categorical clinical research centers		(2,416,000)		---		(2,416,000)
Specialized research centers		(850,000)		---		(850,000)
Fellowships		3,085,000		-428,000		2,657,000
Training		15,047,000		-747,000		14,300,000
Direct Operations:						
Laboratory and clinical research	293	10,100,000	-3	-224,000	290	9,876,000
Collaborative research and development	201	10,092,000	-2	-807,000	199	9,285,000
Biometry, epidemiology and field studies	80	3,028,000	--	-3,000	80	3,025,000
Training activities	2	72,000	--	---	2	72,000
Review and approval of grants	85	2,114,000	--	-20,000	85	2,094,000
Program direction	29	441,000	--	---	29	441,000
Total obligations	690	103,485,000	-5	-2,229,000	685	101,256,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	690	-5	685
Full-time equivalent of all other positions	45	---	45
Average number of all employees	713	---	713
Personnel compensation:			
Permanent positions	$ 7,315,000	$ -40,000	$ 7,275,000
Positions other than permanent	343,000	---	343,000
Other personnel compensation	120,000	-5,000	115,000
Total personnel compensation	7,778,000	-45,000	7,733,000
Personnel benefits	753,000	-3,000	750,000
Travel and transportation of persons	372,000	---	372,000
Transporation of things	83,000	---	83,000
Rent, communications, and utilities	225,000	---	225,000
Printing and reproduction	139,000	---	139,000
Other services	14,519,000	-1,000,000	13,519,000
Supplies and materials	1,270,000	-6,000	1,264,000
Equipment	710,000	---	710,000
Grants, subsidies, and contributions	77,638,000	-1,175,000	76,463,000
Subtotal	103,487,000	-2,229,000	101,258,000
Deduct quarters and subsistence charges	- 2,000	---	- 2,000
Total obligations by object	103,485,000	-2,229,000	101,256,000

Summary of Changes

1970 obligations:

Original estimate	$ 103,485,000
Revised estimate	101,256,000
Net change	-2,229,000

Decreases:

A. Program				
1. Fellowships	---	3,085,000	---	-428,000
2. Training	---	15,047,000	---	-747,000
3. Laboratory and clinical research	293	5,920,000	-3	-185,000
4. Collaborative research and development	201	9,932,000	-2	-797,000
5. Review and approval of grants	85	1,286,000	---	-14,000
B. Centrally furnished services from the National Institutes of Health Management Fund:	---	5,242,000	---	-58,000
Net change	xxx	xxx	-5	-2,229,000

Explanation of Changes

Fellowships-- The decrease of $428,000 will provide for 132 awards, a reduction of 36 from 1970 original estimate.

Training grants-- The decrease of $747,000 will provide for 385 awards, a reduction of 20 from 1970 original estimate.

Laboratory and clinical research-- The decrease of $185,000 will eliminate 3 new positions requested for 1970, reduce logistical support for initial expansion in the new research facility at Bethesda and cancel new programs in neurotology and the expansion of the Laboratory of Neural Control. All research programs will be maintained at the 1969 level.

Collaborative research and development-- The decrease of $797,000 will eliminate 2 new positions requested for 1970, reduce research support for Neurology's epilepsy and head injury programs and the collaborative perinatal project to a level which is $400,000 below that for 1969. The epilepsy collaborative effort is concerned with the development and testing of improved anticonvulsant drugs. Research associated with head injury is concerned with two major programs, the forces of injury and incidence and prevalence.

Review and approval of grants-- The decrease of $14,000 will minimize support for additional administrative needs of the extramural and program analysis staffs, which will be maintained at the 1969 level.

National Institute of Neurological Diseases and Stroke

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	29,403,000	33,613,000	48,966,000	41,487,000
1961	39,662,000	44,362,000	61,550,000	56,600,000
1962	54,100,000	57,624,000	80,000,000	70,812,000
1963	71,206,000	77,506,000	86,506,000	83,506,000
1964	88,407,000	87,675,000	88,407,000	87,675,000
1965	88,608,000	87,889,000	88,089,000	88,089,000
1966	96,403,000	96,403,000	102,153,000	101,153,000
1967	106,418,000	111,296,000	116,296,000	116,296,000
1968	128,633,000	128,633,000	135,633,000	128,633,000
1969	131,195,000	126,674,000	132,674,000	128,934,500
1970	101,256,000 1/			

1/ Excludes funds transferred from this appropriation to the National Eye Institute.

Justification

National Institute of Neurological Diseases and Stroke

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	690	8,531,000	-5	-48,000	685	8,483,000
Other expenses.....	---	94,954,000	--	-2,181,000	---	92,773,000
Total.....	690	103,485,000	-5	-2,229,000	685	101,256,000

General Statement

The total decrease in this estimate is distributed as follows: Fellowships, $428,000; Training, $747,000; Laboratory and Clinical Research, $185,000; Collaborative Research and Development, $797,000; Review and Approval, $14,000; the management fund portion, of Laboratory and Clinical Research, $39,000; of Collaborative Research and Development $10,000; Biometry, Epidemiology and Field Studies, $3,000; and Review and Approval of Grants, $6,000. Following is the analysis of each activity.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total fellowships.....	3,085,000	-428,000	2,657,000

Funds requested for the 1970 revised estimate will provide for 132 awards, compared to 168 in the 1970 original estimate, a decrease of 36.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total training grants..	15,047,000	-747,000	14,300,000

Funds requested for the 1970 revised estimate will provide for 385 awards, compared to 405 in the 1970 original estimate, a decrease of 20.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	293	4,113,000	-3	-30,000	290	4,083,000
Other expenses.....	---	5,987,000	--	-194,000	---	5,793,000
Total.....	293	10,100,000	-3	-224,000	290	9,876,000

Laboratory and Clinical Research

The decrease of $224,000 in this activity consists of $30,000 and three positions, $155,000 for institute programs and $39,000 for centrally furnished services of the National Institutes of Health Management Fund. This reduction will keep intramural research at the same level as 1969 and will not allow for expansion of the recently established laboratory of neural control or the initiation of a new laboratory of neuro-otology.

The objectives of the Laboratory of Neural Control are to study the mechanisms through which the nervous system can be made to respond to external stimuli and to study how the nervous system controls voluntary and/or involuntary movement. In addition, studies will be made of ways in which the effectiveness of the normal or damaged control mechanisms can be increased by supplementing with or supplanting by artificial elements.

The laboratory of neuro-otology plans a multidisciplinary approach to a program of research in communicative disorders. The mission of this laboratory is to conduct long-range research on the normal processes of the sensory, central, and efferent mechanisms which are used for human communication, and to study the identification, and amelioration of aberration in these mechanisms.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	201	3,181,000	-2	-18,000	199	2,163,000
Other expenses.....	---	7,911,000	--	-789,000	---	7,122,000
Total....	201	10,092,000	-2	-807,000	199	9,285,000

Collaborative Research and Development

Of the total decrease indicated above, $18,000 will apply to personal services, $779,000 is associated with institute programs and $10,000 is for centrally furnished services of the National Institutes of Health Management Fund.

Collaborative Research and Development (con't)

The reduction of two positions will be affected in the head injury and epilepsy programs. The program decrease of $779,000, reducing collaborative research $400,000 below 1969, will decrease the collaborative perinatal project by $400,000, head injury research by $332,000 and the epilepsy drug research program by $47,000.

a. The collaborative perinatal project which is a comprehensive investigation of medical and obstetrical complications of pregnancy, and the genetic and other factors operating in pregnant women which cause neuropsychiatric damage in their children; b. The epilepsy program which is a collaborative effort concerned with development and testing of improved anticonvulsant drugs. In 1970 this program planned to conduct extensive clinical investigation of anticonvulsant drugs; c. The head injury program plans in 1970 were to develop an incidence and prevalence survey to determine the role of head injury in the total picture of accidental injuries, and the development of field activities related to the physiologic problems of head injury. The major emphasis of this program, the head model construction will continue to the extent possible and has as its goal the development of accurate physical and mathematical models of the head which can be used for intensive studies of the characteristics and effects upon the brain of various forces of injury.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	85	964,000	--		85	964,000
Other expenses.....	--	1,150,000	--	-20,000	--	1,130,000
Total.....	85	2,114,000	--	-20,000	85	2,094,000

A decrease of $14,000 is associated with normal operating expenses of the extramural programs and $6,000 for centrally furnished services of the "National Institutes of Health Management Fund." Operation of this program will continue at the same level as 1969.

New Positions Requested

Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No	Grade	Salary	No	Grade	Salary
Laboratory and Clinical Research						
Medical officer	1	GS-14	$21,406	--	--	---
Secretary	1	GS-5	5,732	--	--	---
Clerk-Typist	1	GS-4	5,145	--	--	---
	(3)		32,283			
Collaborative Research and Development						
Medical officer	1	GS-15	23,734	--	--	---
Medical officer	1	GS-13	19,206	--	--	---
	(2)		42,940			
Total new positions all activities	(5)		75,223	--	--	---

Appropriation Estimate

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

For expenses, not otherwise provided for, necessary to carry out title IV, part D of the Public Health Service Act with respect to allergy and infectious diseases, [$103,922,000] $102,389,000, of which not to exceed $700,000 shall be available for payment to the Gorgas Memorial Institute for maintenance and operation of the Gorgas Memorial Laboratory.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations).....	$103,922,000	$-1,533,000	$102,389,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research.....		$60,582,000		+$18,000		$60,600,000
General research support grants..		(5,871,000)		(+18,000)		(5,889,000)
Gorgas Memorial Laboratory.....		(500,000)		(0)		(500,000)
Categorical clinical research centers.....		(1,100,000)		(0)		(1,100,000)
International centers for medical research and training....		(2,300,000)		(0)		(2,300,000)
Fellowships.....		4,191,000		-610,000		3,581,000
Training.....		9,118,000		-146,000		8,972,000
Direct operations:						
Laboratory and clinical research.	618	15,182,000	-15	-110,000	603	15,072,000
Collaborative research and development.....	42	12,855,000	-3	-673,000	39	12,182,000
Training activities.....	6	155,000	0	0	6	155,000
Review and approval of grants.....	47	1,531,000	-1	-11,000	46	1,520,000
Program direction.	24	308,000	0	-1,000	24	307,000
Total obligations.....	737	103,922,000	-19	-1,533,000	718	102,389,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	737	-19	718
Full-time equivalent of other positions	10	0	10
Average number of all employees	720	-7	713
Personnel compensation:			
Permanent positions	$6,979,000	-$69,000	$6,910,000
Positions other than permenant	95,000	0	95,000
Other personnel compensation	126,000	0	126,000
Total personnel compensation	7,200,000	-69,000	7,131,000
Personnel benefits	791,000	-8,000	783,000
Travel and transportation of persons	320,000	0	320,000
Transportation of things	100,000	0	100,000
Rent, communications, and utilities	303,000	0	303,000
Printing and reproduction	60,000	0	60,000
Other services	18,872,000	-718,000	18,154,000
Supplies and materials	1,900,000	0	1,900,000
Equipment	500,000	0	500,000
Grants, subsidies and contributions	73,891,000	-738,000	73,153,000
Subtotal	103,937,000	-1,533,000	102,404,000
Deduct quarters and subsistance charges	-15,000	0	-15,000
Total obligations by object	103,922,000	-1,533,000	102,389,000

Summary of Changes

1970 obligations:

Original estimate	$103,922,000
Revised estimate	102,389,000
Net change	-1,533,000

	Original estimate		Amendment	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Program				
1. Research grants	...	$60,582,000	...	+$18,000
Subtotal, increases				+18,000
Decreases:				
A. Program				
1. Fellowships	...	4,191,000	...	-610,000
2. Training grants	...	9,118,000	...	-146,000
3. Laboratory and clinical research	618	10,703,000	-15	-60,000
4. Collaborative research and development	42	12,817,000	-3	-671,000
5. Review and approval of grants	47	689,000	-1	-6,000
Subtotal, program decreases			-19	-1,493,000
B. Payments to the "National Institutes of Health management fund" for centrally furnished services	...	5,386,000	...	-58,000
Subtotal, decreases			-19	-1,551,000
Net change	xxx	xxx	-19	-1,533,000

Explanation of Changes

Research grants--The increase of $18,000 will provide the Institute's proportionate share for general research support grants.

Fellowships--The decrease of $610,000 will provide a total of $3,581,000 for approximately 205 awards, or 35 awards below the 1970 original estimate.

Training grants--The decrease of $146,000 will provide a total of $8,972,000 for approximately 153 projects, or 3 grants below the 1970 original estimate.

Laboratory and clinical research--The program decrease of $60,000 and 15 positions will eliminate the 1970 original proposed increased research effort in clinical allergy and immunology, chronic and degenerative, and viral diseases.

Collaborative research and development--The program decrease of $671,000 and 3 positions will eliminate the 1970 original estimated increase of $225,000 and 3 positions for increased research in the transplantation and immunology program and reduces this research area an additional $376,000 below the 1969 level of support. In addition, the scientific and administrative support of the U.S.-Japan Cooperative Medical Sciences program original 1970 estimated increase of $46,000 is eliminated with a further reduction of $24,000 below the 1969 level of support.

Review and approval of grants--The program decrease of $6,000 will eliminate the one additional position requested in the 1970 original estimate for the grants management activity.

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
1960	24,071,000	30,286,000	41,000,000	34,054,000
1961	34,739,000	38,439,000	48,234,000	44,000,000
1962	48,322,000	52,182,000	60,000,000	56,091,000
1963	59,342,000	62,142,000	68,142,000	66,142,000
1964	69,226,000	68,723,000	69,226,000	68,723,000
1965	68,600,000	70,100,000	70,400,000	70,100,000
1965	74,987,000	74,987,000	77,987,000	77,987,000
1967	85,702,000	88,670,000	90,670,000	90,670,000
1968	94,422,000	94,422,000	98,922,000	94,422,000
1969	98,562,000	95,119,000	99,119,000	96,840,500
1970	102,389,000			

Justification

National Institute of Allergy and Infectious Diseases

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	737	$7,991,000	-19	-$77,000	718	$7,914,000
Other expenses	...	95,931,000	...	-1,456,000	...	94,475,000
Total	737	103,922,000	-19	-1,533,000	718	102,389,000

General Statement

The National Institute of Allergy and Infectious Diseases 1970 revised estimate of $102,389,000 represents a reduction of $1,533,000 below the 1970 original estimate of $103,922,000. This net decrease is to be directed toward research of allergic and infectious diseases in the following areas: (1) research grants +$18,000; fellowships -$610,000; training grants -$146,000 for a total net reduction of -$738,000 in extramural activities; (2) -$135,000 for intramural research and (3) -$660,000 for the contract program.

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research projects	$50,761,000	$0	$50,761,000
Special programs	9,821,000	+$18,000	9,839,000
Total research grants	60,582,000	+18,000	60,600,000

The increase of $18,000 in the special programs represents the Institute's proportionate share for the general research support grants.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total fellowships	$4,191,000	-$610,000	$3,581,000

Funds requested for the 1970 revised estimate will provide 205 awards, compared to 240 awards in the 1970 original estimate, a decrease of 35 awards.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total training grants	$9,118,000	-$146,000	$8,972,000

Funds requested for the 1970 revised estimate will provide for 153 awards, compared to 156 in the 1970 original estimate, a decrease of 3 awards.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	618	$6,591,000	-15	-$60,000	603	$6,531,000
Other expenses		8,591,000		-50,000		8,541,000
Total	618	15,182,000	-15	-110,000	603	15,072,000

The decrease of $110,000 includes a program decrease of $60,000 and 15 positions included in the 1970 original estimate for increased research effort in clinical allergy and immunology, chronic and degenerative, and viral diseases, and will fund these areas of research at the same level as in 1969. The remaining decrease of $50,000 is for centrally furnished services and supplies from the National Institutes of Health management fund.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	42	$487,000	-3	-$11,000	39	$476,000
Other expenses		12,368,000		-662,000		11,706,000
Total	42	12,855,000	-3	-673,000	39	12,182,000

The total decrease of $673,000 and 3 positions eliminates the 1970 original estimated increases of $225,000 and 3 positions for increased research in the transplantation and immunology program involving studies of human tissue typing, and $46,000 for scientific and administrative support of the U.S.-Japan Cooperative Medical Sciences program. An additional reduction of $376,000 and $24,000 below the 1969 level of support is made in these programs respectively. The remaining decrease of $2,000 is for centrally furnished services and supplies from the National Institutes of Health management fund.

Training Activities

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	6	$90,000	...	$0	6	$90,000
Other expenses	...	65,000	...	0	...	65,000
Total	6	155,000	...	0	6	155,000

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	47	$541,000	-1	-$6,000	46	$535,000
Other expenses	....	990,000	...	-5,000	....	985,000
Total	47	1,531,000	-1	-11,000	46	1,520,000

The program decrease of $6,000 will eliminate the one position requested in the 1970 original estimate for the grants management activity. The decrease also includes $5,000 for centrally furnished services from the National Institutes of Health management fund.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	24	$282,000	....	$0	24	$282,000
Other expenses		26,000		-1,000		25,000
Total	24	308,000	....	-1,000	24	307,000

The decrease of $1,000 is in centrally furnished services from the National Institutes of Health management fund.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Laboratory and clinical research:						
Medical Officer.....	3	GS-13	$54,747	...	.....	.....
Virologist.....	4	GS-11	40,812	...	.....	.....
Maintenance Engineer....	1	GS-11	10,203	...	.....	.....
Research Technician.....	2	GS-7	13,962	...	.....	.....
Animal Caretaker.....	5	WB-4	26,830	...	.....	.....
Total Laboratory and clinical research....	15		146,554			
Collaborative research and development:						
Medical Officer.....	1	GS-15	21,098	...	.....	.....
Medical Officer.....	1	GS-14	19,771	...	.....	.....
Clerk-Stenographer.....	1	GS-5	5,732	...	.....	.....
Total Collaborative research and development.....	3		46,601			
Review and approval of grants:						
Scientist Administrator..	1	GS-13	14,409	...	.....	.....
Total all activities.....	19		207,564			

Appropriation Estimate

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

For expenses, not otherwise provided for, necessary to carry out title IV, part E of the Public Health Service Act with respect to general medical sciences, including the training of clinical anesthesiologists, [$157,803,000] $154,288,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$157,803,000	$-3,515,000	$154,288,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research		$84,263,000		+$7,000		$84,270,000
General research support grants		(8,120,000)		(+7,000)		(8,127,000)
Scientific evaluation grants		(1,437,000)		(---)		(1,437,000)
Pharmacology-Toxicology research		(3,500,000)		(---)		(3,500,000)
Anesthesiology and Diagnostic Radiology centers		(1,000,000)		(---)		(1,000,000)
Fellowships		20,040,000		-2,414,000		17,626,000
Training		45,568,000		-1,091,000		44,477,000
Direct operations:						
Collaborative research and development	---	3,288,000	---	---	---	3,288,000
Training activities	22	337,000	---	-1,000	22	336,000
Review and approval of grants	124	3,251,000	---	-14,000	124	3,237,000
Program direction	56	1,056,000	---	-2,000	56	1,054,000
Total obligations	202	157,803,000	---	-3,515,000	202	154,288,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions.....	202	0	202
Full-time equivalent of all other positions.....	6	0	6
Average number of all employees.....	202	0	202
Personnel compensation:			
Permanent positions.....	$2,160,000	0	$2,160,000
Positions other than permanent.....	67,000	0	67,000
Other personnel compensation.....	16,000	0	16,000
Total personnel compensation.....	2,243,000	0	2,243,000
Personnel benefits.....	223,000	0	223,000
Travel and transportation of persons..	164,000	0	164,000
Transportation of things.....	17,000	0	17,000
Rent, communications, and utilities...	129,000	0	129,000
Printing and reproduction.....	139,000	0	139,000
Other services.....	4,907,000	-17,000	4,890,000
Supplies and materials.....	77,000	0	77,000
Equipment.....	33,000	0	33,000
Grants, subsidies, and contributions..	149,871,000	-3,498,000	146,373,000
Total obligations by object.....	157,803,000	-3,515,000	154,288,000

Summary of Changes

1970 obligations:

Original estimate	157,803,000
Revised estimate	154,288,000
Net change	-3,515,000

	Original estimate		Amendment	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Program:				
1. Research grants	---	$84,263,000	---	+$7,000
Subtotal, increases	---	84,263,000	---	+7,000
Decreases:				
A. Program:				
1. Fellowships	---	20,040,000	---	-2,414,000
2. Training grants	---	45,568,000	---	-1,091,000
B. Payment to the "NIH Management Fund" for centrally furnished services	---	1,499,000	---	-17,000
Subtotal, decreases	---	---	---	-3,522,000
Net change	---	---	---	-3,515,000

Explanation of Changes

Research grants--The $7,000 increase is for general research support grants.

Fellowships--The decrease of $2,414,000 to a 1970 level of 1,634 awards reflects a reduction of 357 new awards. This represents a reduction of 263 predoctoral awards, 72 postdoctoral and 22 special awards.

Training grants--The decrease of $1,091,000 to a 1970 level of 513 awards reflects a decrease of 12 awards and 133 trainees in graduate training.

National Institute of General Medical Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1966	$124,538,000	$124,538,000	$129,388,000	$127,188,000
1967	137,175,000	142,613,000	145,113,000	145,113,000
1968	160,284,000	160,284,000	164,284,000	160,284,000
1969	165,777,000	161,250,000	166,250,000	163,513,500
1970	154,288,000			

Note: Included in "General Research and Services, National Institutes of Health," appropriation prior to 1966.

Justification

National Institute of General Medical Sciences

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	202	$2,466,000	--	---	202	$2,466,000
Other expenses.....	--	155,337,000	--	-$3,515,000	--	151,822,000
Total.....	202	157,803,000	--	-3,515,000	202	154,288,000

General Statement

The National Institute of General Medical Sciences is requesting a total of $154,288,000 for F.Y. 1970, a decrease of $3,515,000 from the original estimate.

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Regular program.....	$70,206,000	---	$70,206,000
Special program.....	14,057,000	+$7,000	14,064,000
Total research grants.....	84,263,000	+7,000	84,270,000

Funds requested for the 1970 revised estimate will provide an increase of $7,000 for the General Research Support Grants program.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Fellowships.....	$20,040,000	-$2,414,000	$17,626,000

Funds requested for the 1970 revised estimate will provide for 1,634 awards, compared to 1,991 in the 1970 original estimate, a decrease of 357. $15,565,200 would be required for funding of noncompeting continuations and $2,060,800 for competing.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Training Grants.....	$45,568,000	-$1,091,000	$44,477,000

Funds requested for the 1970 revised estimate will provide for 513 awards, compared to 525 in the 1970 original estimate, a decrease of 12 in the Fundamental Sciences' program.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Total other expenses.....	--	$3,288,000	--	---	--	$3,288,000

Funds requested for the 1970 revised estimate are unchanged from the original estimate.

Training Activities

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	22	$233,000	--	---	22	$233,000
Other expenses.....	--	104,000	--	-$1,000	--	103,000
Total.....	22	337,000	--	-1,000	22	336,000

Funds requested for the 1970 revised estimate reflects a $1,000 decrease from the original estimate in payment to the "National Institutes of Health Management Fund" for centrally furnished services.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	124	$1,511,000	--	---	124	$1,511,000
Other expenses.....	--	1,740,000	--	-$14,000	--	1,726,000
Total.....	124	3,251,000	--	-14,000	124	3,237,000

Funds requested for the 1970 revised estimate reflects a $14,000 decrease from the original estimate in payment to the "National Institutes of Health Management Fund" for centrally furnished services.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	56	$722,000	--	---	56	$722,000
Other expenses.....	--	334,000	--	-$2,000	--	332,000
Total.....	56	1,056,000	--	-2,000	56	1,054,000

Funds requested for the 1970 revised estimate reflects a decrease from the original estimate of $2,000 in payment to the "National Institutes of Health Management Fund" for centrally furnished services.

Appropriation Estimate

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

For expenses, not otherwise provided for, necessary to carry out title IV, part E of the Public Health Service Act with respect to child health and human development, [$78,411,000] $75,852,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH
National Institute of Child Health and Human Development

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations).....	$78,411,000	$-2,559,000	$75,852,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research.....		$46,564,000		-$1,437,000		$45,127,000
General research support grants.....		(4,469,000)		-(387,000)		(4,082,000)
Scientific evaluation...		(100,000)		...		(100,000)
Categorical clinical research centers.....		(500,000)		...		(500,000)
Mental retardation research centers.....		(3,000,000)		-(1,000,000)		(2,000,000)
Fellowships.....		4,027,000		-411,000		3,616,000
Training.....		9,621,000		-229,000		9,392,000
Direct Operations:						
Laboratory and clinical research.....	279	6,373,000	-43	-352,000	236	6,021,000
Collaborative research and development.....	32	6,721,000	+5	...	37	6,721,000
Biometry, epidemiology and field studies.....	23	2,176,000	...	-90,000	23	2,086,000
Training activities.....	4	85,000	...	...	4	85,000
Review and approval of grants.....	88	2,037,000	-3	-26,000	85	2,011,000
Program direction.....	49	807,000	-2	-14,000	47	793,000
Total obligations.....	475	78,411,000	-43	-2,559,000	432	75,852,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions..	475	-43	432
Full-time equivalent of all other positions.....	16	...	16
Average number of all employees.....	456	-22	434
Personnel compensation:			
Permanent positions.....	$ 4,442,000	$ -309,000	$ 4,133,000
Positions other than permanent.....	89,000	...	89,000
Other personnel compensation.....	117,000	...	117,000
Total personnel compensation.....	4,648,000	-309,000	4,339,000
Personnel benefits.....	532,000	-31,000	501,000
Travel and transportation of persons.	193,000	...	193,000
Transportation of things.....	52,000	...	52,000
Rent, communications, and utilities..	180,000	...	180,000
Printing and reproduction.....	107,000	...	107,000
Other services.....	11,599,000	-142,000	11,457,000
Supplies and materials.....	385,000	...	385,000
Equipment.....	503,000	...	503,000
Grants, subsidies, and contributions..	60,212,000	-2,077,000	58,135,000
Total obligations by object.....	78,411,000	-2,559,000	75,852,000

Summary of Changes

1970 Obligations:

Original Estimate	$78,411,000
Revised Estimate	75,852,000
Net Change	-2,559,000

	Original Estimate		Amendment	
	Positions	Amount	Positions	Amount
Increases:				
A. Program				
1. Collaborative research and development	32	$6,721,000	+5	...
Subtotal increases	...	...	+5	...
Decreases:				
A. Program				
1. Research grants	...	46,564,000	...	$-1,437,000
2. Fellowships	...	4,021,000	...	-411,000
3. Training grants	...	9,621,000	...	-229,000
4. Laboratory & clinical research	279	4,459,000	-43	-266,000
5. Biometry, epidemiology, & field services	23	2,154,000	...	-89,000
6. Review & approval of grants	88	1,392,000	-3	-20,000
7. Program direction	49	763,000	-2	-12,000
Subtotal	...	...	-48	-2,464,000
B. Centrally furnished services from the "National Institutes of Health Management Fund"	...	2,656,000	...	-95,000
Subtotal decreases	...	...	-48	-2,559,000
NET CHANGE	xxx	xxx	-43	-2,559,000

Explanation of Changes

Research Grants -- The decrease of $1,437,000 will be distributed as follows: $50,000 - competing projects in the regular program; $1,000,000 - Mental Retardation Research Centers; and $387,000 - General Research Support Grants.

Fellowships -- The decrease of $411,000 will provide for 186 fellowships compared to 207 in the 1970 original estimate.

Training Grants -- The decrease of $229,000 will provide for 116 grants compared to 127 in the 1970 original estimate.

Laboratory and Clinical Research -- The decrease of 43 positions and $266,000 will be distributed among four of the five major program areas of the Institute - Perinatal Biology and Infant Mortality, Growth and Development, Aging, and Mental Retardation. The other Institute program, Reproduction and Population Research will receive 14 positions, and $524,000, the entire increase in the Intramural program in 1970.

Collaborative Research and Development -- The increase of five positions in the Collaborative program will be to support the Center for Population Research, which administers the expanding contract program in Population research.

Biometry, Epidemiology and Field Studies - The decrease of $89,000 will come from reductions in epidemiologic contracts and in other object expenses, other than those related to population research.

Review and Approval -- The decrease of 3 positions and $20,000 will come from the grants management support staff, which will continue to operate at its 1969 level.

Program Direction -- The decrease of 2 positions and $12,000 will come from the central administrative activities of the Institute, which will continue to operate at the 1969 level.

This request contains $15,541,000 in the Institute's program, Population and Family Planning, which is an increase of 23 positions and $4,735,000 over the 1969 level and the same amount as shown in the original 1970 estimate.

National Institute of Child Health and Human Development

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1964	($34,000,000)	($34,000,000)	($34,000,000)	($34,000,000)
1965	43,169,000	43,696,000	42,696,000	42,696,000
1966	53,524,000	53,524,000	55,024,000	55,024,000
1967	61,448,000	61,422,000	64,922,000	64,922,000
1968	68,621,000	68,621,000	74,621,000	68,621,000
1969	75,394,000	70,859,000	76,359,000	73,126,500
1970	75,852,000			

Justification

National Institute of Child Health and Human Development

	1970 Original Estimate		1970 Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	475	$5,180,000	-43	-$340,000	432	$4,840,000
Other expenses		73,231,000		-2,219,000		71,012,000
Total	475	78,411,000	-43	-2,559,000	432	75,852,000

General Statement

The request of $75,852,000 in the revised 1970 estimate is $2,559,000 below the original 1970 estimate. This reduction will be achieved by decreasing the grant program $2,077,000 and by decreasing the direct operations of the Institute $482,000. In grants, the reduction is divided as follows: $1,437,000 from Research Grants, of which $1,000,000 will be taken from the Mental Retardation Research Centers; $411,000 from Fellowships; and $229,000 from Training Grants. In direct operations the reduction was achieved, primarily, by reducing the intramural research program $266,000. The remainder of the reduction in direct operations is split in smaller amounts between three other activities: Biometry, Epidemiology and Field Studies - $89,000; Review and Approval - $20,000; and Program Direction - $12,000. In addition, payment to the National Institutes of Health Management Fund for centrally furnished services has been reduced $95,000.

This request contains $15,541,000 in the Institute's program, Population and Family Planning, which is an increase of 23 positions and $4,735,000 over the 1969 level and the same amount as shown in the original 1970 estimate.

Research Grants

	1970 Original Estimate	1970 Amendment	1970 Revised Estimate
Regular projects	$38,495,000	-$50,000	$38,445,000
Special program	8,069,000	-1,387,000	6,682,000
Total research grants	46,564,000	-1,437,000	45,127,000

Funds requested for the 1970 revised estimate will provide for 963 awards in the regular program compared to 964 in the 1970 original estimate, a decrease of one.

In the special research grant programs, the reduction of $1,387,000 will be divided between two programs: $387,000 from General Research Support Grants and $1,000,000 from Mental Retardation Research Centers. Funds requested for the 1970 revised estimate for Mental Retardation Research Centers will provide for 8 awards compared to 15 in the 1970 original estimate, a decrease of seven.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Fellowships.....	$4,027,000	$ -411,000	$3,616,000

Funds requested for the 1970 revised estimate will provide for 186 awards, compared to 207 in the 1970 original estimate, a decrease of 21.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Training Grants.....	$9,621,000	-$229,000	$9,392,000

Funds requested for the 1970 revised estimate will provide for 116 awards, compared to 127 in the 1970 original estimate, a decrease of 11.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	279	$2,886,000	-43	-$359,000	236	$2,527,000
Other expenses.....		3,487,000		+7,000		3,494,000
Total.....	279	6,373,000	-43	-352,000	236	6,021,000

The reduction of 43 positions and $266,000 from the budget for Laboratory and Clinical Research will eliminate expansion of four of the five major program areas of the Institute - Perinatal Biology and Infant Mortality, Growth and Development, Aging, and Mental Retardation. There is also a decrease of $89,000 for centrally furnished services from the National Institutes of Health Management Fund.

Collaborative Research and Development

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	32	$374,000	+5	+$59,000	37	$433,000
Other expenses		6,347,000		-59,000		6,288,000
Total	32	6,721,000	+5	...	37	6,721,000

Five positions have been added to the Collaborative program to strengthen the support for the Center for Population Research.

Biometry, Epidemiology and Field Studies

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	23	$241,000	...	...	23	$241,000
Other expenses		1,935,000		-$90,000		1,845,000
Total	23	2,176,000	...	-90,000	23	2,086,000

The reduction of $90,000 in this activity will decrease by $89,000 the amount of funds available for epidemiologic research contracts and staff support, and by $1,000 the amount available for centrally furnished services from the National Institutes of Health Management Fund.

Training Activities

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnl compensation and benefits	4	$48,000	...	...	4	$48,000
Other expenses		37,000		...		37,000
Total	4	85,000	...	...	4	85,000

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	88	$1,010,000	-3	-$24,000	85	$986,000
Other expenses		1,027,000		- 2,000		1,025,000
Total	88	2,037,000	-3	-26,000	85	2,011,000

The reduction of 3 positions and $20,000 in this activity will eliminate the additional staff planned for grant managment support, which will be maintained at the 1969 level. There is also a reduction of $6,000 in the National Institutes of Health Management Fund for centrally furnished services.

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	49	$621,000	-2	-$16,000	47	$605,000
Other expenses		186,000		+2,000		188,000
Total	49	807,000	-2	-14,000	47	793,000

A reduction of 2 positions and $12,000 will maintain the central administrative activities of the Institute at the 1969 level. The payment to the National Institutes of Health Management Fund from centrally furnished services is reduced $2,000.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
Laboratory and clinical research	No.	Grade	Salary	No.	Grade	Salary
Medical Officer	1	GS-15	$19,780	1	GS-15	$19,780
Veterinarian	1	GS-14	16,946	...	...	...
Psychologist	1	GS-14	16,946	...	...	...
Physiologist	1	GS-13	14,409	1	GS-13	14,409
Biochemist	2	GS-13	28,818	...	...	...
Medical Officer	1	GS-12	12,174	1	GS-12	12,174
Biochemist	1	GS-12	12,174	...	...	...
Physiologist	1	GS-12	12,174	...	...	...
Physiologist	1	GS-11	10,203	...	...	...
Medical Officer	2	GS-11	20,406	1	GS-11	10,203
Physiologist	1	GS- 9	8,462	1	GS- 9	8,462
Chemist	3	GS- 9	25,386	1	GS- 9	8,462
Biologist	4	GS- 7	27,924	2	GS- 7	13,962
Chemist	5	GS- 7	34,905	1	GS- 7	6,981
Psychologist	3	GS- 5	17,196	1	GS- 5	5,732
Secretary	1	GS- 5	5,732	...	...	...
Chemist	5	GS- 5	28,660	1	GS- 5	5,732
Biologist	3	GS- 5	17,196	1	GS- 5	5,732
Biological-laboratory technician (histology)	1	GS- 5	5,732	...	...	...
Clerk typist	4	GS- 4	20,580	1	GS- 5	5,145
Biological laboratory technician	2	GS- 4	10,290	...	...	...
Biological laboratory aid	3	GS- 3	13,800	...	...	...
Clerk typist	1	GS- 3	4,600	...	...	...
Electroencephalographic technician	1	GS- 3	4,600	...	...	...
Physical science technician	1	GS- 3	4,600	...	...	...
Biological laboratory aid (animal)	2	GS- 2	8,462	...	...	...
Animal caretaker	5	WB	21,238	1	WB	4,248
Dishwasher	1	WB	3,723	...	...	...
	57	...	427,116	14	...	121,022
Collaborative Research and Development						
Biologist						
Biologist	1	GS-15	19,780	1	GS-15	19,780
Psychologist	1	GS-14	16,946	1	GS-14	16,946
Health scientist administrator	...	...	...	1	GS-14	16,946
Physiologist	1	GS-13	14,409	1	GS-13	14,409
Health scientist administrator	...	...	...	2	GS-13	28,818
Program management officer	...	...	...	1	GS-12	12,174
Program analyst	...	...	...	1	GS-11	10,203
	3	...	51,135	8	...	119,276
Biometry, Epidemiology and Field Studies						
Mathmatical statistician	1	GS-13	14,409	1	GS-13	14,409
	1	...	14,409	1	...	14,409
Review and Approval						
Health scientist administrator	1	GS-14	16,946	...	...	...
Health scientist administrator	2	GS-13	28,818	...	...	...
	3	...	45,764	...	...	...

New Positions Requested
Fiscal Year 1970
(Continued)

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Program direction						
Program management officer.....	1	GS-12	12,174	...	...	...
Program analyst	1	GS-11	10,203	...	...	...
	2	...	22,377			
Total new positions, all activities	66	...	560,801	23	...	254,707

Appropriation Estimate

NATIONAL EYE INSTITUTE

For expenses necessary to carry out title IV, part F, of the Public Health Service Act, with respect to eye diseases and visual disorders, /~~$25,778,000~~/ $23,685,000.

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Estimate
Appropriation (Total Obligations)	**$25,778,000**	**$-2,093,000**	**$23,685,000**

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research	--	$19,660,000	--	$-1,850,000	--	$17,810,000
General research Support grants	--	(2,671,000)	--	(-300,000)	--	(2,371,000)
Scientific evaluation and planning	--	(25,000)	--	----	--	(25,000)
Categorical clinical research centers	--	(734,000)	--	----	--	(734,000)
Fellowships	--	650,000	--	-89,000	--	561,000
Training	--	3,462,000	--	-149,000	--	3,313,000
Direct Operations:						
Laboratory and clinical research	40	754,000	--	-2,000	40	752,000
Collaborative research and development	--	349,000	--	-----	--	349,000
Biometry, epidemiology and field studies	15	317,000	--	-----	15	317,000
Review and approval of grants	15	466,000	--	-3,000	15	463,000
Program direction	8	120,000	--	-----	8	120,000
Total obligations	78	25,778,000	--	-2,093,000	78	23,685,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	78	--	78
Full-time equivalent of all other positions	6	--	6
Average number of all employees	76	--	76
Personnel compensation:			
Permanent positions	$ 777,000	--	$ 777,000
Other personnel compensation	28,000	--	28,000
Total personnel compensation	805,000	--	805,000
Personnel benefits	58,000	--	58,000
Travel and transportation of persons	51,000	--	51,000
Transportation of things	12,000	--	12,000
Rent, communications, and utilities	34,000	--	34,000
Printing & reproduction	16,000	--	16,000
Other services	942,000	-5,000	937,000
Supplies and materials	47,000	--	47,000
Equipment	41,000	--	41,000
Grants, subsidies, and contributions	23,772,000	-2,088,000	21,684,000
Total Obligations by object	25,778,000	-2,093,000	23,685,000

Summary of Changes

1970 Obligations:

Original Estimate	$25,778,000
Revised Estimate	23,685,000
Net Change	-2,093,000

	Original Estimate Pos.	Original Estimate Amount	Amendment Pos.	Amendment Amount
Decreases:				
A. Program				
1. Research grants	---	$19,660,000	---	$-1,850,000
2. Fellowships	---	650,000	---	- 89,000
3. Training	---	3,462,000	---	- 149,000
B. Payment to "National Institutes of Health Management Fund" for centrally furnished services	---	424,000	---	- 5,000
Net Change	xxx	xxx	xxx	-2,093,000

Explanation of Changes

Research Grants: The reduction of $1,850,000 will result in a decrease of 46 research grant awards from the original estimate, for a total of 394 awards.

Fellowships: The decrease of $89,000 will reduce the number of fellowships to be awarded under the original estimate by 4, for a total of 31 awards.

Training Grants: The decrease of $149,000 will reduce the number of awards by 4 from the original estimate, for a total of 76 awards.

National Eye Institute

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$23,685,000 1/			

1/ Prior year appropriation for this Institute was included within the National Institute of Neurological Diseases and Stroke.

Justification

National Eye Institute

Personnel Compensation and Benefits.....	78	$ 863,000	--	$--	78	$ 863,000
Other Expenses.....	--	24,915,000	--	-2,093,000	--	22,822,000
Total.....	78	25,778,000	--	-2,093,000	78	23,685,000

General Statement

The total decrease in this estimate is distributed as follows: Research Grants, $1,850,000; Fellowships, $89,000; Training, $149,000; the management fund portion of Laboratories and Clinical Research, $2,000; and the management fund portion of Review and Approval, $3,000.

Following is a detailed analysis of each activity:

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research Projects.....	$16,989,000	$-1,550,000	$15,439,000
Special Programs.....	2,671,000	-300,000	2,371,000
Total	19,660,000	-1,850,000	17,810,000

The original 1970 estimate provided $19,660,000 for this program or an increase of approximately $3,000,000 for new awards over 1969. The revised estimate of $17,810,000 will allow $1,825,000 over 1969 for new programs.

The emphasis placed on the establishment of the new Eye Institute requires that funding support be sufficient to launch new or expanded programs on research associated with blinding eye disorders and visual impairment. Accordingly, the revised estimate for 1970 will provide for 39 new awards compared to 85 under the original estimate for a decrease of 46 grants.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Fellowships.....	$650,000	$-89,000	$561,000

Funds requested for the 1970 revised estimate will provide for 31 awards, compared to 35 in the 1970 original estimate, a decrease of 4.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Training Grants.....	$3,462,000	$-149,000	$3,313,000

Funds requested for the 1970 revised estimate will provide for 76 awards compared to 80 in the 1970 original estimate, a decrease of 4.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	40	$474,000	--	----	40	$474,000
Other expenses.....	--	280,000	--	-2,000	--	278,000
Total.....	40	754,000	--	-2,000	40	752,000

The estimates reflect a decrease of $2,000 in the National Institutes of Health Management Fund for centrally provided services.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	15	$190,000	--	------	15	$190,000
Other expenses.....	--	276,000	--	-3,000	--	273,000
Total.....	15	466,000	--	-3,000	15	463,000

The estimates reflect a decrease of $3,000 in the National Institutes of Health Management Fund for centrally provided services.

Appropriation Estimate

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

To carry out, except as otherwise provided for, sections 301 and 311 of the Public Health Service Act, with respect to environmental health activities, [$19,004,000] $18,328,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institute of Environmental Health Sciences

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligation)	$19,004,000	$-676,000	$18,328,000

Obligations by Activity

	1970 Original Est.		Amendment		1970 Revised Est.	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Research.....		$8,967,000		$-516,000		$8,451,000
General research support grants...		(567,000)		(-16,000)		(551,000)
Environmental Health Sciences Centers.		(3,500,000)		(-500,000)		(3,000,000)
Fellowships.....		194,000		-30,000		164,000
Training.....		3,740,000		-123,000		3,617,000
Direct operations:						
Laboratory and clinical research..	186	5,322,000	---	-6,000	186	5,316,000
Review and approval of grants.....	23	443,000	---	-1,000	23	442,000
Program direction....	20	338,000	---	---	20	338,000
Total obligations..	229	19,004,000	---	-676,000	229	18,328,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions..	229	...	229
Full time equivalent of all other positions.....	9	...	9
Average number of all employees.....	220	...	220
Personnel compensation:			
Permanent positions.....	$2,191,000	...	$2,191,000
Positions other than permanent.....	64,000	...	64,000
Other personnel compensation.....	7,000	...	7,000
Total personnel compensation.....	2,262,000	...	2,262,000
Personnel benefits.....	225,000	...	225,000
Travel and transportation of persons.	180,000	...	180,000
Transportation of things.....	50,000	...	50,000
Rent, communications, and utilities..	350,000	...	350,000
Printing and reproduction.....	40,000	...	40,000
Other services.....	1,658,000	$-7,000	1,651,000
Supplies and materials.....	581,000	...	581,000
Equipment.....	757,000	...	757,000
Grants, subsidies, and contributions.	12,901,000	-669,000	12,232,000
Total obligations by object.....	19,004,000	-676,000	18,328,000

Summary of Changes

1970 Obligations:	
Original estimate	$19,004,000
Revised estimate	18,328,000
Net change	-676,000

	Original Estimate Pos.	Original Estimate Amount	Amendment Pos.	Amendment Amount
Decreases				
A. Program				
1. Research grants	---	$8,967,000	---	$-516,000
2. Fellowships	---	194,000	---	-30,000
3. Training grants	---	3,740,000	---	-123,000
B. Payment to "National Institutes of Health management fund" for centrally furnished services	---	278,000	---	-7,000
Total decreases	---	---	---	-676,000
Net changes	xxx	xxx	xxx	-676,000

Explanation of Changes

Research grants -- The decrease of $516,000 will eliminate $16,000 for general research support grants and $500,000 for the initiation of two additional Environmental Health Sciences Centers.

Fellowships -- The decrease of $30,000 reduces the number of fellowships in 1970 from 18 to 15.

Training grants -- The decrease of $123,000 will reduce the number of training grants awarded in 1970 from 47 to 45.

National Institute of Environmental Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1965	$10,920,000	$9,380,000	$9,730,000	$9,380,000
1966	15,933,000	15,933,000	15,983,000	15,983,000
1967	24,312,000	24,298,000	24,298,000	24,298,000
1968	20,615,000	17,289,000	20,615,000	17,289,000
1969	18,099,000	17,541,000	18,099,000	17,820,000
1970	18,328,000			

Justification

National Institute of Environmental Health Sciences

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	229	$2,487,000	---	---	229	$2,487,000
Other expenses.....	---	16,517,000	---	$-676,000	---	15,841,000
Total.....	229	19,004,000	---	-676,000	229	18,328,000

This revised estimate is $676,000 less than the original request, reductions having been made in Center Grants, Fellowships, Training Grants and the cost of centrally furnished services financed through the NIH Management Fund.

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research projects.....	$4,900,000	---	$4,900,000
Special programs.....	4,067,000	$-516,000	3,551,000
Total research grants.	8,967,000	-516,000	8,451,000

The amendment eliminates $16,000 for general research support grants and $500,000 to initiate 2 new Environmental Health Sciences Centers.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total Fellowships.....	$194,000	$-30,000	$164,000

The 1970 revised estimate will provide for 15 awards, compared to 18 in the 1970 original estimate, a decrease of 3.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Training grants.....	$3,740,000	$-123,000	$3,617,000

The 1970 revised estimate will provide for 45 awards, compared to 47 in the 1970 original estimate, a decrease of 2.

Laboratory and Clinical Research

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	186	$1,968,000	---	---	186	$1,968,000
Other expenses	---	3,354,000	---	$-6,000	---	3,348,000
Total	186	5,322,000	---	-6,000	186	5,316,000

The amendment decreases $6,000 from centrally furnished services financed through the NIH Management Fund.

Review and Approval of Grants

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	23	$261,000	---	---	23	$261,000
Other expenses	---	182,000	---	$-1,000	---	181,000
Total	23	443,000	---	-1,000	23	442,000

The amendment decreases $1,000 from centrally furnished services financed through the NIH Management Fund.

New Positions Requested

Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Laboratory and Clinical Research						
Associate Director of Office	1	GS-16	$22,835	1	GS-16	$22,835
Scientist	1	GS-16	22,835	1	GS-16	22,835
Chief of Branch	1	GS-15	19,780	1	GS-15	19,780
Medical Officer	2	GS-15	39,650	2	GS-15	39,650
Scientist	2	GS-15	39,650	2	GS-15	39,650
Medical Officer	3	GS-14	50,838	3	GS-14	50,838
Scientist	2	GS-14	33,892	2	GS-14	33,892
Scientist	4	GS-13	57,636	4	GS-13	57,636
Scientist	7	GS-12	85,218	7	GS-12	85,218
Scientist	1	GS-11	10,203	1	GS-11	10,203
Research Assistant	3	GS-9	25,386	3	GS-9	25,386
Laboratory Assistant	2	GS-3	9,200	2	GS-3	9,200
Animal Caretaker	4	GS-2	16,924	4	GS-2	16,924
Animal Caretaker	2	GS-1	7,778	2	GS-1	7,778
Total new positions	35		441,825	35		441,825

Appropriation Estimate

GENERAL RESEARCH AND SERVICES

For the activities of the National Institutes of Health, not otherwise provided for, including research fellowships, grants for research projects and training grants pursuant to section 301 of the Public Health Service Act; and grants of therapeutic and chemical substances for demonstrations and research; [$74,809,000] $69,698,000: Provided, That funds advanced to the National Institutes of Health management fund from appropriations included in this Act shall be available for the cost of sharing medical care facilities and resources pursuant to section 328 of the Act, purchase of not to exceed fourteen passenger motor vehicles for replacement only; and not to exceed $5,000 for entertainment of visiting scientists when specifically approved by the Surgeon General.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

General Research and Services

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations).....	$74,809,000	$-5,111,000	$69,698,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Division of Research Facilities and Resources:						
Grants:						
Research.....		$64,831,000		$-3,960,000		$60,871,000
Fellowships.....		146,000		-20,000		126,000
Training.....		364,000		-12,000		352,000
Direct Operations:						
Collaborative research and development...	2	1,483,000	--	--	2	1,483,000
Review and approval of grants.....	108	1,615,000	-4	-35,000	104	1,580,000
Program direction.....	36	641,000	--	-1,000	36	640,000
Division of Computer Research and Technology:						
Direct Operations.	112	4,753,000	--	-107,000	112	4,646,000
Engineering Development:						
Direct Operations:						
Collaborative research and development...	--	750,000	--	-750,000	--	--
Program direction.....	2	226,000	-2	-226,000	--	--
Total obligations.....	260	74,809,000	-6	-5,111,000	254	69,698,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions...	260	-6	254
Full-time equivalent of all other positions.....	11	--	11
Average number of all employees.....	263	-1	262
Personnel compensation:			
Permanent positions.....	$2,754,000	$-136,000	$2,618,000
Positions other than permanent.....	101,000	-2,000	99,000
Other personnel compensation.....	7,000	-1,000	6,000
Total personnel compensation.....	2,862,000	-139,000	2,723,000
Personnel benefits.....	276,000	-16,000	260,000
Travel and transportation of persons..	157,000	-7,000	150,000
Transportation of things.....	32,000	-5,000	27,000
Rent, communications, and utilities...	158,000	-7,000	151,000
Printing and reproduction.....	87,000	-9,000	78,000
Other services.....	5,719,000	-920,000	4,799,000
Supplies and materials.....	51,000	-4,000	47,000
Equipment.....	126,000	-12,000	114,000
Grants, subsidies, and contributions..	65,341,000	-3,992,000	61,349,000
Total obligations by object.....	74,809,000	-5,111,000	69,698,000

Summary of Changes

1970 obligations:

Original estimate	$74,809,000
Revised estimate	69,698,000
Net change	-5,111,000

	Original estimate		Amendment	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Program				
1. Division of Research Facilities and Resources:				
(a) Research grants: General clinical research centers		$38,964,000		$-3,960,000
(b) Fellowships		146,000		-20,000
(c) Training		364,000		-12,000
(d) Review and approval of grants	108	1,513,000	-4	-30,000
2. Division of Computer Research and Technology: Direct operations	112	4,645,000	--	-105,000
3. Engineering Development:				
(1) Collaborative Research and development	--	750,000	--	-750,000
(2) Program direction	2	224,000	-2	-224,000
B. Payment to the "National Institutes of Health management fund" for centrally furnished services	--	247,000	--	-10,000
Subtotal, decreases	xxx	xxx	-6	-5,111,000
Net change	xxx	xxx	-6	-5,111,000

Explanation of Changes

Research grants--The program decrease of $3,960,000 for the General Clinical Research Center program will result in a reduction of beds currently in use from 645 to 510 due to the rising costs for hospitalization and technical personnel in the continuing and activated centers.

Fellowships--The program decrease of $20,000 will result in a decrease from 15 to 14 in the number of grants awarded, and the average amount of each grant will be reduced.

Training grants--The program decrease of $12,000 will result in no change in the number of grants awarded, however, the average amount of each grant will be reduced.

Review and approval--The program decrease of $30,000 will eliminate the four positions requested to provide additional staff for the scientific administration of the several grant programs.

Computer research and technology--The decrease of $105,000 will eliminate the increase requested for entry into the implementation phase for more powerful and efficient programming tools to exploit the new remote terminals and special purpose computer systems now being acquired by NIH laboratories.

Engineering development--The decrease of $974,000 and two positions will abolish this division.

General Research and Services

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$28,974,000	$36,404,000	$49,585,000	$45,994,000
1961	47,260,000	52,600,000	104,405,000	83,900,000
1962	95,341,000	119,275,000	140,000,000	127,637,000
1963	147,826,000	155,826,000	161,826,000	159,826,000
1964	164,674,000	163,869,000	164,674,000	163,869,000
1965	163,715,000	162,959,000	164,759,000	164,759,000
1966 1/	58,719,000	59,969,000	60,469,000	60,469,000
1967	67,821,000	68,534,000	68,534,000	68,534,000
1968	81,141,000	81,141,000	81,141,000	81,141,000
1969	87,000,000	82,719,000	94,823,000	84,809,500
1970	69,698,000			

1/ Excludes the "National Institute of General Medical Sciences" established as a separate appropriation in 1966.

Justification

General Research and Services

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	260	$3,138,000	-6	$-155,000	254	$2,983,000
Other expenses	--	71,671,000	--	-4,956,000	--	66,715,000
Total	260	74,809,000	-6	-5,111,000	254	69,698,000

General Statement

The revised 1970 request is $5,111,000 below the original 1970 request. The reduction will come from the following activities: $4,028,000 from the Division of Research Facilities and Resources; $107,000 from the Division of Computer Research and Technology; and $976,000 from the Engineering Development activity, which will abolish this program.

Division of Research Facilities and Resources

Research Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
General clinical research centers	$38,964,000	-$3,960,000	$35,004,000
Scientific evaluation	305,000	--	305,000
Special research resources	10,494,000	--	10,494,000
Animal resources	4,568,000	--	4,568,000
Primate centers	10,500,000	--	10,500,000
Total research grants	64,831,000	-3,960,000	60,871,000

General Clinical Research Centers

Program Plans in 1969 and 1970

The $35,004,000 requested in the revised estimate, a decrease of $3,960,000 below the original estimate of $38,964,000, will provide support for 2,000 of the 2,540 currently approved positions and for slightly less than 50% bed occupancy (510 of the 1,040 beds available). This compares with the original request for support of 2,080 positions and maintenance of the current bed occupancy rate of 62%. The estimated reduction below the present rate of occupancy is due to the increased cost of hospitalization and pay raises for nurses, technicians and other paramedical personnel.

Fellowships

	1970 Original Estimate	Amendment	1970 Revised Estimate
Fellowships	$146,000	-$20,000	$126,000

The $126,000 requested in the revised estimate, a decrease of $20,000 from the original estimate for 1970 of $146,000 will provide support for 14 grants at a reduced level per grant compared to 15 in the original estimate.

Training Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Training grants.....	$364,000	-$12,000	$352,000

The $352,000 requested in the revised estimate, a decrease of $12,000 from the original estimate of $364,000 will provide support for nine training grants the same number as in the original estimate at, however, a reduced amount per grant.

Review and Approval

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	108	$1,229,000	-4	-$30,000	104	$1,199,000
Other expenses.....	--	386,000	--	-5,000	--	381,000
Total.....	108	1,615,000	-4	-35,000	104	1,580,000

The program decrease of $30,000 and four positions will eliminate the requested additional staff for the scientific administration of the several grant programs.

The reduction of $5,000 is for centrally furnished services from the "National Institutes of Health management fund".

Program Direction

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	36	$487,000	--	--	36	$487,000
Other expenses.....	--	154,000	--	-$1,000	--	153,000
Total.....	36	641,000	--	-1,000	36	640,000

The reduction of $1,000 is for centrally furnished services from the "National Institutes of Health management fund".

Division of Computer Research and Technology

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	112	$1,361,000	--	$-105,000	112	$1,256,000
Other expenses	--	3,392,000	--	-2,000	--	3,390,000
Total	112	4,753,000	--	-107,000	112	4,646,000

The reduction of $105,000 will eliminate the increase requested for the development of more powerful and efficient programming tools to exploit the new remote terminals and special purpose computer systems now being acquired by NIH laboratories.

The reduction of $2,000 represents the Division's decrease in payment to the "National Institutes of Health management fund" for centrally furnished services.

Engineering Development

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Collaborative research and development	--	$750,000	--	$-750,000	--	--
Program direction	2	226,000	-2	-226,000	--	--
Total obligations	2	976,000	-2	-976,000	--	--

The reduction of $976,000 will abolish the Division of Engineering Development.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Division of Research Facilities and Resources						
Review and approval of grants						
Scientist	1	GS-14	$16,946	...	.....	.....
Administrative staff assistant	1	GS-13	14,409	...	.....	.....
Secretary	2	GS-6	12,642	...	.....	.....
Total new positions	4		43,997			

Appropriation Estimate

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

For the John E. Fogarty International Center for Advanced Study in the Health Sciences,

[$3,460,000] $2,954,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center for
Advanced Study in the Health Sciences

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation...(total obligations)	$3,460,000	-$506,000	$2,954,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Operations:						
(a) Grants:						
(1) Research ...	...	$ 150,000	...	....	...	$ 150,000
(2) Fellowships...	...	1,570,000	...	-$503,000	...	1,067,000
(b) International center.....	58	1,740,000	-6	- 3,000	52	1,737,000
Facility planning and construction...	...	....	...	....	...	....
Total.....	58	3,460,000	-6	-506,000	52	2,954,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions.	58	-6	52
Full-time equivalent of all other positions.....	3	..	3
Average number of all employees.....	57	-2	55
Personnel compensation:			
Permanent positions.....	$ 680,000	...	$ 680,000
Positions other than permanent....	25,000	...	25,000
Other personnel compensation.....	2,000	...	2,000
Total, personnel compensation...	707,000	...	707,000
Personnel benefits.....	84,000	...	84,000
Travel and transportation of persons.....	228,000	...	228,000
Transportation of things.....	41,000	...	41,000
Rent, communications and utilities..	93,000	...	93,000
Printing and reproduction.....	68,000	...	68,000
Other services.....	309,000	-$3,000	306,000
Supplies and materials.....	74,000	...	74,000
Equipment.....	136,000	...	136,000
Grants, subsidies, and contributions.....	1,720,000	- 503,000	1,217,000
Total obligations by object.....	3,460,000	- 506,000	2,954,000

Summary of Changes

1970 obligations:

Original estimate	$3,460,000
Revised estimate	2,954,000
Net change	-506,000

	Original estimate Pos.	Original estimate Amt.	Amendment Pos.	Amendment Amt.
Decreases:				
A. Program:				
1. International center	58	$1,655,000	-6	....
2. Fellowships	...	1,570,000	...	-$503,000
B. Centrally furnished services from the "National Institutes of Health Management Fund"	...	85,000	...	-3,000
Total decreases	xxx	xxx	-6	-506,000
Net change	xxx	xxx	-6	-506,000

Explanation of Changes

1. Fellowships - Funds requested for the 1970 revised estimate will provide for 129 awards, compared to 183 in the 1970 original estimate, a decrease of 54.

2. International Center - The reduction of 6 positions will decrease the support of the scientific administration of the Scholars-in-Residence and the Fogarty International Center Conference Programs.

John E. Fogarty International Center for Advanced Study in the Health Sciences

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$ 500,000	$500,000	$725,000	$500,000
1969	600,000	600,000	600,000	600,000
1970 1/	2,954,000			

1/ Includes activities previously funded in the appropriation "General Research and Services, NIH".

Justification

John E. Fogarty International Center for
Advanced Study in the Health Sciences

	1970 original estimate		Amendment		1970 revised estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	58	$ 791,000	-6	....	52	$ 791,000
Other expenses.....	--	2,669,000	--	-$506,000	--	2,163,000
Total	58	3,460,000	-6	- 506,000	52	2,954,000

The decrease in 6 positions and $506,000 will reduce the International Postdoctoral Fellowship Program and planned expansion and development of the scholars-in residence and the Fogarty Center conference programs.

Fellowships

	1970 original estimate	Amendment	1970 revised estimate
International Postdoctoral Fellowships.....	$1,400,000	-$503,000	$ 897,000
Fogarty Scholarships.....	170,000	....	170,000
Total Fellowships.....	1,570,000	- 503,000	1,067,000

Funds requested for the 1970 revised estimate will provide for 113 awards, compared to 167 in the 1970 original estimate, a decrease of 54.

International Center

	1970 original estimate		Amendment		1970 revised estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	58	$ 791,000	-6	....	52	$ 791,000
Other expenses.....	..	949,000	..	-$3,000	..	946,000
Total	58	1,740,000	-6	- 3,000	52	1,737,000

The decrease in 6 positions will reduce planned expansion and development of the scholars-in-residence and the Fogarty Center conference programs. The request for funds for centrally furnished services from the "National Institutes of Health Management Fund" has been decreased $3,000.

New Positions Requested

Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
International Center	No.	Grade	Salary	No.	Grade	Salary
Deputy Director.....	1	GS-15	$19,780	...	...	...
Science Administrator.....	1	GS-15	19,780	...	...	...
Conference Manager.....	1	GS-12	12,174	...	...	...
Secretary.....	1	GS-6	6,321	...	...	...
Secretary.....	1	GS-5	5,732	...	...	...
Clerk-typist.....	1	GS-4	5,145	...	...	...
Total new positions..	6		68,932	...		...

Appropriation Estimate

HEALTH MANPOWER

To carry out, to the extent not otherwise provided, sections 301, 306, 309, and 311, titles VII, and title VIII of the Public Health Service Act, [$218,824,000] $218,021,000: Provided, That the amount available for scholarship grants to schools of nursing for the current fiscal year under such title VIII shall include, in addition to funds appropriated herein, funds appropriated for nursing educational opportunity grants for the fiscal year ending June 30, 1969, but not allotted to States for that fiscal year.

Loans, grants, and payments for the next succeeding fiscal year: For making, after March 31 of the current fiscal year, loans, grants, and payments under section 306, parts C, F, and G of title VII, and parts B and D of title VIII of the Public Health Service Act for the first quarter of the next succeeding fiscal year, such sums as may be necessary, and obligations incurred and expenditures made hereunder shall be charged to the appropriation for that purpose for such fiscal year: Provided, That such payments pursuant to this paragraph may not exceed 50 per centum of the amounts authorized in section 306, parts C and G of title VII, and part B of title VIII for these purposes for the next succeeding fiscal year.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Health Manpower

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation.....	$218,824,000	-$803,000	$218,021,000
Unobligated balance brought forward.....	1,000,000	---	1,000,000
Total available for obligation.1/	219,824,000	-803,000	219,021,000

1/ Excludes estimated obligations due to advance obligational authority.

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Institutional support:						
(a) Medical, dental, and related.....	---	$96,400,000	---	+$5,000,000	---	$101,400,000
(b) Nursing.....	---	7,000,000	---	---	---	7,000,000
(c) Public health.....	---	9,471,000	---	---	---	9,471,000
(d) Allied health professions.....	---	10,988,000	---	---	---	10,988,000
Student assistance:						
(a) Traineeships.....	---	20,670,000	---	---	---	20,670,000
(b) Scholarships.....	---	29,000,000	---	---	---	29,000,000
(c) Loans.....	---	29,610,000	---	-5,000,000	---	24,610,000
Manpower requirements and utilization:						
(a) Grants.....	---	4,425,000	---	-198,000	---	4,227,000
(b) Direct operations..	374	10,870,000	-10	-602,000	364	10,268,000
Program direction and management services....	85	1,390,000	---	-3,000	85	1,387,000
Total NOA available..	459	219,824,000	-10	-803,000	449	219,021,000

ADVANCE OBLIGATIONAL AUTHORITY

	1970 Original Estimate	Amendment	1970 Revised Estimate
NOA available	$219,824,000	-$803,000	$219,021,000
Appropriation available from subsequent year	88,800,000	---	88,800,000
Appropriation available in prior year	-63,160,000	+2,500,000	-60,660,000
Total obligations	245,464,000	+1,697,000	247,161,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	459	-10	449
Full-time equivalent of all other positions	43	-1	42
Average number of all employees	482	-10	472
Personnel compensation:			
Permanent positions	$5,124,200	-$112,200	$5,012,000
Positions other than permanent	343,900	-4,000	339,900
Other personnel compensation	26,000	---	26,000
Total personnel compensation	5,494,100	-116,200	5,377,900
Personnel benefits	497,600	-10,700	486,900
Travel and transportation of persons	590,800	-9,900	580,900
Transportation of things	43,500	---	43,500
Rent, communications, and utilities	270,100	-9,100	261,000
Printing and reproduction	159,700	-1,000	158,700
Other services	5,036,800	-445,000	4,591,800
Supplies and materials	102,300	-5,100	97,200
Equipment	65,100	-8,000	57,100
Investments and loans	30,500,000	-2,500,000	28,000,000
Grants, subsidies, and contributions	202,704,000	+4,802,000	207,506,000
Total obligations by object	245,464,000	+1,697,000	247,161,000

Summary of Changes

1970 obligations:

Original estimate	$219,824,000
Revised estimate	219,021,000
Net change 1/	-803,000

	Original Estimate		Amendment	
	Positions	Amount	Positions	Amount
Increases:				
A. Program				
1. Institutional support: Health professions educational improvement grants	---	$96,400,000	---	+$5,000,000
Decreases:				
A. Program				
1. Student assistance: Health professions student loans	---	20,000,000	---	-5,000,000
2. Manpower requirements and utilization:				
Research grants: Physician manpower	---	1,002,000	---	-100,000
Research training grants: Nursing	---	798,000	---	-98,000
Direct operations:				
Physician manpower	90	3,068,400	---	-273,000
Allied health manpower	53	1,444,600	---	-108,000
Health manpower educational services	73	2,017,000	-10	-211,000
B. Payment to "National Institutes of Health management fund" for centrally furnished services.	---	226,000	---	-13,000
Subtotal, decreases	---	---	-10	-5,803,000
Total net change requested	---	---	-10	-803,000

1/ Excludes advance obligational authority.

Explanation of Changes

Institutional support

Health professions educational improvement grants

The $5,000,000 increase is proposed to be added to special improvement grants specifically to accelerate enrollment in medical schools.

Decreases

Health professions student loans

The $5,000,000 decrease will reduce the number of students receiving loans by approximately 4,400, assuming the average amount loaned per student remains the same.

Research grants--Physician manpower

The $100,000 decrease is from noncompeting continuation costs.

Research training grants--Nursing

The $98,000 decrease is from noncompeting continuation costs.

Direct operations--Physician manpower

The $273,000 decrease is from increased continuation costs for contracts.

Direct operations--Allied health manpower

The $108,000 decrease is from increased continuation costs of contracts.

Direct operations--Health manpower educational services

The $211,000 decrease is from increased continuation costs of contracts of $51,000 and staff increases of ten positions and $160,000.

Health Manpower

	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1967	$750,000	$750,000	0	$500,000
1968 1/	160,630,000	154,528,000	$155,278,000	155,028,000
1969	186,227,000	172,176,000	172,176,000	172,176,000
1970	218,021,000			

1/ Excludes amounts for "Dental Health" which were carried as a part of this appropriation.

Justification

Health Manpower

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	459	$5,991,700	-10	-$126,900	449	$5,864,800
Other expenses	---	213,832,300	---	-676,100	---	213,156,200
Total (excludes advance obligational authority)	459	219,824,000	-10	-803,000	449	219,021,000

INSTITUTIONAL SUPPORT

	1970 Original Estimate	Amendment	1970 Revised Estimate
	Amount	Amount	Amount
Personnel compensation and benefits	---	---	---
Other expenses	$123,859,000	+$5,000,000	$128,859,000
Total	123,859,000	+5,000,000	128,859,000
Subactivities:			
Medical, dental and related:			
Health professions educational improvement grants	$96,400,000	+$5,000,000	$101,400,000
Nursing:			
Project grants for improvement of nurse training	7,000,000	---	7,000,000
Public health:			
Grants to schools of public health	4,554,000	---	4,554,000
Project grants for graduate public health training	4,917,000	---	4,917,000
Allied health professions:			
Educational improvement grants	9,750,000	---	9,750,000
New methods grants	1,238,000	---	1,238,000
Total	123,859,000	+5,000,000	128,859,000

Health Professions Educational Improvement Grants	1970 Original Estimate	Amendment	1970 Revised Estimate
Basic (formula)	$46,500,000	---	$46,500,000
Special	49,900,000	+$5,000,000	54,900,000
Total	96,400,000	+5,000,000	101,400,000

The shortages of physicians' services are clearly evident. Significant increases in output will require new support. Even the maintenance of current health manpower output is threatened by the limited financial resources of some medical schools. A number require substantial assistance. The Health Manpower Act of 1968 specifically authorizes assistance to such schools through the special project grant authority. These schools are not only under severe stress to increase their enrollments; at the same time they are under stress to accept more students from lower income families, to improve the quality of education, to develop teaching and training methods, and to provide more health services to the community. We must develop this additional health manpower if we are to improve the serious deficiency in delivery of health services that prevails today.

In responding to the public demand for comprehensive personal health care for everyone, the most specific issue requiring immediate action is that involving the need for a marked increase in the number of physicians being trained.

The amendment proposes that an additional $5,000,000 be added to special improvement grants specifically to accelerate enrollments in medical schools and that another $5,000,000 of the current request of $49,900,000 for special project grants in 1970 to assist schools of medicine, dentistry, osteopathy, optometry, podiatry, pharmacy, and veterinary medicine, be used to aid medical schools in their enrollment increases.

This $10,000,000 to assist medical schools to increase their enrollments through special improvement grants would be specifically available for a special "physicians augmentation program" which could make significant increases in enrollment in the fall of 1970 beyond expansions already planned by the schools. Grants will be awarded to schools of medicine and osteopathic medicine on the basis of merit, the priority being given to those projects which indicate the greatest potential for increasing enrollments. The merit of individual projects will be determined through the process of review which pertains to all special project grants and awarded on a competitive basis.

The institutions would be required to share in the costs of the increased enrollment as a condition for participation.

The past year has witnessed a new wave of interest in significantly expanding physician output. Both the Association of American Medical Colleges and the American Medical Association have endorsed the goal of increasing medical school enrollment to a level that permits all qualified students to be admitted.

A number of schools are making great efforts to maintain and increase enrollments. With financial help we feel that significant expansion of their first-year classes could take place in the fall of 1970. The additional numbers of physicians needed at this time exceed 50,000. In order to exploit the opportunities which these interests and efforts present, the additional resources requested would enable us to undertake an experimental program involving negotiations with individual medical schools which would, we believe, stimulate them to expand the entering freshman class by approximately 1,000 over the expansion presently planned of approximately 600.

STUDENT ASSISTANCE

	1970 Original Estimate Amount	Amendment Amount	1970 Revised Estimate Amount
Personnel compensation and benefits	---	---	---
Other expenses	$79,280,000	-$5,000,000	$74,280,000
Total	79,280,000	-5,000,000	74,280,000
Subactivities:			
Traineeships:			
Nurse fellowships	$650,000	---	$650,000
Nurse traineeships	10,470,000	---	10,470,000
Public health traineeships	8,000,000	---	8,000,000
Allied health traineeships	1,550,000	---	1,550,000
Scholarships:			
Nurse scholarships	13,000,000	---	13,000,000
Health professions scholarships	16,000,000	---	16,000,000
Loans:			
Health professions student loans	20,000,000	-5,000,000	15,000,000
Nursing student loans	9,610,000	---	9,610,000
Total	79,280,000	-5,000,000	74,280,000

	1970 Original Estimate	Amendment	1970 Revised Estimate
Health Professions Student Loans	$20,000,000	-$5,000,000	$15,000,000

The original request for fiscal year 1970 provided for loans averaging $1,146 to 18,416 students, 23 percent of estimated enrollments in 263 participating schools. More than half of these loans are to medical students. The reduction of $5,000,000 would lower the number of students receiving loans to 14,055 or about 18 percent of enrollment, assuming the average loan remains at $1,146.

It is expected that the students who will not be able to obtain a loan under this program will be primarily from families with higher income and will be able to obtain assistance through the Office of Education Guaranteed Loan Program.

MANPOWER REQUIREMENTS AND UTILIZATION

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	374	$14,774,700	-10	-$126,900	364	$14,647,800
Other expenses	---	10,520,300	---	-673,100	---	9,847,200
Total	374	15,295,000	-10	-800,000	364	14,495,000
Subactivities:						
Grants:						
Research grants:						
Physician manpower	---	$1,002,000	---	-$100,000	---	$902,000
Nursing	---	2,625,000	---	---	---	2,625,000
Research training grants:						
Nursing	---	798,000	---	-98,000	---	700,000
Direct operations:						
Physician manpower	90	3,113,000	---	-275,000	90	2,838,000
Nursing	148	4,248,000	---	-4,000	148	4,244,000
Allied health manpower	53	1,467,000	---	-110,000	53	1,357,000
Health manpower educational services	83	2,042,000	-10	-213,000	73	1,829,000
Total	374	15,295,000	-10	-800,000	364	14,495,000

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research Grants (Physician Manpower)	$1,002,000	-$100,000	$902,000

Funds requested for the 1970 revised estimate will exclude increases for noncompeting grant continuations. New and competing grant amounts are not affected.

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research Training Grants (Nursing)	$798,000	-$98,000	$700,000

Funds requested for the 1970 revised estimate will exclude increases for noncompeting grant continuations. New and competing grant amounts are not affected.

	1970 Original Estimate	Amendment	1970 Revised Estimate
Direct Operations (Physician Manpower)	$3,113,000	-$275,000	$2,838,000

The budget amendment reduces contract continuation increases by $273,000 in such areas as physician utilization, physician education, and continuing education. It also reduces the payment to the NIH management fund by $2,000.

	1970 Original Estimate	Amendment	1970 Revised Estimate
Direct Operations (Nursing)	$4,248,000	-$4,000	$4,244,000

The budget amendment reduces the payment to the NIH management fund by $4,000.

	1970 Original Estimate	Amendment	1970 Revised Estimate
Direct Operations (Allied Health)	$1,467,000	-$110,000	$1,357,000

The budget amendment reduces contract continuation increases by $108,000 in the areas of manpower supply and distribution, utilization, and recruitment. It also reduces the payment to the NIH management fund by $2,000.

	1970 Original Estimate	Amendment	1970 Revised Estimate
Direct Operations (Educational Services)	$2,042,000	-$213,000	$1,829,000

The budget amendment reduces contract continuation increases by $51,000 in the areas related to data collection and dissemination and maintains staff at the 1969 level by eliminating the requested ten positions and $160,000 for administration of grants and Intelligence System. It also reduces the payment to the NIH management fund by $2,000.

PROGRAM DIRECTION AND MANAGEMENT SERVICES

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	85	$1,217,000	---	---	85	$1,217,000
Other expenses.....	---	173,000	---	-$3,000	---	170,000
Total.....	85	1,390,000	---	-3,000	85	1,387,000

The budget amendment reduces the payment to the NIH management fund by $3,000.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
Health Manpower Educational Services	No.	Grade	Salary	No.	Grade	Salary
Public Health Program Specialist	2	GS-14	$33,892	---	---	---
Public Health Program Specialist	2	GS-13	28,818	---	---	---
Public Health Program Specialist	2	GS-12	24,348	---	---	---
Public Health Program Specialist	1	GS-11	10,203	---	---	---
Public Health Program Specialist	1	GS-9	8,462	---	---	---
Clerical Assistant	2	GS-6	12,642	---	---	---
Total new positions	10		118,365	---	---	---

Appropriation Estimate

DENTAL HEALTH

To carry out, to the extent not otherwise provided, sections 301 and 311 of the Public Health Service Act, and for training grants under section 422 of the Act, [$11,888,000] $10,887,000.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Dental Health

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$11,888,000	-$1,001,000	$10,887,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
1. Grants:						
(a) Research.....	---	$1,339,000	---	-$80,000	---	$1,259,000
(b) Fellowships..	---	150,000	---	---	---	150,000
(c) Training.....	---	5,276,000	---	-840,000	---	4,436,000
2. Direct operations	243	5,123,000	---	-81,000	243	5,042,000
Total NOA available.....	243	11,888,000	---	-1,001,000	243	10,887,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	243	---	243
Full-time equivalent of all other positions	20	---	20
Average number of all employees.	258	---	258
Personnel compensation:			
Permanent positions	$2,570,200	---	$2,570,200
Positions other than permanent	194,000	---	194,000
Other personnel compensation	4,000	---	4,000
Total personnel compensation	2,768,200	---	2,768,200
Personnel benefits	316,500	---	316,500
Travel and transportation of persons	200,500	---	200,500
Transportation of things	30,000	---	30,000
Rent, communications, and utilities	162,800	---	162,800
Printing and reproduction	67,000	---	67,000
Other services	1,423,000	-$81,000	1,342,000
Supplies and materials	94,000	---	94,000
Equipment	61,000	---	61,000
Grants, subsidies, and contributions	6,765,000	-920,000	5,845,000
Total obligations by object.	11,888,000	-1,001,000	10,887,000

Summary of Changes

1970 obligations:

Original estimate	$11,888,000
Revised estimate	10,887,000
Net change	-1,001,000

	Original Estimate Pos.	Original Estimate Amount	Amendment Pos.	Amendment Amount
Decreases				
A. Program:				
1. Research grants	---	$1,339,000	---	-$80,000
2. Dental auxiliary utilization grants	---	4,420,000	---	-740,000
3. Research training grants	---	556,000	---	-50,000
4. Continuing education	---	300,000	---	-50,000
5. Direct operations	243	5,055,000	---	-80,000
B. Payment to "National Institutes of Health management fund" for centrally furnished services	---	68,000	---	-1,000
Net change	---	---	---	-1,001,000

Explanation of Changes

Decreases

Research grants

This revised estimate will provide for support of approximately 40 research projects in 1970, the same number as in 1969 but at a reduced level.

Dental auxiliary utilization grants

This revised estimate will provide for the introduction of programs to train dental students in the use of auxiliaries in the three new schools which become eligible in 1970. In 1969, 49 dental school programs were supported.

Research training grants

This revised estimate will provide for continued support of five long-range graduate training programs at a reduced level.

Continuing education grants

This revised estimate will provide for support of six projects for upgrading the skills of dental practitioners in 1970. In 1969, five projects were supported.

Direct operations

This revised estimate will require reductions below the original estimate in studies relating to cleft lip and cleft palate and in dental care for children. The programs will operate at approximately the same level as in 1969.

Dental Health

	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1962	$2,182,000	$2,182,000	$2,500,000	$2,500,000
1963	2,506,000	2,506,000	3,006,000	3,006,000
1964	6,287,000	6,270,000	6,270,000	6,270,000
1965	6,719,000	6,708,000	7,228,000	7,228,000
1966	7,903,000	7,903,000	8,383,000	8,383,000
1967	9,196,000	9,193,000	9,693,000	9,693,000
1968 1/	9,783,000	9,635,000	9,635,000	9,635,000
1969	11,173,000	10,224,000	11,173,000	10,224,000
1970	10,887,000			

1/ Included in Health Manpower Appropriation in Fiscal Year 1968.

Justification
Dental Health

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	243	$3,084,700	---	---	243	$3,084,700
Other expenses.....	---	8,803,300	---	-1,001,000	---	7,802,300
Total.....	243	11,888,000	---	-1,001,000	243	10,887,000

Grants

	1970 Original Estimate	Amendment	1970 Revised Estimate
Research.....	$1,339,000	-$80,000	$1,259,000
Fellowships.....	150,000	---	150,000
Training.....	5,276,000	-840,000	4,436,000
Total.....	6,765,000	-920,000	5,845,000

Research Grants

1970 Original Estimate	Amendment	1970 Revised Estimate
$1,339,000	-$80,000	$1,259,000

Funds requested for the 1970 revised estimate will exclude increases for non-competing grant continuations. New and competing grant amounts are not affected.

Research Training Grants

1970 Original Estimate	Amendment	1970 Revised Estimate
$556,000	-$50,000	$506,000

The $50,000 reduction will curtail the development of the five long-range training programs now under way by changing the scope and plan of these projects.

Continuing Education Grants

1970 Original Estimate	Amendment	1970 Revised Estimate
$300,000	-$50,000	$250,000

The $50,000 reduction eliminates support for one of two additional projects to be funded in fiscal year 1970 which would contribute to up-grading skills of dental practitioners.

Dental Auxiliary Utilization Grants	1970 Original Estimate	Amendment	1970 Revised Estimate
	$4,420,000	-$740,000	$3,680,000

The reduction of $740,000 will maintain the DAU program at its present level in schools which now have them and will provide for the introduction of three new programs in fiscal year 1970 for the new schools that become eligible.

Expanded use of other types of auxiliaries such as dental hygienists and technicians in teaching dental students in the effective utilization of auxiliaries will be postponed.

The reduction will also not permit a planned increase in the hours of instruction for dental students in auxiliary utilization as a means of assuring that this experience will be incorporated into their practice after graduation.

Direct Operations	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	243	$3,084,700	---	---	243	$3,084,700
Other expenses.....	---	2,038,300	---	-$81,000	---	1,957,300
Total.....	243	5,123,000	---	- 81,000	243	5,042,000

Contract funds (1) to support the further analysis of epidemiologic data being obtained on cleft lip and cleft palate in twins and (2) for the expansion of a dental care project for children in a multi-county area will be reduced by $80,000. These studies are directed toward solving difficult and complex problems in dental diseases and care.

A reduction of $1,000 will be applied to the NIH management fund for centrally furnished services.

Appropriation Estimate

NATIONAL LIBRARY OF MEDICINE

To carry out, to the extent not otherwise provided for, section 301 with respect to health information communication, and part H of title III (relating to the National Library of Medicine) and part I of title III, of the Public Health Service Act, [$22,182,000] $19,682,000, of which [$1,950,000] $1,842,000 shall remain available until June 30, 1971.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation
(New Obligational Authority Basis)

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation	$22,182,000	-$2,500,000	$19,682,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Training	--	$1,000,000	--	$-17,000	--	$983,000
Special scientific projects	--	100,000	--	-95,000	--	5,000
Research	--	1,080,000	--	-490,000	--	590,000
Library resources	--	2,350,000	--	-245,000	--	2,105,000
Regional medical libraries	--	1,950,000	--	-108,000	--	1,842,000
Publications support	--	400,000	--	-133,000	--	267,000
Total, grants	--	6,880,000	--	-1,088,000	--	5,792,000
Direct operations:						
Library operations	264	7,193,000	-16	---	248	7,193,000
Toxicology information	20	1,628,000	-2	-100,000	18	1,528,000
National Medical Audio-visual Center	105	2,341,000	--	-212,000	105	2,129,000
Lister Hill National Center for Biomedical Communications	15	1,998,000	-4	-1,100,000	11	898,000
Review and approval of grants and contracts	33	594,000	--	---	33	594,000
Program direction	55	1,548,000	--	---	55	1,548,000
Total, direct operations	492	15,302,000	-22	-1,412,000	470	13,890,000
Total obligations	492	22,182,000	-22	-2,500,000	470	19,682,000

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation
(Total Obligational Authority Basis)

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation	$22,182,000	-$2,500,000	$19,682,000
Unobligated balance brought forward	700,000	...	700,000
Total obligations	22,882,000	-2,500,000	20,382,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Grants:						
Training	--	$1,000,000	--	$-17,000	--	$983,000
Special scientific projects	--	100,000	--	-95,000	--	5,000
Research	--	1,480,000	--	-490,000	--	990,000
Library resources	--	2,350,000	--	-245,000	--	2,105,000
Regional medical libraries	--	2,250,000	--	-108,000	--	2,142,000
Publications support	--	400,000	--	-133,000	--	267,000
Total, grants	--	7,580,000	--	-1,088,000	--	6,492,000
Direct operations:						
Library operations	264	7,193,000	-16	---	248	7,193,000
Toxicology information	20	1,628,000	-2	-100,000	18	1,528,000
National Medical Audio-visual Center	105	2,341,000	--	-212,000	105	2,129,000
Lister Hill National Center for Biomedical Communications	15	1,998,000	-4	-1,100,000	11	898,000
Review and approval of grants and contracts	33	594,000	--	---	33	594,000
Program direction	55	1,548,000	--	---	55	1,548,000
Total, direct operations	492	15,302,000	-22	-1,412,000	470	13,890,000
Total obligations	492	22,882,000	-22	-2,500,000	470	20,382,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions.....	492	-22	470
Full-time equivalent of all other positions.....	21	--	21
Average number of all employees.....	491	--	491
Personnel compensation:			
Permanent positions.....	$5,029,000	--	$5,029,000
Positions other than permanent.....	222,500	--	222,500
Other personnel compensation.....	85,000	--	85,000
Total personnel compensation...	5,336,500	--	5,336,500
Personnel benefits.....	404,200	--	404,200
Travel and transportation of persons.	173,300	--	173,300
Transportation of things.....	16,600	--	16,600
Rent, communications, and utilities..	1,637,500	--	1,637,500
Printing and reproduction.....	421,000	--	421,000
Other services.....	6,454,700	$-1,284,000	5,170,700
Supplies and materials.....	407,200	-56,000	351,200
Equipment.....	451,000	-72,000	379,000
Grants, subsidies, and contributions.	7,580,000	-1,088,000	6,492,000
Total obligations by object.....	22,882,000	-2,500,000	20,382,000

Summary of Changes
(New Obligational Authority Basis)

1970 Obligations:

Original estimate	$22,182,000
Revised estimate	19,682,000
Net change	-2,500,000

	Original estimate		Amendment	
	Positions	Amount	Positions	Amount
Increases				
A. Program				
1. Program direction	55	$1,117,000	--	+$30,000
Subtotal, increases	xxx	xxx	--	+30,000
Decreases				
A. Program				
1. Training grants	--	1,000,000	--	-17,000
2. Special scientific project grants	--	100,000	--	-95,000
3. Research grants	--	1,080,000	--	-490,000
4. Library resources grants	--	2,350,000	--	-245,000
5. Regional medical library grants	--	1,950,000	--	-108,000
6. Publications support grants	--	400,000	--	-133,000
7. Library operations (including MEDLARS II)	264	7,193,000	-16	---
8. Toxicology information program	20	1,628,000	-2	-100,000
9. National Medical Audiovisual Center	105	2,341,000	--	-212,000
10. Lister Hill National Center for Biomedical Communications	15	1,998,000	-4	-1,100,000
Subtotal, program decreases	xxx	xxx	-22	-2,500,000
B. Payments to the "National Institutes of Health Management Fund" for centrally furnished services	--	516,000	--	-30,000
Total decreases	xxx	xxx	-22	-2,530,000
Total net change	xxx	xxx	-22	-2,500,000

Summary of Changes
(Total Obligational Authority Basis)

1970 obligations:

Original estimate	$22,882,000
Revised estimate	20,382,000
Net change	-2,500,000

	Original estimate		Amendment	
	Positions	Amount	Positions	Amount
Increases				
A. Program				
1. Program direction	55	$1,117,000	--	+$30,000
Subtotal, increases	xxx	xxx	--	+30,000
Decreases				
A. Program				
1. Training grants	--	1,000,000	--	-17,000
2. Special scientific project grants	--	100,000	--	-95,000
3. Research grants	--	1,480,000	--	-490,000
4. Library resources grants	--	2,350,000	--	-245,000
5. Regional medical library grants	--	2,250,000	--	-108,000
6. Publications support grants	--	400,000	--	-133,000
7. Library operations (including MEDLARS II)	264	7,193,000	-16	---
8. Toxicology information program	20	1,628,000	-2	-100,000
9. National Medical Audiovisual Center	105	2,341,000	--	-212,000
10. Lister Hill National Center for Biomedical Communications	15	1,998,000	-4	-1,100,000
Subtotal, program decreases	xxx	xxx	-22	-2,500,000
B. Payments to the "National Institutes of Health Management Fund" for centrally furnished services	--	516,000	--	-30,000
Total decreases	xxx	xxx	-22	-2,530,000
Total net change	xxx	xxx	-22	-2,500,000

Explanation of Changes

Training Grants

The revised request for 1970 is $983,000, a decrease of $17,000 from the original request. The request will fund the 17 non-competing continuation grants at a reduced level. No new grants are projected in the original or revised request.

Special Scientific Project Grants

The request of $5,000 is $95,000 below the amount originally requested. The lower amount will permit reduced funding for one non-competing continuation grant and no funding for the one remaining non-competing continuation grant or the one new grant projected in the original request.

Research Grants

A decrease of $490,000 for a total amount of $990,000 will support the 26 non-competing continuation grants and provides no funding for eight new grants projected in the original request.

Library Resource Grants

The revised amount of $2,105,000 is $245,000 less than the original request. The revised level provides funding for the 390 non-competing continuation grants at a reduced level. Thirty-four new grants projected in the original request will go unfunded.

Regional Medical Library Grants

The original request of $2,250,000 is reduced to $2,142,000, a decrease of $108,000. No new grants were projected in the original estimate. The eight non-competing continuation projects will be funded at a reduced level.

Publications Support Grants

A decrease of $133,000 for a total amount of $267,000 will provide funding for the eight non-competing continuation grants but no funding for the six new grants projected in the original request.

Library Operations

A decrease of 16 positions and no dollars for a total of 248 positions and $7,193,000 is requested for Library Operations. A decrease of 12 positions relates to development of MEDLARS II while the remaining decrease of four relates to expanded reference and loan demands on the Library. While the number of new positions is reduced, the anticipated number of man-years remains the same. For this reason there is no corresponding reduction in the dollar amount requested.

Toxicology Information

A decrease of two positions and $100,000 for a total of 18 positions and $1,528,000 will provide reduced funding in 1970 for terminology development to provide standardized, precise descriptors for chemical compounds, and user studies to determine specific product needs of toxicologists and other potential users. The decreases for these efforts will result in some setback of the implementation schedule.

National Medical Audiovisual Center

A total of $2,129,000 and 105 positions is requested for this program, a reduction of $212,000 and no positions from the original request. The decrease eliminates the projected establishment of a Videotape Distribution Center that would have extended distribution activities to include television videotapes.

Lister Hill National Center for Biomedical Communications

The revised estimate is $898,000 and 11 positions, a decrease of $1,100,000 and four positions from the original request. Major effects of the decrease are elimination of funding in 1970 to (1) inter-net the Regional Medical Libraries, MEDLARS (bibliographic) search centers, and the the three National libraries; and (2) develop course materials and interconnect regional medical television networks. Support for the Lister Hill Center will be maintained at the 1969 level. The expansion of the Lister Hill National Center for Biomedical Communications will be deferred pending the development and approval of a long range plan for this program.

Program Direction

There is no net change in the dollar amount or number of positions requested for Program Direction. A projected reduction of $30,000 in the Library's payment to the NIH Management Fund is offset by an anticipated increase of this same amount in other objects to support activities which will not be centrally supported through the management fund.

Justification

National Library of Medicine

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	492	$5,740,700	470	$5,740,700	-22	---
Other expenses	--	17,141,300	--	14,641,300	--	$-2,500,000
Total	492	22,882,000	470	20,382,000	-22	-2,500,000

General Statement

The revised 1970 request of $20,382,000 and 470 positions is $2,500,000 and 22 positions below the original request. The revised request includes reductions of $1,088,000 in budget authority for Medical Library Assistance grants in 1970 and $1,412,000 for direct operations of the National Library of Medicine. In program terms the reduction will eliminate all of the 49 new grant awards previously planned in 1970 and will reduce the funding levels for 450 renewal awards an average of 2% in each of six categories of support. The amendment in direct operations will reduce the amount requested for the Lister Hill National Center for Biomedical Communications from $1,998,000 to $898,000, eliminating virtually all new project contract starts for biomedical communications network development in 1970. The National Medical Audiovisual Center's plan to develop a videotape distribution center in cooperation with the Veterans Administration will be eliminated with a reduction in the Center's 1970 request of $212,000. The Toxicology Information Program's further identification of user needs will be postponed with the reduction of $100,000. The effect of the decrease on specific programs is discussed below:

Training Grants

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	17	$1,000,000	17	$983,000	--	-$17,000
New grants	--	---	--	---	--	---
Total	17	1,000,000	17	983,000	--	-17,000

The revised request for 1970 is $983,000, a decrease of $17,000 from the original request. The 17 non-competing continuation grants will be funded at a lower level under the revised request. No new grants are projected in either the original or revised request.

Special Scientific Project Grants

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants.....	2	$50,000	1	$5,000	-1	-$45,000
New grants.....	1	50,000	--	---	-1	-50,000
Total.....	3	100,000	1	5,000	-2	-95,000

The request of $5,000 is $95,000 below the amount originally requested. One non-competing continuation grant will be funded at a lower level. The other non-competing continuation grant and the one new grant projected in the original request will not be funded.

Research Grants

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants.....	26	$948,000	26	$990,000	--	+$42,000
New grants.....	8	532,000	--	---	-8	-532,000
Total.....	34	1,480,000	26	990,000	-8	-490,000

The revised request of $990,000 is $490,000 below the original 1970 request. The revised amount provides funding for the 26 non-competing continuation grants but the eight new grants projected in the original request will not be funded. The average level at which the non-competing continuation grants will be funded increases slightly over the original estimate because later analysis shows that investigators are drawing upon more sophisticated methods, including computers.

Library Resources Grants

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants.....	390	$2,142,000	390	$2,105,000	--	$-37,000
New grants.....	34	208,000	--	---	-34	-208,000
Total.....	424	2,350,000	390	2,105,000	-34	-245,000

The revised amount of $2,105,000 is $245,000 less than the original request. The revised level provides funding for the 390 non-competing continuation grants and no funding for 34 new grants projected in the original request.

Regional Medical Libraries

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	8	$2,250,000	8	$2,142,000	--	-$108,000
New grants	--	---	--	---	--	---
Total	8	2,250,000	8	2,142,000	--	108,000

The original request of $2,250,000 is reduced to $2,142,000, a decrease of $108,000. No new grants were projected in the original estimate. The 8 non-competing continuation projects will be funded at a reduced level.

Publications Support

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	No. of Awards	Amount	No. of Awards	Amount	No. of Awards	Amount
Non-competing continuation grants	8	$225,000	8	$267,000	--	+$42,000
New grants	6	175,000	--	---	--	-175,000
Total	14	400,000	8	267,000	--	-133,000

The original request of $400,000 is reduced to $267,000, a decrease of $133,000. The revised estimate provides funding for the eight non-competing continuation grants but provides no funding for the six new grants projected in the original request. The funding level for the non-competing continuation grants is slightly higher than that of the original 1970 request because later information indicates that the continuation years of several will involve higher funding than the initial year.

Library Operations

	1970 Original Estimate		1970 Revised Revised		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	264	$2,933,400	248	$2,933,400	-16	---
Other expenses	--	4,259,600	---	4,259,600	--	---
Total	264	7,193,000	248	7,193,000	-16	---

The revised amount for Library Operations excludes all new positions for these activities in 1970. The original 1970 request included 12 new positions related to the development of a second-generation, computer-based Medical Literature Analysis and Retrieval System (MEDLARS II) and four new positions in other Library operations. The revised estimate excludes the 16 new positions but retains funds for the corresponding four man-years required to meet increased work loads in 1970. The increase in man-years without additional positions will be achieved through greater utilization of available positions.

Toxicology Information

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	20	$324,600	18	$324,600	-2	---
Other expenses	--	1,303,400	--	1,203,400	--	-$100,000
Total	20	1,628,000	20	1,528,000	-2	-100,000

The revised amount for the Toxicology Information Program provides for a decrease of $100,000 and two positions for a total of $1,528,000 and 18 positions. The revised amount will provide reduced funding for terminology development and user studies in 1970. The purpose of the terminology effort is to develop standardized, precise descriptors for chemical compounds while that of user studies is to determine the specific product needs of potential users. The decreases for these tasks will result in some deferal in development and implementation of a toxicology information storage and retrieval system that will provide the potential manufacturer of a food or drug, the regulatory agency which must determine whether it is safe for marketing, the environmental scientist, and other interested researchers with access to all existing research upon the effect of a given chemical compound.

National Medical Audiovisual Center

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	105	$1,194,100	105	$1,194,100	--	---
Other expenses	--	1,146,900	--	934,900	--	-$212,000
Total	105	2,341,000	105	2,129,000	--	-212,000

The revised request for the National Medical Audiovisual Center is $2,129,000 and 105 positions, a decrease of $212,000 and no positions from the original request. The Center produces, stores, and distributes various types of audiovisuals to doctors, other health specialists, and the general population. The decrease eliminates the projected establishment of a Videotape Distribution Center that would have extended distribution activities to include television videotapes.

Lister Hill National Center for Biomedical Communications

	1970 Original Estimate		1970 Revised Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	15	$214,700	11	$214,700	-4	---
Other expenses	--	1,783,300	--	683,300	--	-1,100,000
Total	15	1,998,000	11	898,000	-4	-1,100,000

The revised estimate is $898,000 and 11 positions, a decrease of $1,100,000 and four positions from the original request. Support for the Lister Hill Center will be maintained at the 1969 level. Expansion will be deferred pending the development and approval of a long range plan for this program. Major effects of the decrease are elimination of funding in 1970 to (1) inter-net the Regional Medical Libraries, MEDLARS (bibliographic) search centers, and the three National libraries; and (2) develop course materials and interconnect regional medical television networks with the aim of improving continuing medical education.

National Library of Medicine

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$1,566,000	$1,566,000	$1,566,000	$1,566,000
1961	1,738,000	1,738,000	1,738,000	1,738,000
1962	2,066,000	2,066,000	2,066,000	2,066,000
1963	3,335,000	3,335,000	3,335,000	3,335,000
1964	4,074,000	4,074,000	4,074,000	4,074,000
1965	3,678,000	3,858,000	4,058,000	3,958,000
1966	9,185,000	9,185,000	9,685,000	9,685,000
1967	19,231,000	20,092,000	20,192,000	20,192,000
1968	21,162,000	18,662,000	21,162,000	19,912,000
1969	19,172,000	17,149,000	19,172,000	18,160,500
1970	19,682,000			

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Library Operations						
Public Health Program Specialist	2	GS-15	$39,560	--	---	---
Deputy Chief of Office.....	1	GS-15	19,780	--	---	---
Chief of Division.....	1	GS-15	19,780	--	---	---
Systems Analyst.....	2	GS-14	33,892	--	---	---
Systems Analyst.....	3	GS-13	43,227	--	---	---
Public Health Program Specialist	1	GS-12	12,174	--	---	---
Programmer.....	2	GS-12	24,348	--	---	---
Programmer.....	2	GS-11	20,406	--	---	---
Public Health Program Specialist	1	GS-9	8,462	--	---	---
Secretary.....	1	GS-5	5,732	--	---	---
	16		227,361	--		---
Toxicology Information						
Chief of Section.....	1	GS-15	19,780	--	---	---
Public Health Program Specialist	1	GS-13	14,409	--	---	---
	2		34,189	--		---
Lister Hill National Center for Biomedical Communications						
Director of Division.....	2	GS-15	39,560	--	---	---
Administrative Officer.....	1	GS-13	14,409	--	---	---
Secretary.....	1	GS-6	6,321	--	---	---
	4		60,290	--		---
Total, new positions.....	22		321,840	--		---

Appropriation Estimate

BUILDINGS AND FACILITIES

For construction, major repair, improvement, extension, alteration, and equipment, including acquisition of sites, of facilities of or used by the National Institutes of Health, where not otherwise provided; [$4,400,000] $1,000,000, to remain available until expended.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation	$4,400,000	$-3,400,000	$1,000,000
Unobligated balance brought forward	9,505,000	---	9,505,000
Unobligated balance transferred to: "Buildings and Facilities", Health Services and Mental Health Administration	-2,953,000	---	-2,953,000
"Buildings and Facilities", Consumer Protection and Environmental Health Service	-3,777,000	---	-3,777,000
Unobligated balance carried forward	-501,000	+301,000	-200,000
Total Obligations	6,674,000	-3,099,000	3,575,000

Obligations by Activity

Description	1970 Original Estimate	Amendment	1970 Revised Estimate
Combined Services Facility and Warehouse	$ 150,000	$ ---	$ 150,000
Dental Health Center Addition	1,500,000	-1,500,000	---
Expansion of Clinical Center Facilities	154,000	---	154,000
Incinerator Facility	105,000	---	105,000
Lister Hill National Center for Biomedical Communications	900,000	-900,000	---
Master Utilities Extension	1,300,000	-199,000	1,101,000
Multilevel Parking - Additional, Bldg. 31	6,000	---	6,000
National Environmental Health Sciences Center	1,300,000	---	1,300,000
Neurology-Allergy Virus Research Facility	500,000	-500,000	---
NIH Animal Center	207,000	---	207,000
Repairs and Improvements	552,000	---	552,000
Total Obligations	6,674,000	-3,099,000	3,575,000

Obligations by Object

Description	1970 Original Estimate	Amendment	1970 Revised Estimate
NATIONAL INSTITUTES OF HEALTH			
Travel and transportation of persons	$ 10,000	$ ---	$ 10,000
Printing and reproduction	5,000	---	5,000
Other services	1,915,000	---	1,915,000
Equipment	154,000	---	154,000
Lands and structures	105,000	---	105,000
Total, National Institutes of Health	2,189,000	---	2,189,000
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
Travel and transportation of persons	4,000	---	4,000
Printing and reproduction	27,000	---	27,000
Other services	1,500,000	-1,300,000	200,000
Equipment	1,500,000	-1,500,000	---
Lands and structures	1,454,000	-299,000	1,155,000
Total, General Services Administration	4,485,000	-3,099,000	1,386,000
Total obligations	6,674,000	-3,099,000	3,575,000

Summary of Changes

1970 appropriation:

Original estimate	$4,400,000
Revised estimate	1,000,000
Net change	-3,400,000

	Original Estimate	Amendment
Decreases		
A. Program		
1. Dental health center addition - equipment	$1,500,000	-$1,500,000
2. Lister Hill national center for biomedical communications - planning	900,000	-900,000
3. Master utilities extension	1,000,000	-500,000
4. Neurology-allergy virus research facility	500,000	-500,000
5. Repairs and improvements	500,000	---
Net change	xxx	- 3,400,000

Buildings and Facilities

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1961 [1]	$3,135,000	$3,135,000	$3,470,000	$3,470,000
1962	21,745,000	18,230,000 [2]	18,230,000	18,230,000
1963	29,761,000	31,000,000	33,200,000	33,200,000
1964	19,072,000	13,811,000	16,311,000	16,311,000
1965	21,512,000	21,512,000	23,012,000	22,512,000
1966	7,781,000	9,431,000	8,977,000	8,977,000
1967	18,279,000	18,279,000	18,279,000	18,279,000
1968	10,715,000	10,715,000	15,075,000	10,715,000
1969	12,495,000	---	5,310,000	---
1970 [3]	1,000,000			

[1] Prior to 1961 direct construction funds were appropriated on an individual project basis.

[2] Supplemental of $3,515,000 not considered by the House.

[3] Prior to 1970 this appropriation also included direct construction funds for other Public Health Service programs.

Introduction

This appropriation includes all proposed direct construction items of the National Institutes of Health and all continuing projects except the Mental Health-Neurology Research Facility, which was appropriated under "Mental Health Activities" and "Neurology and Blindness Activities" in 1961, and the John E. Fogarty International Center for Advanced Study in the Health Sciences, for which planning funds were appropriated in 1968 under "John E. Fogarty International Center for Advanced Study in the Health Sciences".

Dental Health Center Addition - Equipment

	1970 Original Estimate	Amendment	1970 Revised Estimate
1970 appropriation	$1,500,000	-$1,500,000	$ ---

Planning and construction funds totaling $2,808,000 were appropriated in 1966 and 1968 respectively, for the construction of a wing to the Dental Health Center in San Francisco, California. The reduction of funds in the 1970 original estimate of $1,500,000 will eliminate the procurement of a portion of the specialized equipment and fixtures for the dental clinical and laboratory space and for television and other audiovisual equipment for experimental teaching areas.

Lister Hill National Center for Biomedical Communications - Planning

	1970 Original Estimate	Amendment	1970 Revised Estimate
1970 appropriation	$900,000	-$900,000	$ ---

The reduction of $900,000 in the 1970 original estimate will eliminate the planning funds for the Lister Hill National Center for Biomedical Communications, an annex to the present National Library of Medicine facility.

Neurology - Allergy Virus Research Facility - Planning

	1970 Original Estimate	Amendment	1970 Revised Estimate
1970 appropriation	$ 500,000	-$500,000	$ ---

The reduction of $500,000 in the 1970 original estimate will eliminate the planning funds for a virus research facility to be used jointly by the National Institute of Neurological Diseases and Stroke and the National Institute of Allergy and Infectious Diseases.

Master Utilities Extension - Design and Construction

	1970 Original Estimate	Amendment	1970 Revised Estimate
1970 appropriation	$1,000,000	-$500,000	$500,000

The reduction of $500,000 in the 1970 original estimate will eliminate design funds for extending the master utilities system to serve buildings now in the planning stage.

Appropriation Estimate

Salaries and Expenses, Office of the Director

For expenses necessary for the Office of the Director, National Institutes of Health, [$7,193,000.] $7,093,000

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

Salaries and Expenses, Office of the Director

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (Total obligations)	$7,193,000	-$100,000	$7,093,000

Obligations by activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Management and central services	467	$7,193,000	-7	-$100,000	460	$7,093,000
Total obligations	467	7,193,000	-7	-100,000	460	7,093,000

Obligations by object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions...	467	-7	460
Full-time equivalent of all other positions.....	15	...	15
Average number of all employees.....	467	-10	457
Personnel compensation:			
Permanent positions.....	$4,917,000	-$81,000	$4,836,000
Positions other than permanent.....	105,000	.....	105,000
Other personnel compensation.....	84,000	.....	84,000
Total personnel compensation.....	5,106,000	-81,000	5,025,000
Personnel benefits.....	413,000	-9,000	404,000
Travel and transportation of persons	102,000	.....	102,000
Transportation of things.....	8,000	.....	8,000
Rent, communications and utilities..	112,000	.....	112,000
Printing and reproduction.....	180,000	.....	180,000
Other services.....	1,086,000	-3,000	1,083,000
Supplies and materials.....	103,000	-2,000	101,000
Equipment.....	88,000	-5,000	83,000
Subtotal.....	7,198,000	-100,000	7,098,000
Quarters and subsistence.....	-5,000	.....	-5,000
Total obligations by object.....	7,193,000	-100,000	7,093,000

Summary of Changes

1970 obligations:

Original estimate	$7,193,000
Revised estimate	7,093,000
Net change	-100,000

	Original estimate Pos.	Original estimate Amount	Amendment Pos.	Amendment Amount
Decreases:				
A. Management and central services	467	$7,193,000	-7	-$100,000
Net change	xxx	xxx	-7	-100,000

Explanation of Changes

The reduction of $100,000 will eliminate seven positions for strengthening planning and analysis of NIH programs and reduce man-year support in the financial and personnel areas.

Salaries and Expenses, Office of the Director

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$7,093,000 1/			

1/ Included in the appropriations of the various Institutes and Divisions of NIH prior to 1970.

Justification

Salaries and Expenses, Office of the Director

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits.....	467	$5,514,000	-7	-$90,000	460	$5,424,000
Other expenses.....	...	1,679,000	...	-10,000	...	1,669,000
Total.....	467	7,193,000	-7	-100,000	460	7,093,000

Management and Central Services

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Direction.....	132	$2,531,000	-7	-$67,000	125	$2,464,000
Supporting Management Services.....	335	4,662,000	...	-33,000	335	4,629,000
Total.....	467	7,193,000	-7	-100,000	460	7,093,000

Program direction: The decrease will eliminate seven positions and $67,000 for strengthening the Director's staff for analyzing program progress, developing policy positions, and evaluating trends in the availability of resources to support NIH programs.

Supporting management services: The decrease of $33,000 will reduce man-year support in the financial and personnel areas.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Management and central services						
Scientist administrator.....	1	GS-15	$19,780	...	...	...
Program analyst.....	1	GS-13	14,409	...	...	...
Program analyst.....	1	GS-12	12,174	...	...	...
Program analyst.....	1	GS-11	10,203	...	...	...
Programmer.....	1	GS-9	8,462	...	...	...
Secretary.....	1	GS-6	6,321	...	...	...
Secretary.....	1	GS-5	5,732	...	...	...
Total new positions....	7		77,081	...		...

Appropriation Estimate

GENERAL RESEARCH SUPPORT GRANTS

For general research support grants, as authorized in section 301(d) of the Public Health Service Act, there shall be available from appropriations available to the National Institutes of Health and the appropriation to the Health Services and Mental Health Administration for "Mental health", the sum of [$61,500,000] $60,700,000: Provided, That none of these funds shall be used to pay a recipient of such a grant any amount for indirect expenses in connection with such project.

29-867 O—69—pt. 4——87

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

General Research Support Grants

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation (total obligations)	**$61,500,000**	**$-800,000**	$60,700,000

Obligations by Activity

	1970 Original Estimate	Amendment	1970 Revised Estimate
Grants:			
(a) Traditional general research support	$49,000,000	-$800,000	$48,200,000
(b) Biomedical sciences support.	7,500,000	---	7,500,000
(c) Health sciences advancement awards	5,000,000	---	5,000,000
Total obligations	61,500,000	-800,000	60,700,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Grants, subsidies, and contributions (total obligations)	$61,500,000	-$800,000	$60,700,000

Summary of Changes

1970 obligations:

Original estimate	$61,500,000
Revised Estimate	60,700,000
Net change	-800,000

A. Decrease:

	Original Estimate	Amendment
1. Traditional general research support	$61,500,000	-800,000

Explanation of Change

Funds requested for the 1970 revised estimate will provide traditional general research support awards to some 344 eligible institutions, the same number as in the 1970 origional estimate at however reduced amounts.

General Research Support Grants

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1962	$14,500,000	$16,000,000	$20,000,000	$20,000,000
1963	30,000,000	30,000,000	30,000,000	30,000,000
1964	30,000,000	30,000,000	30,000,000	30,000,000
1965	40,000,000	40,000,000	45,000,000	45,000,000
1966	45,200,000	45,200,000	50,000,000	45,200,000
1967	51,700,000	51,700,000	51,700,000	51,700,000
1968	61,700,000	61,700,000	75,000,000	61,700,000
1969	60,700,000	60,700,000	60,700,000	60,700,000
1970	60,700,000			

Distribution of Funds by Program Area in 1970

The requested amount of $60,700,000 would be distributed as follows: $48,200,000 for the General Research Support to approximately 344 institutions; $7,500,000 for Biomedical Sciences Support Grants to approximately 115 institutions; and $5,000,000 for Health Sciences Advancement Awards to approximately 12 institutions.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institutes of Health Management Fund

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Advances and Reimbursements from:			
Formula advances -- NIH appropriation	$42,425,000	$-567,000	$41,858,000
Non-formula receipts:			
NIH appropriation	463,000	--	463,000
Other Federal sources	7,645,000	--	7,645,000
Total	50,533,000	-567,000	49,966,000

Obligations by Activity

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Reimbursable obligations:						
Research services	928	15,181,000	-6	-128,000	922	$15,053,000
Clinical services	1,579	19,483,000	-5	-182,000	1,574	19,301,000
Administrative management	733	7,475,000	-9	-215,000	724	7,260,000
Grant Review and approval	538	8,394,000	-3	-42,000	535	8,352,000
Total obligations	3,778	50,533,000	-23	-567,000	3,755	49,966,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Total number of permanent positions	3,778	-23	3,755
Full-time equivalent of all other positions	145	--	145
Average number of all employees	3,807	-17	3,790
Personnel compensation:			
Permanent positions	$30,601,000	$-119,000	$30,482,000
Positions other than permanent	994,000	--	994,000
Other personnel compensation	1,473,000	-1,000	1,472,000
Total personnel compensation	33,068,000	-120,000	32,948,000
Personnel benefits	2,950,000	-11,000	2,939,000
Travel and transportation of persons	411,000	-7,000	404,000
Transportation of things	54,000	--	54,000
Rent, communications, and utilities	3,085,000	-19,000	3,066,000
Printing and reproduction	535,000	-29,000	506,000
Other services	4,092,000	-38,000	4,054,000
Supplies and materials	4,910,000	-133,000	4,777,000
Equipment	1,468,000	-210,000	1,258,000
Quarters and subsistence charges	-40,000	--	-40,000
Total obligations by object	50,533,000	-567,000	49,966,000

Summary of Changes

1970 obligations

Original estimate	$50,533,000
Revised estimate	49,966,000
Net change	-567,000

	Original Estimate		Amendment	
	Pos.	Amount	Pos.	Amount
Decreases				
A. Program:				
1. Research services	928	$15,181,000	-6	$-128,000
2. Clinical services	1,579	19,483,000	-5	-182,000
3. Administrative management	733	7,475,000	-9	-215,000
4. Grant Review and approval	538	8,394,000	-3	-42,000
Net change	xxx	xxx	-23	-567,000

Explanation of Changes

Research services -- The reduction of the original 1970 estimate of six positions and $128,000 will reduce the staff and funds for the maintenance and operation of two new facilities to be completed during 1969 and for increased costs of ongoing support.

Clinical services -- The funds requested in the 1970 revised estimates is a decrease of 5 positions and $182,000 compared to the original 1970 estimate and will retain the program at the 1969 level.

Administrative management -- The decrease will eliminate nine positions and $215,000 for servicing facilities, managing research contract workloads, equipment for implementation of the Metcalf and Eddy study for waste handling and refuse collection, and the replacement of passenger carrying vehicles. The decrease will also eliminate replacement of material handling and warehouse equipment, increases for data processing, printing, communications and supplies.

Grant Review and Approval -- The funds requested in the 1970 revised estimate is a decrease of 3 positions and $42,000 compared to the original 1970 estimate and will retain the program at the 1969 level.

Research Services

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	928	$9,273,000	-6	$-43,000	922	$9,230,000
Other expenses	--	5,908,000	--	-85,000	--	5,823,000
Total	928	15,181,000	-6	-128,000	922	15,053,000

Introduction

The reduction of 6 positions and $128,000 will permit the maintenance of the 1969 level of operation, reducing the original 1970 request for the staff to operate and maintain the new facilities which will be completed during 1969 and funds to provide for increased utility services. Both the General Office Building Extension and the Isotope Laboratory Addition will be completed during the latter part of 1969.

Clinical Services

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	1,579	14,917,000	-5	-36,000	1,574	14,881,000
Other expenses	--	4,566,000	--	-146,000	--	4,420,000
Total	1,579	19,483,000	-5	-182,000	1,574	19,301,000

Introduction

The reduction of 5 positions and $182,000 will require reduction in services provided to the various institutes and allow only minimum required coverage in servicing new facilities. In addition, the increasing cost of supplies, maintenance service, and equipment will require further reduction in services provided.

Administrative Management

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	733	$5,721,000	-9	$-42,000	724	$5,679,000
Other expenses	--	1,754,000	--	-173,000	--	1,581,000
Total	733	7,475,000	-9	-215,000	724	7,260,000

Introduction

The revision will eliminate nine positions and $215,000 for servicing new buildings, managing research contract workloads, replacement of vehicles and the procurement of additional trucks for refuse handling. The revision will also eliminate replacement of worn-out equipment, the increases for equipment repair, communications, printing, supplies and data processing.

Grant Review and Approval

	1970 Original Estimate		Amendment		1970 Revised Estimate	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Personnel compensation and benefits	538	$6,067,000	-3	$-21,000	535	$6,046,000
Other expenses	--	2,327,000	--	-21,000	--	2,306,000
Total	538	8,394,000	-3	-42,000	535	8,352,000

Introduction

Funds requested for the 1970 revised estimate will provide for continued grant review and approval services of the Division. Compared to the 1970 original estimate, the revision eliminates three proposed additional positions and $42,000 which were to provide for the further development of the data system and scientific evaluation of research data.

New Positions Requested
Fiscal Year 1970

	1970 Original Estimate			1970 Revised Estimate		
	No.	Grade	Salary	No.	Grade	Salary
Research Services						
Fixed industrial equipment operator	6	WG-10	$44,304	--	--	--
Total	6	--	44,304	--	--	--
Clinical Services						
Scientist	1	GS-9	10,154	--	--	--
Medical staff assistant	1	GS-6	6,955	--	--	--
Medical staff assistant	1	GS-5	6,690	--	--	--
Clerical assistant	1	GS-4	5,145	--	--	--
Clerical assistant	1	GS-3	4,600	--	--	--
Total	5	--	33,544	--	--	--
Administrative Management						
Contract negotiator	1	GS-12	12,174	--	--	--
Contract negotiator	1	GS-11	10,203	--	--	--
Clerk-stenographer	1	GS-5	5,732	--	--	--
Guard	3	GS-3	13,800	--	--	--
Mail clerk	1	GS-2	4,231	--	--	--
Medium truck driver	1	WB-06	6,302	--	--	--
Laborer	1	WB-03	5,678	--	--	--
Total	9	--	58,120	--	--	--
Grant Review and Approval						
Research scientists	2	GS-13	28,818	--	--	--
Program analyst	1	GS-11	10,203	--	--	--
Total	3	--	39,021	--	--	--
Total new positions, all activities	23	--	174,989	--	--	--

Appropriation Estimate

SCIENTIFIC ACTIVITIES OVERSEAS (SPECIAL FOREIGN CURRENCY PROGRAM)

For payments in foreign currencies which the Treasury Department determines to be excess to the normal requirements of the United States, for necessary expenses for conducting scientific activities overseas, as authorized by law, /~~$15,322,000~~/ $3,455,000, to remain available until expended: Provided, That this appropriation shall be available, in addition to other appropriations for such activities, for payments in the foregoing currencies.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Scientific Activities Overseas (Special Foreign Currency Program)

Amounts Available for Obligation

	1970 Original Estimate	Amendment	1970 Revised Estimate
Appropriation	$15,322,000	-$11,867,000	$3,455,000
Unobligated balance brought forward	...	...	...
Total obligations	15,322,000	-11,867,000	3,455,000

Obligations by Activity

	1970 Original Estimate	Amendment	1970 Revised Estimate
Foreign health research	$15,322,000	-$11,867,000	$3,455,000

Obligations by Object

	1970 Original Estimate	Amendment	1970 Revised Estimate
Travel and transportation of persons	$400,000	-$280,000	$120,000
Other services:			
Project contracts	14,522,000	-11,287,000	3,235,000
Grants, subsidies and contributions	400,000	-300,000	100,000
Total obligations by object	15,322,000	-11,867,000	3,455,000

Summary of Changes

1970 obligations:

Original estimate	$15,322,000
Revised estimate	3,455,000
Net change	-11,867,000

	1970 Original Estimate	Amendment	1970 Revised Estimate
A. Increases:			
1. Program			
(a) National Institutes of Health	$7,200,000	-$5,578,000	$1,622,000
(b) Health Services and Mental Health Administration	6,741,000	-5,221,000	1,520,000
(c) Consumer Protection and Environmental Health Service	1,376,000	-1,066,000	310,000
(d) Office of International Health	5,000	-2,000	3,000
Total program increases	15,322,000	-11,867,000	3,455,000
B. Decreases:			
1. Nonrecurring program cost prior year	-17,460,000	...	-17,460,000
Net change	-2,138,000	-11,867,000	-14,005,000

Explanation of Changes

Due to the severely constrained budget under which the Department will be operating in 1970, the P.L. 480 appropriation has been amended to provide excess foreign currencies equivalent to $3,455,000.

Scientific Activities Overseas (Special Foreign Currency Program)

The budget amendment reduces the pending estimate for the Scientific Activities Overseas Appropriation for FY 1970 by an amount equivalent to $11,867,000. The excess foreign currencies provided, equivalent to $3,455,000, represent a reduction of $14,005,000 below the amount available for the program in FY 1969. The effects this amendment has on the programs that the three agencies of the Public Health Service planned under the original appropriation estimate are as follows:

National Institutes of Health (NIH)

The 5,578,000 dollar equivalent reduction in the NIH program will limit support of the SEATO-Cholera Laboratory to one year instead of three and will permit support of only 2 or 3 of the 21 projects planned under the original FY 1970 budget estimate. These will be selected from the program areas of cancer, dental, cardiovascular, sensory and infectious diseases, nutrition, metabolism, and population research and from information exchange activities (translating and abstracting).

Health Services and Mental Health Administration (HSMHA)

The amendment reduces the original estimate by 5,221,000 dollar equivalents. The overall HSMHA program will be reduced by approximately 80%. The funds provided will be allocated according to priority among the major areas of family planning, nutrition, health services, and communicable disease research and the International Fellowship Program.

Consumer Protection and Environmental Health Services (CPEHS)

The reduction of 1,066,000 dollar equivalents in foreign currencies from the original budget estimate for the CPEHS program will eliminate all planned projects in the program areas of toxicity and pharmacology studies of drugs and chemical agents such as pesticides and mycotoxins; epidemiological investigation of pesticides; environmental stress studies on urban populations; studies on the accoustical and behaviorial impact of industrial and urban noise; research concerning air pollution abatement; and studies of carcinogenic potential and other undesirable side effects of oral contraceptives. Only the existing program for translating air pollution research and technology literature can be supported under the revised budget estimate.

A summary of estimated obligations by country follows:

	1970 Original Estimate	Amendment	1970 Revised Estimate
Ceylon	125,000	-125,000	...
Guinea	439,000	-439,000	...
India	4,086,400	-3,453,550	632,850
Israel	...	...	...
Morocco	431,000	-431,000	...
Pakistan	2,941,000	-1,984,550	956,450
Poland	2,251,400	-1,767,700	483,700
Tunisia	536,000	-415,000	121,000
U.A.R. (Egypt)	471,000	-367,000	104,000
Yugoslavia	4,041,200	-2,884,200	1,157,000
Total	15,322,000	-11,867,000	3,455,000

Scientific Activities Overseas (Special Foreign Currency Program)

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1960	$3,707,000	N.C.	0	0
1961	3,707,000	$3,707,000	$3,707,000	$3,707,000
1962	10,084,000	8,000,000	10,084,000	9,000,000
1963	2,800,000	2,800,000	2,800,000	2,800,000
1964	6,647,000	4,000,000	4,000,000	4,000,000
1965	1,000,000	1,000,000	1,000,000	1,000,000
1966	6,000,000	6,000,000	5,000,000	5,000,000
1967	19,217,000	19,217,000	10,000,000	10,000,000
1968	18,685,000	15,000,000	15,000,000	15,000,000
1969	30,000,000	15,000,000	15,000,000	15,000,000
1970	3,455,000			

LIST OF WITNESSES

	Page
Akers, Mrs. E. L	725
Baldwin, C. B., Jr	821
Baylis, W. G	436
Berliner, Dr. R. W	1, 887, 1163
Berquist, B. G	1225
Boettner, Dr. C. H	966
Bowery, Dr. T. G	887, 1099
Bramlet, R. H	766
Browning, E. L	198
Brust, G. A	177
Cardwell J. B	1, 177, 198, 309, 436, 535, 614, 657, 725, 766, 821, 887, 928, 966, 1099, 1127, 1163, 1184, 1225
Christoferson, H. C	385
Cooper, D. T	309
Cummings, Dr. M. M	1, 1127, 1163
Cyphers, D. F	436
Davis, Dr. D. J	657, 1127
Diefenbach, Dr. V. L	966, 1099
Eagles, Dr. E. L	535, 614
Ehrlich, Dr. S. P., Jr	1198
Eipf	614
Endicott, Dr. K. M	198
Fenninger, Dr. L. D	1, 887, 966, 1099, 1225
Fuller, M. J., Jr	657
Gallagher, Dr. J. A	966, 1099
Gehrig, Dr. L. J	1198
Grainger, Dr. R. M	385
Greulich, Dr. R. C	385
Grubbs, Mrs. E	177
Hambleton, J. W	887, 966, 1099, 1225
Hatch, T. D	966, 1099
Henschel, R. H	309
Holliday, R	1163
Hubscher, E. M	821
Kefauver	1099, 1127
Kennedy, Dr. T. J., Jr	1, 1184
Kingman, G. M	766
Klovdahl, G. J	725
Kotin, Dr. P	766
Kreshover, Dr. S. J	385
Lamont-Havers, Dr. R	1
LaVeck, Dr. G. D	821
Learmouth, R. E	198
Leavitt, Dr. M. D., Jr	928
Leroy, Dr. V	1163
MacNichol, Dr. E. F., Jr	535, 614
Magruder, W. H	657
Marston, Dr. R. Q	177, 198, 309, 385, 436, 535, 614, 657, 725, 766, 821, 887, 928, 966, 1099, 1127, 1184, 1225
May, L. B	1, 535, 614, 657, 725, 766, 821, 928, 966, 1099

Page

McKee, Dr. F. W---- 966, 1099
Murray, Dr. R---- 177
Pratt, Dr. A. W---- 887
Presson, G. E---- 928
Reeder, J---- 309
Russell, G. F., Jr---- 1127
Scott, Miss J---- 966, 1099
Seal, Dr. J. R---- 657
Seggel, R. L---- 1, 887, 1163, 1184
Sherman, Dr. J. F---- 1, 1184
Sharkey, J. E---- 1, 177, 198,
309, 436, 535, 614, 657, 725, 766, 821, 887, 1127, 1163, 1184, 1225
Sithens R. L---- 535, 614
Smith, K. A---- 1225
Steinfeld, J. L---- 198
Stone, Dr. F. L---- 725
Whedon, Dr. G. D---- 436
Whiteside, Dr. D. F---- 966
Wipf, E---- 535

INDEX

NATIONAL INSTITUTES OF HEALTH

A

Page

Appendix ---- 1241

B

Buildings and facilities ---- 1163
Justification material ---- 1174

C

Construction of health educational, research, and library facilities ---- 1099
Justification material ---- 1111

D

Dental health (*See also* National Institute of Dental Research.) ---- 1059
Cleft lip and palate ---- 1069, 1074
Dental auxiliaries ---- 1073, 1084
Dental care programs, inadequacy of ---- 1062
Dental hygienists, training of ---- 1080
Dental problems of the handicapped ---- 1083
Dental services to the poor ---- 1081
Dentist-patient ration in the Armed Forces ---- 1076
Fluoridation ---- 1062, 1076
Gingivitis ---- 1061
Hemodialysis, use of fluoridated water in ---- 1064
Justification material ---- 1086
Management fund payment ---- 1075
Oral cancer ---- 1068, 1079
Periodontal treatment ---- 1082
Prepaid dental care ---- 1083
Pyorrhea ---- 1061
Statement of the Director ---- 1061
Training programs ---- 1072
Division of Biologics Standards ---- 177
Justification material ---- 188

G

General Research and Services ---- 877
Automobiles, replacement of ---- 903
Computer facilities ---- 903
Computer research and technology ---- 899
Drug addiction ---- 893, 902
Entertainment expenses ---- 892
General clinical research centers ---- 893, 900
Heuristics ---- 898
Image processing project ---- 900
Justification material ---- 905
Primate centers ---- 896
Special resource centers ---- 895
Statement of the Director ---- 888

29-867 O—69—pt. 4——88

Page

General research support grants 1225
Justification material 1235

H

Health Manpower 966
Allied health educational improvement grants 984
Awards in fiscal year 1968 for health professions special-improvement grants 980
Bloc grant for medical schools 981
Continuing education of physicians 988
Federal assistance, percentage of students receiving 1001
Grants to schools of pharmacy and veterinary science 979
Health manpower research 996
Health professions student loans 985
Justification material 1003
Medical and dental schools in serious financial need, supplemental funds for 999
Medical school admission requirements 991
Medical school enrollments, expansion of 992, 993
Medical student selection 994
Nurse scholarships, unobligated balance for 989
Nurse training 997
Cost 998
Nurses aide training 983
Nursing schools 982
Construction 995
Institutional grants 994
Nursing student loans 985
Obligational authority, advance 989
Organization 998
Recruitment of students in the health field 999
Scholarships 987
Statement of the Director, Bureau of Health Professions Education and Manpower Training 970
Student assistance 990
Summary tables 966–970

J

John E. Fogarty International Center for Advanced Study in the Health Sciences 928
Budget reduction 938
Centralization of international health activities 932
International Advisory Committee 942
International Fellowship Review Committee 943
International health activities not under the Fogarty center 936
International postdoctoral fellowships 944
Justification material 950
Research in foreign countries, results of 939
Statement of the Director 930
United States-Japan cooperative program 931

N

National Cancer Institute 198
Anticancer programs, effects of 269
Cancer incidence:
Increase 229
Reporting 227
Urban-rural ratios 230
Cancer victims, survival rate 247
Chemotherapy 213–215, 220, 268
Special research report 204

	Page
National Cancer Institute—Continued	
Cigarette, less hazardous	244
Construction authority	244
Etiology of cancer	202
Foreign research grants	235
Accomplishments from	242
Funds, uses of	221
Hodgkins disease	210
Industrial chemicals	252
Justification material	283
Karolinska Institute, awards to	234
Leukemia	211
Special report	212
Lung cancer task force	218, 270
Management fund	228
National cancer survey	225
Pap test	233
Pesticides and cancer	251
Radiation therapy prototype machine	246
Regional cancer institutes	271
Remission and recurrence	210, 211
Research career awards	227
Research results	220
Research support methods, possible changes in	223
Sloan-Kettering system	226
Statement of the Director	200
Task force on breast cancer laboratories	244
Tobacco and health, special report on	245
Viruses and cancer	219, 269
National Eye Institute	614
Budget increase compared with other institutes	627
Clinical research centers	632
Clinical research projects	633
Glaucoma	628, 634, 637
Justification material	639
Myopia	628
Research problems	631
Special report on blindness	618
Statement of the Acting Director	615
National Heart Institute	309
Anthracosilicosis	318
Arteriosclerosis	327
Artificial heart	320, 328, 333
Artificial pacemaker	321
Atromid-S	315
Blood fractions, use of	326
Blood transfusions	322
Cardiovascular research centers	334
Coronary drug project—Atromid-$_S$	315
Fellowships and training grants	335
Heart attack, relative risk of	340
Heart cooperative drug study	334
Heart disease, special report on	344
Heart pacemaker	343
Heart transplants	318, 328–330, 336
Special report on	330
Hepatitis	323
Hypertension	321
Justification material	358
Mechanical heart assistance devices	336, 342
Medical assistance for heart attack victims	340
National blood resource program	335
National registry of organ transplants	335
Obstructive respiratory disease	317
Program direction, additional positions for	335

	Page
National Heart Institute—Continued	
Research projects, reduction in	316
Research results, dissemination of	334
Septicemia	339
Shock	322
Special report on heart disease	344
Specialized research centers	332
Statement of the Director	311
Synthetic blood	324
Transportation costs, budget increase for	333
National Institute of Allergy and Infectious Diseases	657
Allergies	680
Autoimmune diseases	677
Budget increases requested	681
Continuation grants	682
Geographic medicine program	697
Gorgas Memorial Laboratory	671
Hong Kong flu	659
Infections acquired in hospitals	661
Interferon	664
International centers for medical research and training	695
International research career development program	698
John E. Fogarty Center	673
Justification material	699
Kidney transplants, cost of	679
Laboratory and clinical research, budget increase for	679
Pneumonia vaccine	693
Research fellowships	685
Research grant applications, review and approval of	687
Research results	688, 689
Rubella vaccine	694
SEATO chlorea research program	696
Skin cancer immunotherapy	674
Special report on Interferon research	669
Statement of the Director	659
Training grants	686
Transplantation immunology	677
United States-Japan cooperative program	674
National Institute of Arthritis and Metabolic Diseases	436
Arthritis	480
Artificial kidney	443
Costs	455, 462, 478
Cystic fibrosis	442, 481
Diabetes and arthritis	444
Dialysis	443, 455, 462
Justification material	493
Kidney transplants	479
Liver transplants	442
Nutrition	482
Pancreas transplants	480
Positions, new	458
Special report on arthritis	445
Special report on cystic fibrosis	458
Special report on diabetes	449
Special report on kidney disease and the artificial kidney	463
Special report on nutrition	484
Special report on organ transplantation	473
Statement of the Director	438
Training grants, reduction in funds for	453
National Institute of Child Health and Human Development	821
Agency for International Development family planning research	850
Aging	844, 848, 849
Artificial insemination	832
Birth control research	834, 847
Disadvantaged children study	844

Page

National Institute of Child Health and Human Development—Continued
Family planning in foreign countries 838
Headstart program 849
Illegitimacy 846
Intellectual development of children 845
Intramural research 831
Justification material 854
Malnutrition 842
Mental retardation research centers 829, 841
Oral contraceptives, adverse reactions associated with 826
Psychosocial and behavioral research 836
Research on aging 844
Statement of the Director 823
National Institute of Dental Research 385
Caries prevention in children 404
Caries task force 402
Cleft lip and palate 396
Dental care 410
Dental plaque 395
Dentist training 831
Fluoridation 391, 394
Justification material 413
Nutrition 412
Oral cancer 403
Organization of dental health activities 402
Orthodontists 408
Periodontists 409
Public information activities 393
Budget for 402
Restorative materials 410
Statement of the Director 387
Tooth transplantation 400
University dental research institutes 403, 407
National Institute of Environmental Health Sciences 766
Air pollution 795
Budget projections 784
Chemical manufacturing, monitoring of 778
Environmental control 797
Environmental health sciences centers 776, 793
Establishment of the Institute 780, 785
Funding increase, need for 782
Justification material 802
Laboratory and clinical research, budget increase for 733
Laboratory facilities, cost of 783, 785
Lung cancer task force 790
Pesticides 774, 779
Positions, new 779
Research, responsibility for 798
Research career development awards 801
Research grants 777
Revenue and Expenditure Control Act of 1968 (Public Law 90-364), effect of 785
Scientific information program 787
Smoking and health 786, 788
Statement of the Director 768
Task force on research planning 800
Toxicity of new chemicals 777
Uranium miners, studies of 775
National Institute of General Medical Sciences 725
Automation of clinical laboratories 731, 739
Behavioral sciences 735
Drug research 730
Genetics 734, 738
Indiana University research training grant 737

National Institute of General Medical Sciences—Continued Page
Justification material 740
Miniaturization 732
Oral contraceptive research 736
Statement of the Director 727
Trauma 733
National Institute of Neurological Diseases and Stroke 535
Brain and spinal cord injuries 574
Drugs, new, marketing of 584
Fellowship and training grant reductions 578
Fellowship awards, reduction in 572
Human communicative disorders 578
Justification material 585
L-Dopa 576, 581, 584
Neurosensory medical fields, number of physicians entering 573
Other services 572
Positions, increase in 569
Puerto Rico, facilities in 566
Research career development awards 583
Special reports 541
Spinal cord injuries 568, 574, 580
Statement of the Director 535
Stroke clinical research centers 583
Training program 567
Transfer of activities to the Eye Institute 564
Travel and transportation 572
Youth opportunity program 569, 570
National Library of Medicine 1127
Justification material 1139

S

Salaries and expenses, Office of the Administrator 1184
Justification material 1139
Scientific activities overseas (Special foreign currencies program) 1198
Justification material 1215
Statistics and program data 65

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