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DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR 1978

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS HOUSE OF REPRESENTATIVES

NINETY-FIFTH CONGRESS

FIRST SESSION

SUBCOMMITTEE ON THE DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE

DANIEL J. FLOOD, Pennsylvania, *Chairman*

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NEAL SMITH, Iowa
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DAVID R. OBEY, Wisconsin
EDWARD R. ROYBAL, California
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HENRY A. NEIL, Jr., FREDERICK F. PFLUGER, ROBERT L. KNISELY, NICHOLAS G. CAVAROCCHI, MICHAEL A. STEPHENS, and BETTILOU TAYLOR, *Subcommittee Staff*

PART 3

NATIONAL INSTITUTES OF HEALTH

Printed for the use of the Committee on Appropriations

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DEPARTMENTS OF LABOR AND HEALTH, EDUCATION, AND WELFARE APPROPRIATIONS FOR FISCAL YEAR 1978

FRIDAY, MARCH 4, 1977.

NATIONAL INSTITUTES OF HEALTH

WITNESSES

DR. DONALD S. FREDRICKSON, DIRECTOR

ACCOMPANIED BY—

DR. DeWITT STETTEN, JR., DEPUTY DIRECTOR FOR SCIENCE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT
CHARLES MILLER, DEPUTY ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. We now continue with the Department of Health, Education and Welfare, and we will hear from the National Institutes of Health.

The presentation will be made by Dr. Donald S. Fredrickson, the Director of the National Institutes of Health. I see we have a biographical sketch of you, which we will place in the record at this point.

[Dr. Fredrickson's biographical sketch follows:]

CURRICULUM VITAE

Name: Donald S. Fredrickson.
Home address: 6615 Bradley Boulevard, Bethesda, Md.
Date and place of birth: August 8, 1924, Canon City, Colo.
Family: Henriette Priscilla Dorothea Ekhof Fredrickson; two children.
Education: University of Colorado, 1942–43; B.S., University of Michigan, 1946; M.D., University of Michigan, 1949; Certified: American Board of Internal Medicine, 1957.
Chronology of employment:

1949–50 House officer, Peter Bent Brigham Hospital, Boston.
1950–51 James Jackson Cabot Research Fellow in Medicine, Harvard Medical School, Boston.
1950–52 Assistant in Medicine, Peter Bent Brigham Hospital, Boston.
1952–53 Research Fellow in Medicine, Massachusetts General Hospital, Boston.
1953–55 Clinical associate, National Heart Institute, National Institutes of Health, Bethesda.
1955–61 Member, senior research staff, Laboratory of Cellular, Physiology and Metabolism, National Heart Institute.
1961–66 Clinical director, National Heart Institute.
1962–66 Head, Section on Molecular Diseases, Laboratory of Metabolism, National Heart Institute.

1966–68 Director, National Heart Institute.
1966–74 Chief, Molecular Disease Branch, National Heart and Lung Institute.
1969–74 Director of Intramural Research, National Heart and Lung Institute.
1974–75 President, Institute of Medicine, National Academy of Sciences, Washington, D.C.
1975– Director, National Institutes of Health.

Present academic appointments: professiorial lecturer in Medicine, George Washington University School of Medicine, Washington, D.C.; lecturer in Preventive Medicine, Georgetown University School of Medicine, Washington, D.C.

Member:

Alpha Omega Alpha.
American Academy of Arts and Sciences.
American Association for the Advancement of Science.
American College of Cardiology, Fellow.
American College of Physicians, Fellow.
American Federation for Clinical Research.
American Heart Association, Council for the Study of Arteriosclerosis.
American Physiology Society.
American Society for Clinical Investigation.
American Society of Human Genetics.
Association of American Physicians.
British Cardiac Society (corresponding member).
Deutsche Gesellschaft für Innere Medizin (corresponding member).
Harvey Society (honorary).
Institute of Medicine, National Academy of Sciences.
Institute of Society, Ethics and the Life Sciences (associate member).
International Society of Cardiology.
Medical Society of Sweden (honorary).
National Academy of Sciences.
Peripatetic Club.
Phi Beta Kappa.
Phi Kappa Phi.

Research interests: Lipoproteins, lipid transport and metabolism; medical genetics, the cause and prevention of arteriosclerosis, health science, education and care systems.

Related professional activities—

Present:

Member, Advisory Council of the American Center for Chinese Medicine.
Life Associate Member, Intra-Science Research Foundation.
Editorial Boards: American Journal of Medicine, Circulation, Circulation Research, Journal of Atherosclerosis.

Previous:

Advisory Council on Research, New York State Heart Association.
Chairman, Council on Arteriosclerosis, and member, Board of Directors and Central Committee, American Heart Association.
American Society for Clinical Investigation, council and secretary-treasurer.
Bethesda Conferences Committee, American College of Cardiology.
Cardiovascular Research Program Evaluation Committee, Veterans Administration.
Board of Directors, Foundation for Advanced Education in the Sciences.
Cardiovascular Study Section, NIH.
Executive Committee, Section on Atherosclerosis, International Society of Cardiology.
NAS–NRC Committee on Fats, Food, and Nutrition Board.
Governing Board, National Research Council, NAS.
Executive Committee, Assembly of Life Sciences, NAS.
NAS–NRC Committee for the Study of Inborn Errors of Metabolism.
Chairman and Member, Medical Board, NIH Clinical Center.
Nutrition Research Advisory Committee, National Dairy Council.
Stouffer Prize Committee.
U.S. Coordinator, Problem Area 1, Prevention of Arteriosclerosis, U.S.–U.S.S.R. Cardiovascular Exchange Program.

Editorial Activities: American Physiology Society, Member and Chairman, Publications Committee; Editorial Boards, Journal of Clinical Investigation, Physiology in Medicine; Editorial and Advisory Board, Journal of Lipid Research.

Honors and other special scientific recognition:

Gold Medal Award, The American College of Cardiology, 1967.
The James F. Mitchell International Award for Heart and Vascular Research, 1968.
Department of Health, Education, and Welfare Superior Service Award, 1970, and Distinguished Service Award, 1971.
Modern Medicine Distinguished Achievement Award, 1971.
The McCollum Award, The American Society for Clinical Nutrition, 1971.
Election to the National Academy of Sciences, 1973.
Jimenez-Diaz Award (Madrid), 1974.
Intrascience Award, 1974.
La Modannina Prize for Science (Milan), 1975.
Honorary Fellow of the Council on Clinical Cardiology, 1975.
The American College of Physicians Award, 1976.
Award of Merit, the American Heart Association, 1976.

Honorary Lectureships:

American Swiss Foundation for Scientific Exchange University Lectures (Basel, Bern, Lausanne, Geneva, Zurich), 1964.
John Kent Lewis Memorial Lecture (Stanford), 1967.
Seventeenth Annual Convocation Lecture (The American College of Cardiology), 1968.
Third Bernard H. Pastor Memorial Lecture (University of Pennsylvania), 1968.
Marcus R. Caro Memorial Lecture (American Academy of Dermatology), 1968.
The Carl Herzog Guest Lecture (The American Dermatological Association, Inc.), 1969.
The Distinguished Lecture (Association of American Physicians), 1969.
Second George C. Griffith Scientific Lecture (Los Angeles County Heart Association), 1969.
Plenary Lecture, Deutsch Gesellschaft fur Klinisch Chemi (Bonn), 1970.
St. Cyres Lecture (National Heart Hospital, London), 1970.
Wall Memorial Lecture (Children's Hospital of the District of Columbia), 1971.
Cardiac Society of Australia and New Zealand and National Heart Foundation Lecturer, 1971.
Alpha Omega Alpha lecture and visiting professorship (Johns Hopkins Medical School), 1972.
Ernest William Goodpasture Lecture (Vanderbilt), 1972.
John C. Higgins Memorial Lecture (University of Oregon), 1972.
Harvey Lecture, 1973.
Samuel Bellet Memorial Lecture (Philadelphia), 1973.
The Jimenez-Diaz Lecture (Madrid), 1974.
Alpha Omega Alpha Lecture (Mount Sinai School of Medicine), 1976.
G. Lyman Duff Memorial Lecture (American Heart Association), 1976.

Mr. FLOOD. Do you have some people with you that you would like us to meet.

Dr. FREDRICKSON. On my left is Leon M. Schwartz, the associate director for administration. On my right is Norman Mansfield, the director of the division of financial management, and to his right is Dr. DeWitt Stetten, the deputy director for science. And I think Dr. Miller you have met earlier.

Mr. FLOOD. More or less, yes.

I see you have a prepared statement, Doctor; how do you want to handle this?

Dr. FREDRICKSON. Mr. Chairman, if you have no objection, I would like to offer my prepared statement for the record and to discuss briefly some major problems, described more extensively there, that relate to some of the major problems common to all the Institutes.

Mr. FLOOD. Suppose you do that.

[Dr. Fredrickson's complete statement follows:]

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE, NATIONAL INSTITUTES OF HEALTH, STATEMENT BY THE DIRECTOR, MARCH 4, 1977

Mr. Chairman and members of the committee, as the Directors of each of the 14 components of NIH for which there are separate appropriations will be here to explain their present activities and future plans, I believe that it is appropriate—and, I hope, helpful to the committee—for me to discuss briefly—

Some activities and problems that concern NIH as a whole;

What we are doing in areas in which NIH has new or expanded legislative mandates; and

Areas that I believe need further development.

The major problems that affect the directions in which NIH will move, and the manner in which its programs will develop, during the next few years are common to all, or most, of the Institutes.

The most important of these common problems is the relationship of NIH, as the principal biomedical research agency of the Federal Government, to the health service community—and the extent to which NIH can, or should, take responsibility for activities that lie at the boundary between the conduct of research and the delivery of health services. As clinical research—that is, research involving human patients as distinct from research done solely in the laboratory or with animals—necessarily includes caring for patients, the boundary between research and service is not easy to define. This, of course, complicates any decision on how far NIH should go in carrying out its primary responsibility for the conduct of research.

There can be no doubt that this responsibility includes the communication of research results. Although much of the research supported by NIH, or conducted in its own facilities, is as far removed from the needs at the bedside as exploring for an oilfield is from pumping gasoline into a car, the end product of all the work we do or support is the prevention, cure or amelioration of disease and disability. Due to the complexity of most disease problems, each investigator is, in effect, a subcontractor working on what is often a very small piece of the problem and his results will usually only be of interest and of use to other investigators working on related pieces. But their collective goal is ultimately to put together information that will have a direct bearing on man's ability to prevent or cope with disease. Research, therefore, is not completed until usable results have been made available to health practitioners and to the general public.

We have just prepared a report on the activities initiated by NIH during 1976 for improving the dissemination of research results. I should like to submit a copy for inclusion in the record of these hearings. It is, in both senses, a progress report: first, because we feel that we have, indeed, made some progress in improving communication with health professionals engaged in primary care, and, second, because this is an ongoing and expanding activity for which, we hope, a final report will never be written. In particular, I looked forward to the development of the Lister Hill Center for Biomedical Communications to enhance the ability of NIH to play a more effective role—construction of the long-delayed building for this center is now scheduled to begin in April. The National Library of Medicine, since it became part of NIH, has already moved far beyond the traditional passive archival role of a library and with the completion of the Lister Hill Center its ability to explore and expand innovative technological approaches to the storage, retrieval and dissemination of information will be greatly enhanced. At the same time, I must point out that communication is not a job that NIH can do alone. Our main mission, and our expertise, is in providing the substance of what must be communicated—and here we must constantly strive to do a better job of selecting and displaying what is immediately useful to practitioners and the public. But other agencies, particularly the professional societies and voluntary health groups, are better situated to reach the wide audience to whom communication must be addressed—they must be encouraged

to take a more active part in the bucket brigade carrying knowledge from the research well to the health services.

A more fundamental—and much more complex—problem at the juncture of research and the delivery of health services is how best to transfer the technology developed as the result of research and, more particularly, how to assess or forecast its long-term effects. Many new developments have dangers as well as benefits and they may have economic and social impact as well as purely medical usefulness. Sometimes ethical questions may also arise. In each case, the pluses and minuses must be balanced and the inevitable differences of opinion, even among scientists, must be weighed. To this end, we must seek a technical consensus not merely to determine the clinical significance of new findings but to assess their ethical, social and economic implications. We cannot, in good conscience, widely disseminate research information just because it exists—we must, in so far as is possible, be certain that the full effects, in the broadest sense, of putting it into practice are understood and that it is accompanied by whatever warnings or safeguards are necessary. A fairly lengthy document on the responsibilities of NIH in this connection is being prepared. A draft has been discussed with Director's advisory committee and is now receiving internal review. It will be published shortly and copies will, of course, be sent to this committee.

The best assessment tool for the results of most clinical research is the so-called clinical trial—that is, putting a new procedure into practice under previously agreed and carefully monitored conditions. The Cancer and Heart Institutes have special legislative mandates to conduct such trials but they are, in fact, also conducted under the aegis of each of the other Institutes. In fiscal year 1975, the latest year for which complete figures are available, NIH supported 755 clinical trials at a cost of $87.8 million. Some of these trials had already been in progress for several years—in fact, $209 million had been spent on them prior to 1975—and many would continue for several more years at a projected cost of $345 million. The total cost of these 755 trials will therefore be about $642 million. The size, complexity and duration of these trials—and, therefore, their individual cost—varies widely. The most expensive were the 26 trials supported by the Heart Institute which will cost an average of a little over $15 million each. Over half of these 755 trials were supported by the Cancer Institute but they account for only 20 percent ($132 million) of the projected cost. The average cost of the clinical trials that were active in 1975 will be about $850,000.

Our involvement in clinical trials has increased during the past 2 years and the future support to which we are now committed is higher than it was in 1975. The time has come to decide how much farther and how rapidly we should go. The first determinant, of course, is what research developments are thought to be ready for clinical trial. This is not always an easy judgment to make and it is here that technical consensus can become particularly important. The public—and, I am sure, the Congress—is anxious that research be brought to its clinical fruition without delay but there can also be real dangers in bringing new techniques into practice too soon. There have been ample tragic warnings that a promising new drug or procedure can do unsuspected harm and it is, I think, abundantly clear that the public interest is best served by prudence and caution. A second factor in planning further trials is, of course, the cost. In this connection, we must consider not only the commitment of future funds for the years it may take to complete the trial but also the difficulty of terminating support when the trial has served its scientific purpose. In too many instances the grant or contract that made the trial possible also had the effect of making possible a service to patients that would, in effect, be terminated when NIH support ceases. With rapidly rising health care cost, ending a trial may raise a serious problem for the institutions in which the trial is being conducted while continuing it would clearly be contrary to the NIH mission and the purpose for which the funds were appropriated. We must, therefore, be careful to enter into costly trials only in circumstances that give assurance that they will produce answers to scientific questions, in a reasonable time, and that the purely service aspect of the clinical work undertaken will be continued under other auspices when the trial has been completed. As research is the primary role of NIH and the principal justification for its budget requests, we must be constantly on guard not to assume—or appear to assume—responsibilities for health care services which we cannot properly undertake.

Among the new and expanded legislative mandates for NIH, the two that have the broadest impact are those for diabetes and arthritis.

The current NIH obligations for diabetes research total $76 million which is slightly more than the $73.3 million recommended for fiscal year 1977 by the Diabetes Commission. Of this amount a little over half—$39.8 million—is in the National Institute of Arthritis, Metabolic and Digestive Diseases which has primary responsibility for diabetes research. But diabetes related research also accounts for $11.9 million in the Heart Institute; $9.1 million in the Eye Institute for diabetic retinopathy; $4.6 million in the Child Health Institutes; $1.9 million in the Neurology Institute; $6.4 million in the Division of Research Resources; and lesser amounts, totalling $2.4 million, in some of the other Institutes. There is, thus, an overall NIH involvement of considerable magnitude and scope in diabetes research. To insure that this broad approach is properly coordinated, I have established an NIH Diabetes Coordinating Committee to complement the activities of the interagency committee and the Diabetes Board already established under Public Law 93-354. A joint advisory group has been set up by the Heart and Arthritis Institutes to assist in arranging a clinical trial on the efficacy of controlling blood glucose in arresting the development of vascular complications of diabetes. The Arthritis Institute is setting up several other advisory groups on various aspects of its diabetes program and is arranging a number of conferences and workshops. Existing advisory groups in other Institutes have also appointed subcommittees or are themselves looking into the diabetic aspects of relevant diseases and conditions. The Institute Directors concerned will testify in more detail on their diabetes related activities.

Research on arthritis is similarly dispersed throughout NIH though in this case the Arthritis Institute continues to carry a larger share of the burden. Our total obligations during fiscal year 1977 will be $30.5 million of which the Arthritis Institute accounts for $24.7 million. There are, however, relevant research activities in eight of the other Institutes. We are in the process of reviewing all our arthritis related programs as part of our preparation of the 1979-83 forward plan. When this is completed I shall appoint a coordinating committee similar to the one for diabetes.

The health problems of the aged also cut across the disease-oriented organizational structure of NIH. Dr. Butler—who became the first Director of the National Institute for Aging on May 1, 1976—is therefore much concerned to coordinate the activities of his Institute with the ongoing disease-oriented programs at NIH and with other agencies that have responsibilities and programs affecting the aged. It will be our joint endeavor to insure that, on the one hand, there is no unnecessary overlap or duplication and, on the other hand, that there is optimal cooperation and collaboration including, where appropriate, joint funding of research projects of mutual interest. It is too early to set forth the details of these arrangements but Dr. Butler will discuss his plans when he testifies later in the hearings.

In addition to such diseases as arthritis and diabetes and the broad spectrum of problems that may afflict the aged, many scientific disciplines and fields of clinical study also cut across the categorical missions of all or several of the Institutes. In most cases the necessary coordination is readily achieved through normal disciplinary channels. There are, however, a few fields in which a more deliberate approach to coordination is desirable.

One such field is research on nutrition which is as yet—at NIH and elsewhere—a vast, diverse, and essentially unstructured set of activities. It is, in fact, an undefined field that figures prominently in home economics courses but is not generally recognized as a scientific discipline. In June 1975, NIH established a Nutrition Coordination Committee as a first step in defining the scope of nutrition activities at NIH and developing a focal point for the exchange of information on nutrition. The time is now ripe to extend these activities to monitoring international research on nutrition, identifying gap areas, facilitating collaboration, and selecting specific nutrition research problems for which discrete NIH programs might be developed. We are developing a Nutrition Plan and considering how we might best assess present knowledge on nutrition in order to respond to the increased demand for prudent advice on the optimal diet for maintaining health and contributing to longevity.

Epidemiology, though well defined and long recognized as important to an understanding of the dynamics of disease, has languished partly because of the relatively low status accorded to this discipline, the traditional practice of restricting epidemiology training to graduates of medical schools, and the limited number of adequate training centers. As a result of these factors, there is now a critical shortage of chronic disease epidemiologists, which, unfortunately, coincides with a growing need for sophisticated epidemiologic studies. As a first step

toward rectifying this situation, I have appointed an NIH Epidemiology Committee and have asked them—

To make an estimate, in conjunction with the American Society of Epidemiology, of the current supply of qualified epidemiologists and the future manpower requirements;

To define the basic requirements and suggest a curriculum for training both MD's and non-MD's; and

To explore the desirability and feasibility of establishing a training program at NIH in cooperation with universities and other Federal agencies.

During the past decade, genetics has made the most dramatic strides of any of the biomedical sciences—indeed, of any of the sciences. From a purely disciplinary point of view, coordination is hardly necessary: Investigators in the field are only too eager to keep abreast of each other's work. However, because the potential impact of genetics research on a wide variety of disease problems is so great, we have established an NIH Genetics Coordinating Committee which has sought to define the areas of interest and assess the current extent of involvement of Federal agencies in genetic diseases. The results of this enquiry will be part of the report to be submitted to the Congress in April as required by the National Sickle Cell Anemia, Cooley's Anemia, Tay-Sachs, and Genetic Diseases Act (Public Law 94-278). The NIH Committee has also suggested that the Secretary establish a formally chartered DHEW Interagency Genetics Coordinating Committee, with NIH acting initially as the lead agency, to guide the implementation of the act which calls for many activities—such as screening, treatment, and genetic counseling—that lie outside the purview of NIH.

A particular aspect of genetic research that has recently attracted a lot of public attention—and, on the part of some, considerable apprehension—is the work that is beginning to be done with what is called "recombinant DNA." The dangers of doing this research that have received so much publicity are purely speculative: No one knows whether they really exist but, on the other hand, no one can be certain that they do not. However, to put this matter into perspective it must be borne in mind that changes in DNA—the nucleic acid that is present in all living organisms and determines their inherited characteristics—also occur spontaneously in nature: They have made possible the never ending process of evolution. We are as we are as the result of a long series of changes in the DNA of our biological ancestry—and aberrations or faults in DNA are undoubtedly responsible for inherited disabilities and predispositions to disease. Research on recombinant DNA therefore holds the promise of becoming a powerful tool in the conquest of disease and, ultimately, in the prevention or correction of inherited malfunctions and disabilities. The potential dangers of such research are, I think, no greater—almost certainly considerably less—than the dangers, less than a century ago, of cultivating, in primitive laboratories, the newly discovered bacteria of dread diseases for which there was then no prevention or cure. Nevertheless, it behooves us to heed the adage that it is better to be safe than sorry. We have therefore developed guidelines which are mandatory for all laboratories using recombinant techniques in research conducted by or supported by any Federal agency. These guidelines have also been adopted by the member industries of the Pharmaceutical Manufacturers Association and the international scientific community has reached agreement that a common set of standards shall govern the use of recombinant DNA techniques. The Interagency Committee on Recombinant DNA Research is now considering how this is to be accomplished and how compliance is to be monitored and enforced.

Under proper safeguards much good can flow from this latest development in the steady progress of science. It is probably not an exaggeration to compare our unfolding ability to split and recombine DNA chains to our ability to split atoms—and I believe that the long-term benefits to mankind will be substantially greater. There is good reason to believe that genetic research—of which the present work on DNA is merely the forerunner—will have as sweeping an impact on health and the practice of medicine during the last quarter of this century as the new science of bacteriology had during its first quarter.

But if biomedical research is entering a new era, so is its relationship to society. It is passing from an extended period of relative privacy and autonomy to an engagement with new ethical, legal, and social imperatives under concerned public scrutiny. NIH has responded to this concern by requiring the formation of review boards to oversee human experimentation, animal care, and now genetic recombination experiments. Similar bodies may soon have to oversee other hazardous laboratory work. These responsibilities are inescapable adjustments to the rising demand for public governance of science, though this need

not—and, indeed, should not—go beyond what is clearly required for public safety lest we inadvertently impede successful research and hamper creativity. The progress of science will continue to depend on the initiative and insights—call it inspiration, if you like—of individual scientists. NIH has no intention of trying to mastermind research.

The NIH budget requests now before you total $2,576,371,000, which is an increase of $44,957,000 over the comparable figure for fiscal year 1977. A third of the funds requested for the research components are for the Cancer Institute. I am satisfied that the distribution of the remaining funds between the other Institutes is reasonable and that the budget requests, as a whole, will enable NIH to maintain its present level of effort. The Directors of Institutes, Research Divisions and the National Library of Medicine will testify for their respective programs.

Dr. FREDRICKSON. These problems affect the directions in which NIH will move and the manner in which its programs will develop during the next few years. Important among these is the relationship of NIH, as the principal biomedical research agency of the Federal Government, to the health service community and the extent to which NIH can, and should, take responsibility for important activities at the boundary between the conduct of research and the delivery of health services.

COMMUNICATION OF RESEARCH RESULTS

Certainly not an issue is the responsibility that NIH clearly has to communicate research results. We have just prepared a report on those activities initiated by NIH during 1976 for improving the dissemination of research results, and I should like to submit a copy for inclusion in the record of these hearings.

Mr. FLOOD. Without objection, that will be done.

[The report follows:]

REPORT ON ACTIVITIES INITIATED BY THE NATIONAL INSTITUTE OF HEALTH DURING 1976 FOR IMPROVING THE DISSEMINATION OF RESEARCH RESULTS

The following report on activities for improving the dissemination of research results describes projects undertaken by the National Institutes of Health since January 1976. Concurrently with the development and initiation of the efforts summarized in the report, the Director, NIH, his staff and the Director's Advisory Committee have devoted considerable time to an assessment of NIH responsibility at the Health Research/Health Care interface. Dissemination of information on findings ready for application to patient care is viewed as an important element of such responsibility.

A plan is in development to establish an overall organizational framework for identifying and fostering the evaluation of new knowledge which is on the verge of transfer to the health care community. The plan will include the design of a permanent organizational structure for the dissemination program.

In considering dissemination improvement projects, priority attention has been given to those involving communication with health professionals engaged in primary care. Such efforts were designed to accelerate the transfer of research findings related to a selected list of clinically significant topics by giving the information "special delivery" treatment, supplemental to its normal diffusion through the channels by which professionals keep informed.

In accordance with the improvement plans previously submitted to the Congress, additional health information materials have been prepared for use by the public media as well, with emphasis on materials for use by radio and television stations. Four public service announcements providing substantive health information have been prepared and distributed to all U.S. radio stations.

A set of dramatized announcements on diabetes and colon cancer is ready for distribution to all TV stations. The NIH produced and distributed to 2,247 high schools a 15-minute health information film accompanied by kits of teaching

materials. The film's principal subject is immunology and it is titled, "Invaders and Defenders of the Human Body."

The activities described in this report are also supplemental to the substantial congressionally-mandated demonstration and information programs carried out by the National Cancer Institute and the National Heart, Lung, and Blood Institute.

The cost of projects under the NIH dissemination improvement program during fiscal year 1976, including the transition quarter, was approximately $200,000.

An amount of $1,692,000 has been budgeted from fiscal year 1977 funds for approved projects which were recommended to the Director by his task force on communications.

Two professionals and one clerical employee are assigned to full time support of dissemination improvement activities.

The following projects have been initiated or completed since the last report to the Congress in January 1976:

1. "FROM THE NIH"

A monthly report on research findings of potential value to the practioner.

The first 2-page section of the Journal of the American Medical Association prepared by the NIH and titled "From the NIH" appeared in the August 9, 1976 issue, and has been published monthly since. Topics are chosen on the basis of their general clinical significance and current research activity relating to them. Editors of two other journals have asked to be provided the same or similar materials and arrangements are being made to supply it.

At this time JAMA is providing space for the NIH series at no charge.

2. VIDEOTAPE PRESENTATIONS FOR WIDESPREAD DISTRIBUTION TO HEALTH PROFESSIONALS

Two videotape productions for health professionals highlighting research developments in the treatment of diabetes and cancer will be put into distribution by February 15, 1977.

The first, "Diabetes," is a review of current knowledge concerning this important disease, and includes presentations by scientists of the National Institute of Arthritis, Metabolism, and Digestive Diseases as well as leading non-Federal clinicians.

The second is titled, "Bedside Clues to the Etiology of Cancer and Other Diseases." It was prepared under the supervision of the National Cancer Institute.

Both programs are approximately 1-hour in length. David Prowitt, known for his award-winning television programs, produced and directed them.

Seven-hundred-and-fifty copies in cassette form will be made for distribution to academic medical centers, hospital departments of continuing medical education, and to professional organizations.

The total cost of the two productions, including distribution, is $250,000.

3. DISTRIBUTION OF VIDEOTYPE CASSETTES OF NOVEMBER 1976 INTERNATIONAL CONFERENCE OF BREAST CANCER

The White House, the National Cancer Institute and the American Cancer Society sponsored a 2-day conference on breast cancer in Washington, November 22, and 23, 1976.

The entire conference was videotaped, using multiple cameras and special equipment for recording charts and other visual aids. This video summary of knowledge about breast cancer has been edited under supervision of the National Cancer Institute and converted to video cassettes.

Duplication of the tapes will be completed in time for their distribution by February 15, 1977. The cassettes have been approved by the American Academy of Family Physicians for continuing education credit. This project will make available to a large percentage of American physicians a full report on current information and research related to the diagnosis and treatment of breast cancer.

Cassettes will be sent at no charge to all medical schools and to the continuing medical education departments of some 700 hospitals.

Officials of the Public Broadcasting System are considering presentation of abridged versions of the Conference tapes.

The cost of the breast cancer information dissemination project is estimated at $175,000.

4. JOINT SPONSORSHIP OF NATIONAL SYMPOSIUM ON RESEARCH RELATED TO CLINICAL PROBLEMS

The National Institutes of Health and the Medical Society of the District of Columbia sponsored a Bicentennial Symposium on September 16–18, 1976. The conference was planned specifically for practitioners. More than 400 physicians from 22 States attended the conference, which was devoted to intensive discussion of current topics of clinical significance. This was the first time that the NIH and a general professional organization of clinicians jointly sponsored a scientific meeting.

Funds have been set aside for publication and distribution of the proceedings of the conference.

The total cost of the NIH–DC Medical Society project, including preparation and distribution of the proceedings, is estimated at $34,000.

5. ASSISTANCE TO PUBLISHER OF REFERENCE MANUAL FOR PHYSICIANS

The National Institutes of Health provided financial assistance tothe Federation of American Societies for Experimental Biology (FASEB) for expert review of data contained in a reference book, "Human Health and Disease." The book will be published in the spring of 1977 and will contain an extensive collection of standard values and data on a variety of disease problems. It is intended for use by physicians and clinical investigators. The editorial advisory board and roster of contributors to the book include many prominent clinicians and scientists.

The NIH contribution was $30,000.

6. SURVEY OF INFORMATION SOURCES USED BY FAMILY PHYSICIANS

A contract has been awarded to the American Academy of Family Physicians for a survey of information resources used by family physicians and of their preferences among them. It is considered essential to the dissemination improvement effort that current patterns of information flow to the family physician be charted. The survey will cover an established panel of 2,500 active physicians. Following the initial study, the panel will be polled periodically in an effort to determine the effectiveness of the improvement projects and to provide guidance for future efforts.

The initial contract will cost $25,000 and will be financed from DHEW evaluation set-aside funds.

Projects under development

Funds have been earmarked for the following projects under development:

1. "NIH grand rounds by satellite".—The Communications Technology Satellite will be used as a two-way audiovisual communications link for a series of joint grand rounds. Presentations will be made from Bethesda and the distant centers connected by satellite with NIH. Face-to-face questions will be entertained from the floor, that is, the audience assembled at each terminal of the closed circuit.

Effort will be made to assemble a number of primary physicians for each of the grand rounds presentations. Arrangements at the distant point will be in charge of the Department of Family Medicine of the involved school of medicine. Continuing education credits will be awarded to participants who qualify.

A tentative schedule has been reserved for the "NIH Grand Rounds by Satellite" as follows:

Bethesda-Lexington, Kentucky, Friday June 17, 1977, 12:15–3:15 p.m. e.s.t.

Bethesda-Denver, Colorado, Tuesday, July 19, 1977, 2:30–5:30 p.m. e.s.t.

Bethesda-Bozeman, Montana, Thursday, August 25, 1977, 1:45–3:15 p.m. e.s.t.

Bethesda-Seattle, Washington, Monday, January 10, 1978, 1:45–3:15 p.m. e.s.t.

[The schedule for completion of the ground installations at sites other than Bethesda is subject to revision, which may alter the order in which the pairings are scheduled.]

Two other times are available for scheduling at sites to be determined.

This project is a modification of that originally proposed for the use of the CTS. The original plan would have used the satellite as a one-way relay for transmitting NIH-originated presentations to teaching hospitals and academic centers. Due to the high cost of receiving units capable of reliable reception at the frequencies employed by CTS, only a limited number (not more than six) could have been purchased and installed. Further, the satellite can transmit to only about one-third of the country at a time. Together these factors would have limited the potential audience for a given live program transmitted by the CTS. The size of the audience available and willing to view the program at the time it was presented would not have justified the cost. Use of the satellite merely to send programs from NIH to be taped for later viewing at the receiving end would have been less cost-effective than simply mailing the tapes.

The point-to-point approach, which the modified plan embodies, will permit concentration of efforts on an identified target audience (for example, general practitioners from the northwest assembled at the University of Washington), and provide a more reliable basis for evaluating the use of the satellite for dissemination of biomedical research findings.

The listed sites were chosen for the grand rounds for three reasons:

A. Two-way terminals are being installed at the selected sites for other CTS experiments. They will be in frequent operation and thus will afford a high degree of technical reliability.

B. It will not be necessary for the NIH to purchase terminal hardware for the grand rounds, because such equipment is being installed by the National Library of Medicine and the Health Resources Administration for the other experiments. Thus the costs of the grand rounds will be for program production only.

C. Effectiveness of the grand rounds approach to dissemination by two-way links can be tested with highly developed medical centers (for example, Seattle) as well as localities having no large medical centers (for example, Bozeman).

The cost of production and promotion of the grand rounds is estimated at $500,000.

2. Distribution of special tapes and films to academic medical centers, teaching hospitals and professional groups.—Each year the NIH sponsors workshops, conferences and seminars on topics of immediate importance to practicing health professionals. Leading scientists and clinicians make authoritative presentations during such conferences which are later published in official proceedings.

In an effort to take further advantage of the potential of such meetings, arrangements were made to film the Bicentennial Colloquium sponsored in May 1976 by the National Library of Medicine, and more recently the Breast Cancer Report to the Professions 1976 (see above). These experiments indicate that by advance preparation of visual materials (charts, et cetera) and by judicious editing, a valuable and effective television tape can be produced, which then can be duplicated and distributed broadly.

Tapes also will be prepared from each of the "NIH Grand Rounds by Satellite."

The budget of the task force provides for video-taping some 20 hours of programs during fiscal year 1977 and for duplication and distribution of 300 copies of each.

The cost is estimated at $225,000.

3. Nationwide survey of primary physicians.—Results of the surveys involving the American Academy of Family Physicians panel of 2,500 (see item 6 initiated projects above) will be continuing sources of information to be used in program planning and evaluation. However, because the panel is made up only of physicians who have volunteered to participate, it may not be representative of the total primary physician population. Evaluation funds have been reserved to finance a survey of the information resources and source preferences of members of the Academy of Family Physicians (AAFP) and the American College of Physicians (ACP). The data derived from the full-scale survey of the AAFP will be useful in evaluating the statistical validity of the volunteer AAFP panel as a sample. The Health Systems Associates, which will conduct the American Academy of Family Physicians panel study, has proposed and tentative approval has been given to a similar study of the information practices of osteopathic physicians.

The estimated cost of the above studies to be financed from DHEW evaluation funds is $75,000.

4. What's new in health research?—The Task Force on Communications is developing an annual self-evaluation questionnaire covering recent clinically related research findings on the general "state of the art" and on ethical and legal matters related to medical practice.

The publication will resemble the multiple choice current affairs quiz formerly published by Time magazine and will be accompanied by an answer key. The publication will provide an annual review of important research developments in a challenging and entertaining form, giving the reader a means for self-assessment.

The Educational Testing Service, Princeton, N.J., has advised on the format of the publication and will prepare the questions. No budget estimate is available at this time.

5. Medicine for the layman.—The Clinical Center NIH will present a series of 12 weekly programs in the fall of 1977 for the general public on current medical topics and related research. Attendance at similar presentations during the Bicentennial Open House at NIH in 1975 and again in 1976 indicated a high level of public interest.

In addition, edited radio and television versions of these "Medicine for the Layman" presentations will be submitted to the Public Broadcasting System.

A budget of $50,000 has been reserved for recording on videotape.

The fall 1977 series will be a test. If successful, it will be repeated in the spring of 1978.

Dr. FREDRICKSON. We feel that we have made considerable progress in improving communication with health professionals throughout the Nation, particularly those engaged in primary care. At the same time I must point out that communication is not a job that NIH can do alone. Our main mission, and our expertise, lies in providing the substance of what must be communicated and used to provide the best standard of care. Other agencies, including the academic medical centers, professional societies and voluntary health groups, must continue also to play a primary role in reaching much of the wide audience to whom communication must be addressed.

TECHNOLOGY ASSESSMENT

A more fundamental—and more complex—problem at the juncture of research and the delivery of health services is how best to validate the technology arising from research and to anticipate its long-term effects. Many new developments have dangers as well as benefits; they have economic and social ethical impacts as well as purely medical usefulness. There is a need to improve the processes for reaching expert consensus on the clinical significance of new findings so that their ethical, social, and economic implications can be determined by the many sectors of society having a stake in them. NIH has been examining, this year, its methods and responsibilities for the evaluation of research developments. We are adding structure and more formality to these examinations. With expenditure of modest resources we believe so-called technology transfer between the researcher and some communities can be improved in important ways. We have nearly completed an analysis of this subject and shortly copies will, of course, be sent to this committee.

CLINICAL TRIALS

The best assessment tool—and the most costly, I am afraid—for the results of most clinical research is the so-called clinical trial—that is, trying out a new procedure in practice under previously agreed and carefully monitored conditions. These practical scientific exercises

have long been part of NIH research. They are becoming increasingly important. In fiscal year 1975, the latest year for which complete figures are available, NIH supported over 755 clinical trials which, by the time they are completed, will cost more than $640 million. Our involvement in clinical trials steadily rises and the future support we have now committed climbs as well. Each year we must carefully determine how much farther and how rapidly we can and should go in this direction. The first set of decisions involve the wise choice of what clinical research developments to test by a clinical trial. Part of the decision must also be the cost. Setting the priorities requires that we also take care to preserve the capacity to seek new knowledge in areas still far away from practical use in medicine. Because in many instances the clinical trial also makes service possible for patients, we must be sure that, when the scientific question has been answered, the purely service aspects of the clinical work undertaken will be continued under other auspices. This allows the research resources, both money and personnel, to turn to other pressing scientific problems. How to amortize the costs of massive clinical studies is a long-range problem for us in budgeting the resources made available to us.

I would like to mention another problem that exists in a vigorous enterprise like biomedical science—the coordination of research that extends across the activities of many institutes. It is a sign of progress when knowledge grows across institute boundaries and makes them fuzzy.

DIABETES

Among the new and expanded legislative mandates for NIH, the two that have the broadest impact are those for diabetes and arthritis. There is now an overall NIH involvement of considerable magnitude and scope in diabetes research, as you are aware, Mr. Chairman. To insure that this broad approach is properly coordinated, I have established an NIH Diabetes Coordinating Committee to complement the activities of the older interagency committee and the Diabetes Board already established under Public Law 93–354. We are prepared to describe for you, or submit for the record, the degree to which the present budget allows us to implement the diabetes plan.

ARTHRITIS

Research on arthritis is similarly dispersed throughout NIH. We have completed a review of all our arthritis-related programs as part of our preparation of the 1979–83 forward plan and I have appointed an NIH coordinating committee similar to the one for diabetes. The advisory boards required by legislation are holding their first meetings this month.

OTHER FIELDS FOR COORDINATION

There are other fields in which a more deliberate approach to coordination is also desirable. We have a Nutrition Coordinating Committee and are drawing up a comprehensive nutrition plan in order to develop a more orderly approach to this field. Nutrition research has

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seen development of much new knowledge over the years which now needs more synthesis into practical ways to advise healthy and sick people better on what they should eat. We have also just set up an NIH Epidemiology Committee to husband the scarce and valuable resources in this vital area. I want it also to suggest ways of overcoming the critical shortage of chronic-disease epidemiologists which coincides with a rapidly growing need for sophisticated epidemiologic studies. There is an NIH Genetics Coordinating Committee and the Secretary has been asked to establish a DHEW Interagency Genetics Coordinating Committee, with NIH acting initially as the lead agency, to guide the implementation of the new Genetic Diseases Act which calls for many activities—including services like screening, routine treatment, and genetic counseling—that lie outside the purview of NIH.

RECOMBINANT DNA RESEARCH

A particular aspect of genetic research that has recently attracted a lot of public attention is the work that is beginning to be done with what are called 'recombinant DNA techniques.' The much-publicized dangers of doing this research remain speculative, as do some of the much-publicized and hoped-for benefits. Nevertheless, I think that DNA, which means deoxyribonucleic acid, is an extraordinarily important area for research at present.

As you know, DNA is the bearer of the genetic code in all living organisms and determines their inherited characteristics. Recombination or changes in DNA occur spontaneously in nature: Such changes have made possible the never-ending process of evolution; and faults in DNA are responsible for inherited disabilities and much predisposition to disease. Research on recombinant DNA holds the promise of becoming a very powerful tool in the conquest of disease. There is good reason to believe that genetic research—of which the present work on laboratory recombination of DNA is only a small part—will have as sweeping an impact on health and the practice of medicine during the last quarter of the 20th century as the new science of bacteriology had during its first quarter. To insure that recombinant DNA techniques are used with due regard for safety, the international scientific community has reached agreement that a common set of standards shall govern the use of them all over the world. NIH has developed guidelines which are now mandatory for all laboratories using recombinant techniques in research conducted by or supported by any Federal agency. These guidelines have also been adopted by the member industries of the Pharmaceutical Manufacturers Association, where most of the industrial work is being carried out. An Interagency Committee on Recombinant DNA Research, of which I am the Chairman, is now developing recommendations as to how Federal standards will be extended to use of the recombinant techniques throughout this country and how compliance is to be monitored and enforced. I expect the committee to make its first report during this month.

GOVERNANCE OF SCIENTIFIC PRACTICES

NIH has previously responded to legitimate public concerns by requiring the formation of review boards to oversee human experimenta-

tion, and animal care. It has developed guides to handling carcinogenic materials in the laboratory and now, with guidelines for genetic recombination experiments, begins a wider examination of ways to protect the workers and the public from other new experimental hazards. Such responsibilities are inescapable adjustments to the rising demand for safe governance of scientific practices. There is, in all this, a delicate requirement to assure public safety while not unnecessarily destroying capacity and opportunity for creative and necessary research.

These, Mr. Chairman, are a few of the problems whose resolution will have an important bearing on the future course of NIH but which, essentially, are not fiscal questions and are therefore not dealt with in our normal budget submissions. Because they are relevant to our program activities, I feel they should be brought to your attention. I am now ready, Mr. Chairman, to answer questions you and the other committee members may have.

NATIONAL EXPENDITURE ON BIOMEDICAL RESEARCH

Mr. FLOOD. Doctor, let's start off with trying to put the NIH budget in a proper perspective. Can you tell us what is the total level of expenditures in 1978 for biomedical research throughout the entire Federal Government?

Dr. FREDRICKSON. We are approximately 60 percent of the total Federal expenditure for biomedical research, so I would have to extrapolate from our 1978 budget of about $2.5 billion to about something beyond $3.5 billion for the total Federal Government.

Mr. FLOOD. All right; but how much more is going to be spent by the private sector?

Dr. FREDRICKSON. The total amount expected to be spent on biomedical research in 1978 is on the order of about $5 billion, Mr. Flood. Of that, probably only about 5 percent will come from private nonprofit sources. The other major source is the $1.4 billion which industry, primarily the pharmaceutical industry, is spending in drug and other product research related to pharmaceutical manufacture.

Mr. FLOOD. You are indicating that the total Federal expenditure for biomedical research will be about $3.5 billion. Out of the $3.5 billion, NIH is $2.3 billion. How much will be left for the private sector, about $1.5 billion?

Dr. FREDRICKSON. About $2 billion, sir.

COORDINATION WITH OTHER AGENCIES

Mr. FLOOD. All rght; now you are the director. How do you, as the director of NIH, coordinate the biomedical research efforts of your outfit, with biomedical research at the other non-HEW agencies such as Defense and the Energy Research and Development Agency? Do you talk with them at all?

Dr. FREDRICKSON. Yes, we do. A most prominent one is our relationship with the National Science Foundation, which funds about $60 million in research related to biology that is very close to the same kind of basic science that we also support. We have a good relationship, particularly through our Institute of General Medical Science, and we tend the boundary carefully. We watch for overlap and make sure there are no gaps.

Mr. FLOOD. With ERDA, as well as Defense?

Dr. FREDRICKSON. We have less formal relationships with Defense but we know what the other agencies—such as ERDA and NASA—are doing. We have frequent relationships with them at the program level where they may be supporting activities that are closely related to ours.

Mr. FLOOD. This has to do with the budget structure. Is there sufficient interagency planning at the very time the budget is prepared, to permit the assigning of mutual tasks of interest to the agency that is most qualified to handle that problem, or is each department constructing its own budget, each independent of the other?

Dr. FREDRICKSON. I think that is a very important question.

Mr. FLOOD. That is why I asked it; I know that.

Dr. FREDRICKSON. And I think that we have recognized that this kind of interagency activity is absolutely essential.

Mr. FLOOD. We agree with that.

Dr. FREDRICKSON. And we do achieve this in a variety of ways.

Mr. FLOOD. You do, very much?

Dr. FREDRICKSON. Yes, and we are doing more of it.

Mr. FLOOD. You think it should be done?

Dr. FREDRICKSON. Yes, I do. We have very close relationships, of course, with ADAMHA, because mental health research is conducted intramurally at NIH. I would point out that we maintain a system, called the CRISP system, at NIH in which we maintain records on all the biomedical research done by ADAMHA. We maintain the records for the FDA. We have common records for certain aspects of the programs of the National Science Foundation with particular regard to recombinant DNA research. We are engaging in talks with the Veterans' Administration. Our clinical trials coordinating committee wants also to do the same with the ADAMHA, and with the Veterans' Administration. So we are opening up channels of communication with the National Center for Health Statistics. We do a lot of epidemiology and they do a great deal. We want to be sure that we use those resources wisely.

ADEQUACY OF NIH BUDGET

Mr. FLOOD. The overall increase at NIH in 1978 is pretty small, about 1.8 percent. However, the regular research grant program is getting a 5.8-percent increase. Some people say that by no means this increase will ever meet the cost of inflation and that being so, NIH is not going to be able to support any new research activities.

What is your reaction to this? Do you think this an adequate budget?

Dr. FREDRICKSON. Given the priorities against which the total administration requirements have been set, I think that we have the opportunity here to do a great deal of profitable and useful research, Mr. Flood.

NEW RESEARCH GRANTS

Mr. FLOOD. I know, but I asked two questions. The last one is the conclusion. Are you going to be able, plus keeping in mind inflation, to support any new research activities?

Dr. FREDRICKSON. We will support some new research activities. Each year a large fraction of our grants, approximately a quarter, come up for renewal and in the competitive process we will be able to fund new grants. In fact, we regard this as absolutely essential in an enterprise like health research.

ANALYSIS OF BIOMEDICAL RESEARCH IN UNITED STATES

Mr. FLOOD. You remember you made quite a point last year, and we were told NIH is about to complete work on a comprehensive analysis of programs and resources of all the biomedical research in the United States.

Have you completed the analysis?

Dr. FREDRICKSON. No, Mr. Chairman, we have not completed an analysis of the biomedical research resources, but we are coming closer to a better understanding of the total organism than I think we ever have.

Mr. FLOOD. Did you go pretty far with it? What did you learn from the study so far? Are we fully utilizing all of our biomedical resources? Do we have an excess capacity from your analysis?

Dr. FREDRICKSON. I have no question but that we do not have an excess capacity to do biomedical research in this country.

Mr. FLOOD. Did you come up with any kind of inventory of the biomedical research that is being conducted in the private sector?

Dr. FREDRICKSON. We are aware of the general display of the total distribution. Those were the figures I gave you earlier.

Mr. FLOOD. When do you think the report is going to be finished? You are not going to have it finished in time to have a copy of the final report in the record, are you?

Dr. FREDRICKSON. I think it will take several more months. But we might be able to provide you some preliminary information for this particular record.

Mr. FLOOD. Go as far as you can.

[The information follows:]

DOLLARS FOR HEALTH RESEARCH AND DEVELOPMENT: 1968-1975

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HIGHLIGHTS

Background

- Between 1960 and 1975, national support of medical and health-related R&D rose from $0.90 billion in 1960 to $4.61 billion in 1975, or at an average annual rate of 11.5 percent (Table A-1). A decline in the growth rate is apparent, however: The 1960-1969 period experienced an average annual growth of 13.3 percent; the 1969-1975 period, 8.9 percent.

- The five-fold rise in current dollars over the 15-year period was severely eroded by inflation: In terms of constant dollars, it was limited to 2-1/2 times the 1960 figure--an average annual growth rate of 6.6 percent (Chart 2-1c).

- During the 1965-1975 decade health R&D increased not only its relative share of total R&D from 9 percent to 13 percent, but also rose slightly in terms of GNP. However, relative to national health expenditures, it declined from a high of 4.9 percent in 1966 to 3.7 percent in 1975--a decrease attributable to burgeoning health-care expenditures (Table A-2).

- Over the decade, Federal agencies funded about three-fifths of national health R&D, and State governments 6-8 percent. Industry's relative share rose from 24 percent in 1965 to 29 percent in 1975 whereas the proportion from the private nonprofit sector--foundations, voluntary health agencies, and other private contributors--declined from 8 percent to 5 percent (Table A-3).

The 1968-1975 Period

- During the period specifically covered by this report (1968-1975), Federal support rose from $1.58 billion to $2.80 billion, a 77 percent increase. The Public Health Service of the Department of Health, Education, and Welfare (HEW) obligated $2.12 billion in FY 1975, of which $1.85 billion represented NIH support. Non-HEW agencies contributed $637 million, a 44 percent increase over FY 1968 (Table A-5).

- The relative share of the National Institutes of Health in Federal health R&D grew from 55 percent in FY 1968 to 66 percent in FY 1975, while the percentages for other Public Health Service agencies (PHS), Department of Defense, Energy Research & Development Administration, and National Aeronautics & Space Administration decreased (Table A-5).

- Between 25 percent and 30 percent of overall Federal health R&D was performed within Federal establishments themselves. About 16-20 percent of NIH R&D funds were spent in in-house or other Government research installations. For agencies outside HEW, intramural research accounted for some 45-50 percent due to the large in-house R&D efforts of the Departments of Agriculture and Defense, and the Veterans Administration. In fact, these three agencies together accounted for over 75 percent of non-HEW intramural health R&D in FY 1975 (Tables A-6 and A-7).

- Academic institutions continued their role as the single largest group performing health R&D. In FY 1975, they received $1.4 billion, or nearly half of the Federal health R&D support. NIH funds, which represented 71 percent of academic health R&D support in FY 1968, rose to nearly 80 percent by FY 1975 (Table A-15).

    - Within the academic framework, medical schools performed an increasing share of health R&D: In FY 1968, they were awarded 52 percent of the then $727 million academic health total; in FY 1975, 61 percent of $1.3 billion. This two-fold increase in medical school R&D funds was almost entirely attributable to NIH (Tables 4-3 and 4-5).

    - Medical school research funds were relatively concentrated, with 30 of the schools receiving nearly two-thirds of the medical school total (Table 4-3).

- Private nonprofit institutions were the second largest recipient group of Federal health R&D funds in 1975 (13 percent), followed by industry (9 percent), and State and local government entities (2 percent) (Table A-7).

- Funds under contracts increased from 28 percent of Federal extramural health R&D to 35 percent between FY 1968 and FY 1975, reflecting the more mission-oriented approach of the Public Health Service, specifically shifts in NIH. For non-HEW agencies, contracts made up approximately 80 percent of extramural R&D throughout the period (Table A-9).

- Research per se--as opposed to development--constituted 88 percent of the Federal health R&D effort (Table A-13). This distribution contrasted sharply with that of the overall Federal R&D effort where only 36 percent represented research. The difference in emphasis is attributable to the high development costs encountered by DOD, ERDA, and NASA, which together supported about 90 percent of the development in the total R&D area.

- California and New York, in that order, led all other States by a wide margin in Federal health R&D support to academic institutions. These two States received $382 million in FY 1975, or 29 percent of all academic health R&D. In terms of medical school R&D support only, however, New York ranked first. The reversal in rank order occurred because in New York 73 percent of academic health R&D was performed by medical schools; in California, only 59 percent of academic health R&D was carried out at medical schools. The next three States in order of support were Massachusetts, Pennsylvania, and Texas (Table A-17).

I. INTRODUCTION

Purpose and and Scope

This report is a summary description of medical and health-related R&D resources funded through government and private sources during the 1968-1975 period. It thus constitutes an update and extension of *Resources for Medical Research* reports published in past years (see inside back cover).[1]

In order to provide a historical framework in which to interpret the 1968-1975 data as well as to incorporate several revisions made for the earlier series, data presented in Section II (National Trends) go back to 1960, with occasional references both in that Section and in other parts of the report to the mid-1950's when this country witnessed a considerable increase in emphasis on biomedical research. Data for earlier periods, however, must be viewed as general indicators rather than as definitive figures.

Areas Covered by this Report

The data covered in this report are presented in three sections: Section II covers aggregate totals on health R&D funded by Federal, State, industry, and private nonprofit sources; distribution of health R&D by sector performing the research; relationship of current and constant dollars; and a comparison of health R&D with selected economic variables. Sections III and IV provide greater detail on the Federal role in health research. Section III presents an overview of DHEW and other agency funding patterns during the 1968-1975 period, also relating health R&D to the total R&D effort. Section IV deals with Federal support to medical schools and to institutions of higher education as a whole, for it is in the academic world, and increasingly at medical schools themselves, that so much of the Federally funded health R&D effort is performed. Included in Section IV are analyses of changes (or lack of changes) in concentration patterns, support of public vs. private institutions, and geographic distribution.

Health R&D Defined

The general definition of research and development is identical to the one employed by the National Science Foundation (see Technical Note). Within this broader context, medical and health-related research and development--referred to as "health R&D" in this report--focus on the following areas:

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[1] Two recent NIH publications, one on foundations and one on voluntary health agencies, provide greater detail on the health R&D activities of these groups. In addition, separate reports are issued on DHEW obligations to academic institutions, medical and other health-professional schools, covering not only R&D but support in other areas--fellowships and training, capitation grants, etc. (see inside back cover).

1. The causes, diagnosis, treatment, control, prevention of and rehabilitation relating to, the physical and mental diseases and other killing and crippling impairments of mankind;

2. The origin, nature and solution of health problems not identifiable in terms of disease entities;

3. Broad fields of science where the research is undertaken to obtain an understanding of processes affecting disease and human well being;

4. All aspects of the organization and delivery of health services;

5. The development of improved methods, techniques, and equipment for research, diagnosis, therapy, rehabilitation, and promotion of public health.

Good data for biomedical R&D as opposed to other types of health R&D are not available because of definitional difficulties. However, it is clear that the vast majority of funds fall under the biomedical heading: All NIH research is biomedical and so is much of research performed by the Alcohol, Drug Abuse, & Mental Health Administration (ADAMHA), a part of DHEW Public Health Service; the Veterans Administration (VA); Energy Research & Development Administration (ERDA); National Aeronautics and Space Administration (NASA); and the Department of Defense (DOD); i.e., agencies contributing the bulk of the Federal health research effort. Industry support as well as that of private nonprofit organizations can also be considered virtually entirely in the biomedical area.

It should be noted that with one exception, the terms "research" and "R&D" are used interchangeably. The only exception is in the discussion on Fields of Science (Section III) from which development has been specifically excluded.

II. NATIONAL HEALTH R&D TRENDS IN PERSPECTIVE

Introduction

Substantial growth in national health R&D occurred during the 1964-75 decade, reflecting the increased emphasis on improving the nation's health and well-being. This growth was accomplished through the support of all sectors--Federal and State governments, industry, foundations and voluntary health agencies, and other private philanthropic sources. Together, the sectors achieved an impressive total of $4.6 billion in 1975, 2-1/2 times the $1.9 billion spent a decade earlier, and a five-fold increase over 1960 (Chart 2-1). The increase, however, was mitigated to a considerable extent by inflation. In constant dollar terms, it was limited to slightly less than 1-1/2 times the 1965 figure (Chart 2-1c).

Sources of National Health R&D Support

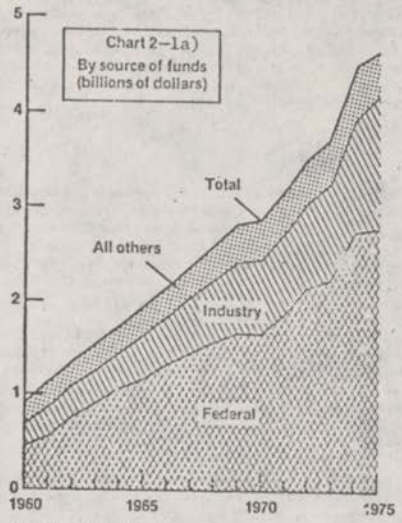
In much of health research, factors other than economic ones dominate particularly the early phases, and economic benefits of basic research cannot readily be captured by the performing sector. Thus, the Federal Government has continued to carry the major burden of the support, providing by 1975 about three-fifths of total health R&D funds expended. Industry contributed another quarter, and the nonprofit sector (private nonprofit institutions as well as State governments) the remainder (Chart 2-1a).

Growth has not proceeded evenly over the years. The rapid expansion carried over from the mid-1950's peaked in 1962. Although the industry growth rate continued to climb virtually each year through 1969, increases in Federal support proceeded at a far slower pace. Between FY 1969 and FY 1970, Federal health R&D funding declined 0.4 percent.[2] As in that year the industry growth rate also dropped precipitously, national health R&D rose by only 1.6 percent--considerably less than the 6 percent inflation rate.

Since 1970, national health R&D support has risen nearly 50 percent--but only 20 percent when account is taken of inflation. Furthermore, annual changes have been somewhat erratic. An 11 percent growth for both 1971 and 1972 was followed in 1973 by one of 6.2 percent. In that year, the Administration did not obligate substantial sums ($162 million for NIH alone) appropriated by Congress, resulting in a 3.6 percent increase for Federal health R&D over the year before, somewhat less than the 4.5 percent inflation rate. The withheld funds, however, were released for obligation in 1974 (with some carryover to 1975) and, together with the 1974 appropriations, precipitated a Federal growth for 1974 of 24 percent over 1973. Coupled with a lesser increase in industry funding, growth in national R&D for that year totaled 20 percent. Between 1974 and 1975, the pattern changed once more. A Federal

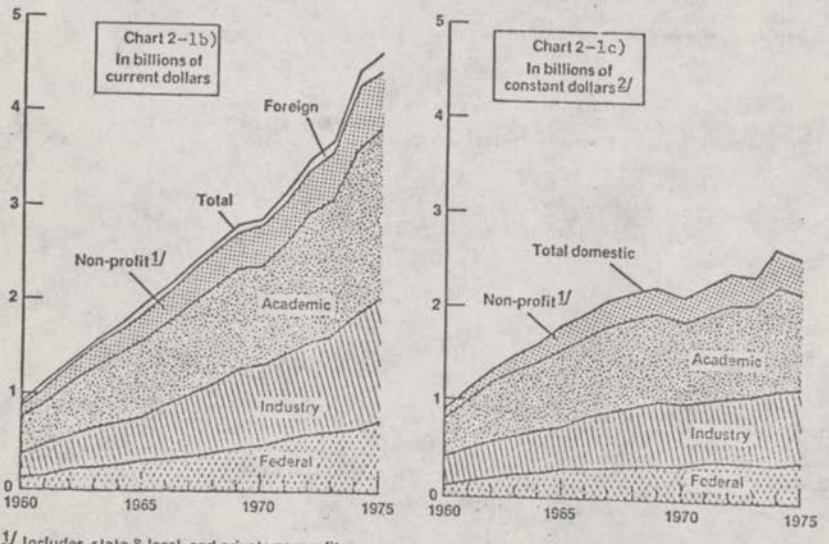
[2] This decline was not limited to health portion of Federal R&D support: Total R&D support by non-HEW agencies declined 2 percent between FY 1968 and FY 1969 and another 0.5 percent between FY 1969 and FY 1970.

Chart 2-1. National Health R&D, by Source of Funds, and by Performer in Current and Constant Dollars, 1960-1975



Source: Table A-1.

By Performance Component



1/ Includes state & local, and private nonprofit.

2/ Biomedical R&D deflator (1965 = 100) not considered applicable to R&D performed abroad.

increase of 2 percent and an industry increase of 11 percent resulted in an overall 5 percent growth. In constant dollars, however, this translates into a 5 percent decline. Preliminary 1976 and estimated 1977 figures indicate a 10 percent growth in national support for each of these years, or a "real" annual increase of about 3 percent.

In sum, although year-to-year fluctuations in funding patterns of any one sector have indeed influenced the short-term relative share of the other contributing sectors, over the entire 1965-1975 decade little change in relative distribution took place. The Federal share rather consistently constituted about three-fifths of the total. A rise in industry's share from about 24 percent to 29 percent occurred at the expense of the private nonprofit sector, whose support dropped from 8.3 percent of the national total in 1965 to 5.4 percent in 1975 (Table A-1).[3]

Performers of Health R&D

The performer pattern of health R&D differs markedly from the one shown for source of funds (Chart 2-1b). R&D at Federal establishments accounted for a rather steady 16 percent of the national total during the 1960-1975 period with a slight rise during 1970-1973. Academic institutions continued their traditional role as the largest single group performing health R&D, utilizing about two-fifths of all funds during the period, but were followed closely by industry with just under 30 percent. Private nonprofit institutions, on the other hand, performed only about 11 percent of all health research.

However, as can be seen from the data on Table A-3, while each sector's performance share remained comparatively stable over the period, the relative importance of the Federal Government as a source of funds has increased. In 1960, for example, little more than half the R&D performed by academic and other nonprofit institutions was funded from Federal sources; in 1975, nearly four-fifths of the research support recorded in the time series for both these groups stemmed from the Federal Government. Even for industry, which has traditionally supported most of its own health research, the Federal share nearly doubled over the years and in 1975 accounted for about 20 percent of the $1.4 billion used by industry within the United States.

In recent years, an increase has also taken place in relative share of funds spent abroad (no data are available for comparable monies flowing into the United States from other countries). Throughout the years, the Federal Government funded research overseas, in part utilizing U.S.-owned foreign currencies as authorized under Public Law 480. Although total Federal dollars spent abroad nearly tripled to $27 million between 1960 and 1962, only occasional shifts have taken place since then. Private nonprofit-institution spending overseas rose from an estimated

[3] See also Koleda, M.S., R. Smith, D. Bourque, "Federal/Foundation Spending: A Look at Patterns, *Foundation News*, Vol. 16, No. 4, July/August 1975, pp. 28-35.

$10 million in 1960 to $17 million by 1975. On the other hand, industry health R&D performed in other countries for pharmaceutical companies (no data are available for the spending patterns of other types of industry-funded health research) increased from $6 million to $57 million between 1960 and 1971, or at an average annual rate of 23 percent. Beginning in 1971, drug-company research abroad has risen at an average annual rate of 29 percent to $158 million in 1975, with a particularly dramatic increase of 65 percent between 1972 and 1973.

The Economic Context of Health R&D

Comparison of health R&D with three commonly used variables--Gross National Product (GNP), total R&D for all functions, and national health expenditures--produces a somewhat divergent set of relationships. Health research has increased over the years in terms of the first two, but--during the past decade at least--has declined as percent of health expenditures.

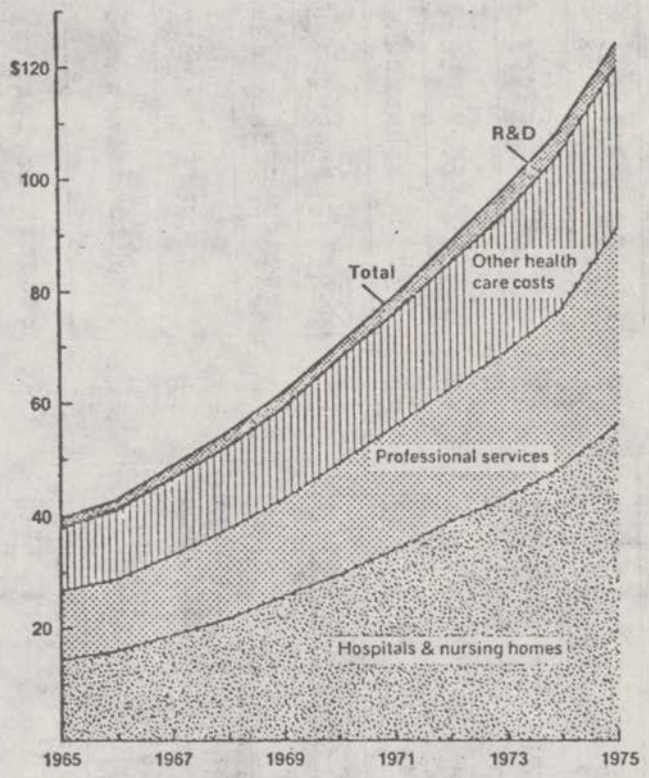
From the mid-Fifties through 1965--a period of rapid expansion of Federal (specifically NIH) health R&D support--health research rose from 4.1 percent of total R&D to 9.1 percent; from 1.5 percent of health expenditures to 4.8 percent; and from 0.07 percent of GNP to 0.28 percent--a two-three, and four-fold relative increase, respectively (Table A-2). By 1975, health R&D had grown to 13 percent of total R&D and to 0.32 percent of GNP. With respect to total R&D, a contributing factor in the changed relationship of health research (as well as of other civilian-oriented R&D) was the decline in relative importance of the defense and space programs. Defense-related R&D dropped from more than 50 percent of U.S. total R&D during the 1957-1960 period to under 30 percent by 1975 although Federal support in absolute terms continued to grow. Federal funds for the space program, on the other hand, after peaking in 1966, declined in absolute terms as well.

A different picture emerges when health research is examined in relation to total health expenditures. Since 1965 such expenditures have tripled, a growth stimulated by the enactment of the Medicare and Medicaid programs, by inflation in the health care industry, and also by technological advances permitting more extensive--but more expensive--care.[4] As a result of this rise, health research as percent of health expenditures had gradually declined from a high of 4.9 percent in 1966 to 3.7 percent in 1975.

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[4] The relative influence of each of the several factors contributing to increased national health expenditures is difficult to ascertain. For a detailed discussion of health expenditures, see Nancy L. Worthington, "National Health Expenditures, 1929-1974," *Social Security Bulletin*, February 1975. Please note that the health R&D figures (and therefore total health expenditures) presented in that report have been adjusted for use in this publication in order to utilize comparable R&D data (see Technical Notes).

Chart 2-4. National Health Expenditures, by Type of Cost, 1965-1975 (Billions of Dollars)



Source: Social Security Administration and NIH.

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Table A-1. National Health R&D, by Source of Funds, 1950-1975

(Millions of dollars)

Year	Total	Government			Industry	Nonprofit organizations			
		Total	Federal	State		Total	Foundations	Voluntary health agencies	Other
1950	$ 161	$ 73	$ 73	$ -	$ 51	$ 37	$12	$ 9	$16
1955	261	144	139	5	62	55	14	17	24
1960	900	526	448	78	253	121	40	36	45
1961	1,096	655	574	81	312	129	40	37	52
1962	1,337	866	782	84	336	135	40	38	57
1963	1,526	1,008	919	89	375	143	41	40	62
1964	1,690	1,140	1,049	91	400	150	43	42	65
1965	1,884	1,277	1,174	103	450	157	42	45	70
1966	2,104	1,428	1,316	112	510	166	44	47	75
1967	2,338	1,581	1,459	122	580	177	46	54	77
1968	2,553	1,707	1,582	125	661	185	49	57	79
1969	2,762	1,817	1,674	143	754	191	47	61	83
1970	2,805	1,817	1,667	150	795	193	47	61	85
1971	3,107	2,040	1,877	163	860	207	57	63	87
1972	3,454	2,326	2,147	179	925	203	53	63	87
1973	3,667	2,426	2,225	201	1,033	208	51	70	87
1974	4,390	2,976	2,754	222	1,187	227	54	84	89
1975	4,610	3,038	2,799	239	1,322	250	64	93	93

Source: National Institutes of Health

Table A-2. Gross National Product, National Health Expenditures, and National Support of Total R&D and of Health R&D, 1955-1975

(Dollars in billions)

Year	GNP	National health expenditures	R&D			Medical and health-related R&D as percent of:		
			Total[1]	Health		GNP	Health expenditures	Total R&D[2]
				Total	Domestic			
1955	$ 381.0	$ 17.4	$ 6.2	$0.3	$0.3	0.069	1.5	4.1
1960	498.3	26.2	13.5	0.9	0.9	0.181	3.4	6.5
1964	616.4	35.9	18.9	1.7	1.6	0.274	4.7	8.7
1965	658.0	39.4	20.0	1.9	1.8	0.286	4.8	9.1
1966	722.4	42.7	21.8	2.1	2.0	0.291	4.9	9.3
1967	773.5	48.6	23.1	2.3	2.3	0.302	4.8	9.8
1968	830.2	54.5	24.6	2.6	2.5	0.308	4.7	10.0
1969	904.2	61.6	25.6	2.8	2.7	0.305	4.5	10.4
1970	960.2	70.2	25.9	2.8	2.7	0.292	4.0	10.5
1971	1,019.8	78.4	26.6	3.1	3.0	0.305	4.0	11.3
1972	1,111.8	88.1	28.3	3.5	3.3	0.311	3.9	11.8
1973	1,238.6	96.8	30.3	3.7	3.5	0.296	3.8	11.6
1974	1,361.2	108.2	32.3	4.4	4.2	0.323	4.1	13.0
1975	1,452.3	123.9	34.6	4.6	4.4	0.317	3.7	12.7

[1]Excludes R&D performed abroad with U.S. funds.
[2]Percentages are based on health R&D funds spent within the U.S. (domestic health R&D).

Sources: National Health Expenditures: *Social Security Bulletin*, January, February, or March of each year, with R&D, and therefore totals, adjusted by NIH; GNP: Department of Commerce *Survey of Current Business, January 1976*, with quarterly series summed by fiscal year; Total R&D: NSF, *National Patterns of R&D Resources, 1953-77*; Medical and health-related R&D: National Institutes of Health.

Table A-3. Transfers of Funds of National Health R&D Support, Distributed by Source, 1960-1975 (1)

(Millions of dollars)

	Total Health R&D	Federal: Total funds used	Federal: Fed. govt.	State and local: Total funds used	State and local: Fed. govt.	State and local: State govt.	Industry: Total funds used	Industry: Fed. gov(4)	Industry: Industry	Academic institutions: Total funds used	Academic institutions: Fed. govt. (5)	Academic institutions: State govt.	Academic institutions: Industry	Academic institutions: PNP (2)	Other PNP (2): Total funds used	Other PNP (2): Fed. govt. (5)(6)	Other PNP (2): Industry	Other PNP (2): PNP (2)	Foreign: Total funds used	Foreign: Fed. govt.	Foreign: Industry	Foreign: PNP (2)
1960	$ 900	$ 138	$ 138	$ 17	$ 5	$ 12	$ 257	$ 27	$ 230	$ 343	$ 200	$ 65	$ 7	$ 71	$ 119	$ 69	$ 10	$ 40	$ 26	$ 10	$ 6	$ 10
1961	1,096	164	164	21	8	13	322	34	288	418	266	67	8	77	139	68	9	42	32	15	7	10
1962	1,337	215	215	21	8	13	354	48	306	536	375	70	9	82	165	110	12	43	46	27	9	10
1963	1,526	250	250	30	16	14	397	58	339	606	434	74	10	88	190	133	12	45	53	29	14	10
1964	1,690	272	272	36	21	15	438	79	359	673	495	75	12	91	215	154	13	43	56	29	16	11
1965	1,884	305	305	41	23	18	483	87	396	749	555	84	14	96	244	178	15	51	62	27	25	10
1966	2,104	345	345	53	31	22	560	116	444	822	613	88	14	103	257	187	18	52	67	24	32	11
1967	2,338	369	369	57	31	26	653	135	518	918	699	94	16	109	266	200	10	56	75	27	36	12
1968	2,553	403	403	79	49	30	725	138	587	983	759	93	18	113	277	205	14	58	86	31	42	13
1969	2,762	458	458	81	48	33	813	137	676	1,035	792	108	18	117	281	205	15	60	94	36	45	13
1970	2,805	489	489	86	49	37	828	122	706	1,024	775	110	21	118	291	214	16	61	87	22	52	13
1971	3,107	568	568	93	52	41	889	129	760	1,127	859	119	24	125	318	233	19	66	112	40	57	15
1972	3,454	609	609	107	60	47	964	159	805	1,303	1,025	129	27	124	353	267	23	64	116	31	71	14
1973	3,787	629	629	129	79	50	1,042	176	866	1,342	1,040	148	28	126	371	281	22	68	134	24	117	13
1974	4,390	668	668	146	92	54	1,230	248	982	1,678	1,348	164	32	134	477	373	26	78	191	29	147	15
1975	4,610	716	716	108	54	54	1,350	256	1,094	1,743	1,375	181	39	148	487	372	31	84	205	30	159	17

Date:02/05/77

(1) Data are based on reports by source of funds.

(2) Private nonprofit. Includes foundations, voluntary health agencies, institutions" own funds, and other philanthropic and nonprofit sources.

(3) Excludes R&D funded by foreign sources.

(4) Includes funds from voluntary health agencies to Federal Government of $0.5-1 million in certain years.

(5) Includes data for Federally funded R&D centers (FFRDC"s) administered by industry, academic institutions, or other nonprofit organizations, respectively (see technical notes for details).

(6) Includes State government funding.

SOURCE: National Institutes of Health.

Table A-5. Federal Obligations for Total R&D, and for Health R&D by Selected Agencies, FY 1968-1975

(Dollars in millions)

Agency	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	FY 1974	FY 1975
Total R&D	$15,921.4	$15,641.1	$15,340.3	$15,564.2	$16,511.9	$16,821.2	$17,438.2	$19,044.3
Health R&D	1,581.9	1,674.1	1,666.6	1,876.6	2,147.3	2,225.3	2,753.6	2,798.9
Health as percent of total	9.9%	10.7%	10.9%	12.1%	13.0%	13.2%	15.8%	14.7%
Department of Health, Education, and Welfare, total	1,139.0	1,191.4	1,177.0	1,316.0	1,584.3	1,609.9	2,092.2	2,162.2
National Institutes of Health	864.0	893.0	873.3	1,038.9	1,271.3	1,323.2	1,736.8	1,845.5
Other Public Health Service	229.1	249.9	270.0	247.6	275.9	255.4	315.2	278.5
Other Department of Health, Education, and Welfare	45.8	48.7	33.8	29.4	37.0	31.3	40.2	38.2
All other agencies	443.0	482.6	489.5	560.6	563.1	615.4	661.4	636.7
Department of Agriculture	45.8	48.8	50.1	60.3	67.3	61.1	59.7	61.4
Department of Defense	114.0	117.5	124.9	124.2	126.0	126.6	119.0	115.9
Department of Interior	2.7	4.4	12.4	22.6	34.9	33.3	33.3	9.0
Department of Transportation	4.5	7.3	9.7	41.9	39.0	65.0	64.8	11.9
Energy Research & Development Administration	95.0	97.9	104.2	104.9	102.7	110.6	121.4	163.9
Environmental Protection Agency[1]	–	–	–	13.1	14.5	20.3	18.8	38.1
National Aeronautics & Space Administration	108.6	116.8	85.9	74.9	50.3	42.3	80.1	74.9
National Science Foundation	21.1	25.6	28.0	34.3	37.2	45.5	47.0	44.7
Veterans Administration	45.6	50.3	58.7	62.7	68.9	74.2	84.0	94.8
All other agencies	5.6	14.0	15.6	21.7	22.2	36.6	33.4	22.0

[1]Established in FY 1970.

Note: Detail may not add to totals because of rounding.

Sources: Total R&D, National Science Foundation; health R&D, National Institutes of Health.

Table A-6. Federal Health R&D Obligations, by Performance Component, FY 1968-1975

(Millions of dollars)

Fiscal year	Total	Intramural	Extramural							
			Total	State and local	Industry[1]	Academic institutions			Other private nonprofit[4]	Foreign
						Total	Institutions[2]	FFRDC[3]		
1968	$1,581.9	$402.2	$1,179.8	$50.6	$138.3	$ 757.7	$ 727.3	$30.5	$202.6	$30.5
1969	1,674.1	456.5	1,217.6	47.7	137.4	792.1	761.8	30.3	203.9	36.4
1970	1,666.6	488.3	1,178.3	49.0	121.7	775.1	744.3	30.8	211.1	21.4
1971	1,876.6	566.5	1,310.1	51.5	128.7	859.4	829.4	30.0	229.7	40.9
1972	2,147.3	608.2	1,539.1	60.2	158.8	1,025.4	994.2	31.2	264.0	30.8
1973	2,225.3	627.3	1,598.0	79.3	176.3	1,039.5	1,004.4	35.2	278.8	24.1
1974	2,753.6	667.9	2,085.8	91.6	248.4	1,347.0	1,305.4	41.6	369.7	29.1
1975	2,798.9	715.7	2,083.1	54.0	256.3	1,374.8	1,321.2	53.6	368.1	30.0

[1]Includes Federally Funded Research and Development Centers (FFRDC's) administered by industry.

[2]Institutions of higher education proper.

[3]FFRDC's administered by institutions of higher education.

[4]Includes FFRDC's administered by private nonprofit institutions.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-7. Federal Obligations for Health R&D
by Agency and Performer, FY 1975
(Millions of dollars)

Agency	Total	Intramural (Fed.)	Extramural								
			Total	State and local	Industry	Institutions of higher education				Other private nonprofit	Foreign
						Total	IHE proper	Medical schools[1]	FFRDC[2]		
Total	$2,798.9	$715.7	$2,083.1	$54.0	$256.3	$1,374.8	$1,321.2	$(837.5)	$53.6	$ 368.1	$ 30.0
Department of Health, Education, and Welfare, total	2,162.2	425.9	1,736.4	52.0	128.6	1,198.1	1,193.6	(808.5)	4.5	323.2	26.4
National Institutes of Health	1,845.5	330.1	1,515.4	33.7	122.9	1,067.6	1,063.1	(750.7)	4.5	272.5	18.7
Other Public Health Service, total	278.5	89.4	189.1	16.0	11.7	116.7	116.7	(50.2)	-	39.0	5.5
Alcohol, Drug Abuse, and Mental Health Administration	139.4	23.2	116.2	14.8	3.8	76.9	76.9	(38.5)	-	19.5	1.3
Center for Disease Control	42.6	27.9	14.7	-	3.6	4.5	4.5	(0.6)	-	5.2	1.3
Food and Drug Administration	35.9	23.1	12.8	0.1	2.5	8.4	8.4	(1.2)	-	1.1	0.7
Health Resources Administration	43.3	10.9	32.4	0.7	1.6	19.8	19.8	(7.8)	-	8.9	1.4
Health Services Administration	17.3	4.3	13.0	0.4	0.3	7.1	7.1	(2.0)	-	4.4	0.8
Other DHEW, total	38.2	6.3	31.9	2.2	2.0	13.7	13.7	(7.7)	-	11.7	2.2
Office of Human Development	16.8	0.6	16.2	1.0	-	10.1	10.1	(7.6)	-	3.3	1.8
Office of the Secretary	6.3	0.4	5.9	-	-	0.9	0.9	-	-	5.0	-
Social and Rehabilitation Service	3.6	0.3	3.3	1.2	1.1	0.1	0.1	-	-	0.5	0.3
Social Security Administration	11.5	5.0	6.4	-	0.9	2.6	2.6	(0.1)	-	3.0	-
Other Departments and agencies	636.7	289.9	346.8	2.1	119.6	176.7	127.6	(29.0)	49.1	44.8	3.6
Department of Agriculture	61.4	46.6	14.8	-	0.4	12.8	12.8	(0.1)	-	0.1	1.6
Department of Commerce	5.5	5.4	0.1	-	0.1	-	-	-	-	-	-
Department of Defense	115.9	83.7	32.2	-	9.4	15.9	15.9	(2.9)	-	6.1	0.8
Department of the Interior	9.0	5.9	3.0	-	0.9	2.2	2.2	-	-	-	-
Department of Labor	2.0	0.2	1.8	-	1.8	-	-	-	-	-	-
Department of State	6.4	0.1	6.3	-	-	2.7	2.7	(0.2)	-	3.2	0.5
Department of Transportation	11.9	3.5	8.5	1.1	5.1	2.1	2.1	-	-	0.3	-
Consumer Products Safety Commission	7.6	4.9	2.6	0.4	0.3	0.6	0.6	-	-	1.3	-
Energy Research & Development Admin.	163.9	7.6	156.3	0.1	39.4	88.3	39.3	(13.3)	49.0	28.1	0.4
Environmental Protection Agency	38.1	25.5	12.6	0.5	6.4	3.3	3.3	(0.5)	-	2.3	0.2
National Aeronautics & Space Admin.	74.9	10.9	64.0	-	54.8	8.8	8.8	(3.9)	-	0.4	-
National Science Foundation	44.7	2.1	42.5	-	0.8	38.8	38.8	(7.7)	0.1	2.7	0.1
Tennessee Valley Authority	0.5	0.5	-	-	-	-	-	-	-	-	-
Veterans Administration	94.8	92.9	1.9	-	0.3	1.1	1.1	(0.3)	-	0.4	-

[1]Included in "IHE, proper."

[2]Federally Funded Research and Development Centers administered by academic institutions.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-8. Federal Extramural Health R&D Obligations, by Funding Mechanism and Performance Component, FY 1968-1975

(Millions of dollars)

Extramural funding mechanism	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	FY 1974	FY 1975
Extramural R&D, total[1]	$1,179.8	$1,217.6	$1,178.3	$1,310.1	$1,539.1	$1,598.0	$2,085.8	$2,083.1
Grants, total	848.2	865.3	824.7	909.7	1,041.3	1,041.8	1,366.0	1,385.5
State and local	45.4	43.1	41.6	42.0	43.6	39.3	44.5	42.7
Industry[2]	-	-	-	-	-	0.3	0.1	0.8
Academic institutions, total	628.4	642.1	625.1	686.1	800.7	811.0	1,074.2	1,105.8
Academic institutions, proper	(628.4)[3]	(641.9)[3]	(625.1)[3]	(686.1)[3]	(799.9)[3]	(809.6)	(1,070.3)	(1,101.3)
Med. school component						*511.7*[4]	*679.0*[4]	*703.1*[4]
FFRDC's administered by academic institutions	-	(0.2)	-	-	(0.7)	(1.4)	(3.9)	(4.5)
Other nonprofit[2]	147.0	150.1	141.0	147.2	173.5	175.4	229.7	225.3
Foreign	27.4	30.1	17.1	34.4	23.4	15.7	17.4	10.9
Contracts, total	331.6	352.3	353.6	400.4	497.8	556.2	719.8	697.7
State and local	5.3	4.7	7.4	9.5	16.6	39.9	47.0	11.3
Industry[2]	138.3	137.4	121.7	128.7	158.7	176.0	248.3	255.4
Academic institutions, total	129.3	150.0	150.0	173.3	224.7	228.6	272.8	269.0
Academic institutions, proper	(98.8)[3]	(119.9)[3]	(119.2)[3]	(143.3)[3]	(194.2)[3]	(194.7)	(235.1)	(219.9)
Med. school component						*106.6*[4]	*130.9*[4]	*134.4*[4]
FFRDC's administered by academic institutions	(30.5)	(30.1)	(30.8)	(30.0)	(30.5)	(33.8)	(37.8)	(49.1)
Other nonprofit[2]	55.6	53.8	70.1	82.5	90.4	103.3	140.0	142.8
Foreign	3.1	6.3	4.3	6.5	7.4	8.4	11.7	19.1

[1]Excludes R&D performed by one Federal agency for another agency.

[2]Includes Federally Funded Research and Development Centers (FFRDC) administered by industry or "other nonprofit" organizations.

[3]Grant/contract breakdown not separately available for all agencies.

[4]Also included in "academic institutions, proper."

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-9. Federal Extramural Health R&D Obligations, by Funding Mechanism and Agency, FY 1968-1975

(Millions of dollars)

Agency	FY 1968	FY 1969	FY 1970	FY 1971	FY 1972	FY 1973	FY 1974	FY 1975
Extramural health R&D, total	$1,179.8	$1,217.6	$1,178.3	$1,310.1	$1,539.1	$1,598.0	$2,085.8	$2,083.1
Grants, total	848.2	865.3	824.7	909.7	1,041.3	1,041.8	1,366.0	1,385.5
Department of Health, Education, and Welfare, total	805.8	818.9	772.1	838.7	978.8	968.0	1,289.1	1,317.9
National Institutes of Health	(626.4)	(629.6)	(602.2)	(678.6)	(797.8)	(817.7)	(1,095.8)	(1,150.6)
Other Public Health Service	(139.3)	(146.4)	(138.7)	(134.4)	(149.7)	(150.2)	(167.5)	(144.1)
Other Department of Health, Education, and Welfare	(40.0)	(42.8)	(31.2)	(25.7)	(31.3)	(20.1)	(25.8)	(23.3)
Department of Agriculture	8.5	8.9	8.7	10.0	11.9	11.3	14.0	13.0
Department of Defense	2.8	2.3	1.5	1.7	0.7	1.2	1.2	1.5
Energy Research & Development Administration[1]	-	-	-	-	-	-	-	-
National Aeronautics & Space Administration	10.0	9.8	13.6	15.4	6.3	4.4	6.3	6.9
All other agencies	21.1	25.4	28.9	43.9	43.5	56.9	55.4	46.1
Contracts, total	331.6	352.3	353.6	400.4	497.8	556.2	719.8	697.7
Department of Health, Education, and Welfare, total	123.0	137.9	150.2	192.9	281.8	296.1	431.1	418.4
National Institutes of Health	(97.4)	(104.5)	(105.5)	(155.8)	(240.1)	(252.4)	(351.8)	(364.8)
Other Public Health Service	(23.5)	(31.9)	(43.4)	(34.9)	(40.4)	(38.2)	(72.9)	(45.0)
Other Department of Health, Education, and Welfare	(2.1)	(1.5)	(1.3)	(2.2)	(1.3)	(5.5)	(6.4)	(8.6)
Department of Agriculture	1.9	1.4	2.1	2.4	2.7	1.9	2.7	1.8
Department of Defense	34.9	34.6	36.1	28.2	32.5	34.4	33.0	30.7
Energy Research & Development Administration[1]	89.0	91.8	97.9	98.3	96.2	103.5	114.4	156.3
National Aeronautics & Space Administration	78.2	75.3	47.0	34.0	22.6	20.2	48.6	57.1
All other agencies	4.5	11.2	20.4	44.6	62.1	100.2	90.1	33.3

[1] Formerly part of Atomic Energy Commission.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-13. Federal Obligations for Health Research by Field of Science, and for Development, by Selected Agencies, FY 1975

(Millions of dollars)

Agency	Total	Research								Development total
		Total	Life sciences	Psychology	Mathematics	Engineering	Environ. sciences	Social sciences	Other, nec	
Total	$2,798.9	$2,454.9	$2,036.2	$ 65.0	$ 21.0	$ 73.3	$ 32.7	$ 53.5	$173.2	$344.0
Department of Health, Education, and Welfare, total	2,162.2	1,889.0	1,618.4	56.2	20.4	15.3	-	47.1	131.6	273.2
National Institutes of Health	1,845.5	1,605.6	1,442.5	13.0	18.1	15.3	-	11.3	105.4	239.9
Other Public Health Service	278.5	245.2	166.6	41.7	2.2	-	-	25.9	8.8	33.3
Other Department of Health, Education, and Welfare	38.2	38.2	9.4	1.6	-	-	-	9.9	17.3	-
All other agencies, total	636.7	565.9	417.8	8.8	0.7	58.0	32.7	6.3	41.6	70.7
Department of Agriculture	61.4	58.6	49.4	-	[1]	1.8	0.3	0.1	7.0	2.8
Department of Defense	115.9	106.2	103.7	1.1	-	1.1	0.1	-	0.2	9.7
Energy Research & Development Administration (AEC)	163.9	163.9	132.4	-	-	9.1	22.5	-	-	-
National Aeronautics and Space Administration	74.9	42.6	5.0	1.7	-	23.2	6.5	-	6.3	32.3
National Science Foundation	44.7	44.7	30.3	0.3	-	3.8	1.4	0.7	8.2	-
Veterans Administration	94.8	87.1	78.3	5.5	-	-	-	0.2	3.0	7.7
All other	81.0	62.8	18.7	0.2	0.6	19.1	1.9	5.3	16.9	18.3

[1]Less than $0.05 million.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-14. Federal Obligations for Health Research in Life Sciences, Psychology, and Engineering, by Selected Agency and Minor Field, FY 1975[1]

(Millions of dollars)

Agency	Life sciences				Psychology				Engineering		
	Total	Biological	Medical[2]	Life sci. nec	Total	Biological aspects	Social aspects	Psych nec	Total	Biomed. eng.	Other health eng.
Total	$2,036.2	$ 878.5	$1,090.3	$67.4	$65.0	$35.5	$26.8	$2.7	$73.3	$20.6	$52.7
Department of Health, Education, and Welfare, total	1,618.4	628.8	923.4	66.2	56.2	30.7	24.2	1.3	15.3	15.3	-
National Institutes of Health	1,442.5	565.8	826.2	50.5	13.0	8.9	4.1	-	15.3	15.3	-
Other Public Health Service	166.6	63.1	92.5	11.0	41.7	21.8	18.6	1.3	-	-	-
Other Department of Health, Education, and Welfare	9.4	-	4.7	4.7	1.6	-	1.6	-	-	-	-
All other agencies	417.8	249.6	167.0	1.2	8.8	4.7	2.6	1.4	58.0	5.3	52.7
Department of Agriculture	49.4	44.2	5.2	-	-	-	-	-	1.8	-	1.8
Department of Defense	103.7	16.9	86.8	-	1.1	0.5	0.6	-	1.1	0.9	0.1
Energy Research & Development Administration (AEC)	132.4	123.4	8.9	-	-	-	-	-	9.1	-	9.1
National Aeronautics and Space Administration	5.0	1.4	3.6	-	1.7	-	0.7	1.0	23.2	1.4	21.7
National Science Foundation	30.3	29.5	0.6	0.2	0.3	-	-	0.3	3.8	-	3.8
Veterans Administration	78.3	19.1	58.2	1.0	5.5	4.3	1.2	0.1	-	-	-
All other	18.7	15.1	3.6	-	0.2	[3]	0.2	-	19.1	2.9	16.2

[1]Detailed field of science breakdowns not available for other fields.

[2]Includes clinical medical and other medical research.

[3]Less than $0.05 million.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table A-16. Federal Health R&D Obligations to Institutions of Higher Education and to Medical Schools, by Geographic Region, FY 1968 and FY 1973-1975

(Thousands of dollars)

Regions (ranked in order of FY 1975 total obligations)	1975			1974			1973			1968		
	Total	Medical school component	Other	Total	Medical school component	Other	Total	Medical school component	Other	Total	Medical school component	Other
Total	$1,321,191	$837,469	$483,722	$1,305,398	$809,716	$495,682	$1,004,351	$618,250	$386,101	$727,278	$379,647	$347,631
Middle Atlantic	273,465	191,893	81,572	257,390	177,433	79,957	201,036	139,864	61,172	153,004	92,637	60,367
Pacific	258,115	152,072	106,043	251,915	147,835	104,080	192,902	109,461	83,441	132,542	59,465	73,077
South Atlantic	184,692	124,691	60,001	181,832	117,695	64,137	138,482	90,409	48,073	95,391	53,164	42,227
East N. Central	180,891	103,958	76,933	178,672	99,594	79,078	141,956	79,356	62,600	115,332	55,536	59,796
New England	133,420	74,098	59,322	133,133	76,827	56,306	102,649	56,849	45,800	69,945	31,899	38,046
West N. Central	96,660	71,271	25,389	98,955	66,757	32,198	78,299	54,721	23,578	54,944	31,339	23,605
West S. Central	86,134	50,337	35,797	89,747	54,326	35,421	65,817	37,340	28,477	48,156	24,786	23,370
East S. Central	53,017	37,709	15,308	54,971	37,297	17,674	41,563	28,173	13,390	29,466	16,707	12,759
Mountain	49,910	28,730	21,180	52,532	29,694	22,838	38,410	20,516	17,894	23,081	10,587	12,494
Outlying areas	4,565	2,710	1,855	4,886	2,258	2,628	3,148	1,561	1,587	1,753	511	1,242
Other[1]	322	-	322	1,365	-	1,365	89	-	89	3,664	3,016	648

[1]Discrepancy is attributable to time lag and differing sources of data and cannot be distributed by geographic region.

Source: National Institutes of Health.

Table A-17. The Ten States Leading in Federal Health R&D Support to Institutions of Higher Education and to Their Medical School Components, FY 1968 and FY 1973-1975

(Thousands of dollars)

State (in order of FY 1975 total obligations)	1975			1974			1973			1968		
	Total	Medical school component	Other	Total	Medical school component	Other	Total	Medical school component	Other	Total	Medical school component	Other
Total, all States	$1,321,191	$837,469	$483,722	$1,305,398	$809,716	$495,682	$1,004,351	$618,250	$386,101	$727,278	$379,647	$347,631
Total, leading 10 States	838,870	534,132	304,738	813,716	512,860	300,856	629,601	391,255	238,346	451,617	239,561	212,056
California	199,631	117,236	82,395	192,940	113,206	79,734	147,828	83,957	63,871	100,038	43,232	56,806
New York	182,237	133,886	48,351	169,977	125,185	44,792	134,641	99,388	35,253	106,229	68,228	38,001
Massachusetts	79,598	37,014	42,564	81,615	41,929	39,686	63,952	30,594	33,358	46,866	18,782	28,084
Pennsylvania	77,506	53,216	24,290	73,791	47,151	26,640	56,780	37,567	19,213	39,050	22,629	16,421
Texas	68,124	40,639	27,485	68,193	42,751	25,442	48,255	27,903	20,352	31,249	16,076	15,173
Illinois	57,011	37,904	19,107	54,994	35,385	19,609	47,161	29,346	17,815	35,030	19,442	15,588
Maryland	50,899	33,817	17,082	48,525	31,179	17,346	36,838	23,868	12,970	24,556	13,943	10,613
North Carolina	44,769	34,154	10,615	48,017	32,047	15,970	34,427	24,640	9,787	23,685	14,567	9,118
Washington	39,685	26,406	13,279	38,147	26,554	11,593	29,267	19,382	9,885	17,523	11,656	5,867
Michigan	39,410	19,840	19,570	37,517	17,473	20,044	30,452	14,610	15,842	27,391	11,006	16,385

Source: National Institutes of Health.

Table 4-3. Federal Health R&D Support to the 30 Medical Schools Receiving the Largest Amounts, Ranked by School for Selected Years, FY 1968-1975

(Dollars in thousands)

Medical schools (listed in order of FY 1975 obligations)	State	FY 1975			FY 1974[1]		FY 1973		FY 1972		FY 1968	
		Rank	Amount	Percent of total	Rank	Amount	Rank	Amount	Rank	Amount	Rank	Amount
Total, all medical schools			$837,469	100.0		$809,716		$618,250		$525,236		$374,611
Total, top 30 medical schools in FY 1975			545,869	65.2		519,881		400,846		341,870		239,713
University of California School of Medicine-San Francisco	Cal	1	30,218	3.6	2	26,604	1	20,212	3	18,000	6	11,411
University of Washington School of Medicine	Wash	2	26,406	3.1	3	26,554	2	19,382	5	17,289	4	11,656
Stanford University School of Medicine	Cal	3	25,631	3.1	4	25,180	4	19,002	4	17,568	9	10,423
University of California School of Medicine-Los Angeles	Cal	4	25,019	3.0	1	28,389	3	19,350	1	19,613	1	14,405
University of Chicago School of Medicine	Ill	5	24,412	2.9	10	21,112	8	17,585	12	12,800	8	11,312
Yeshiva University Einstein College of Medicine	NY	6	23,767	2.8	11	20,389	9	17,481	7	15,637	5	11,470
Washington University School of Medicine	Mo	7	23,614	2.8	7	22,172	11	16,379	10	13,979	14	8,890
Johns Hopkins University School of Medicine	Md	8	23,033	2.7	8	21,947	5	18,921	6	16,162	10	10,075
Columbia University College Physicians and Surgeons	NY	9	22,163	2.6	9	21,937	7	17,822	8	15,271	2	13,369
University of Pennsylvania School of Medicine	Pa	10	21,989	2.6	12	19,640	15	14,246	11	13,141	12	9,454
Yale University School of Medicine	Conn	11	21,669	2.6	6	22,563	10	16,712	13	12,337	15	8,632
Harvard University Medical School	Mass	12	20,199	2.4	5	24,913	6	18,808	2	18,199	3	13,189
University of Minnesota Medical School	Minn	13	19,699	2.3	16	16,387	16	13,772	9	14,876	11	9,497
New York University School of Medicine	NY	14	19,534	2.3	15	18,327	12	15,930	14	11,815	7	11,399
Duke University School of Medicine	NC	15	19,086	2.3	14	18,610	13	15,319	15	10,242	16	8,323
Baylor University College of Medicine	Tex	16	18,766	2.2	13	19,529	14	14,756	19	9,015	13	9,067
University of Rochester School of Medicine and Dentistry	NY	17	17,641	2.1	18	14,412	17	13,133	17	9,696	19	7,386
University of Wisconsin Medical School	Wis	18	17,048	2.0	17	15,435	18	12,070	16	10,121	17	7,832
CUNY Mount Sinai School of Medicine	NY	19	15,755	1.9	19	14,110	28	7,503	18	9,090	21	5,365
University Southern California School of Medicine	Cal	20	13,429	1.6	26	10,811	19	10,591	31	6,050	26	4,555
University of California School of Medicine-San Diego	Cal	21	13,343	1.6	21	12,951	22	9,468	25	7,355	76	1,222
University of Miami School of Medicine	Fla	22	13,299	1.6	29	10,510	24	9,293	26	7,082	22	4,909
University of Michigan Medical School	Mich	23	12,889	1.5	24	11,197	21	9,584	20	8,836	18	7,576
University of Alabama-Medical College of Alabama	Ala	24	12,228	1.5	22	12,865	20	10,054	22	7,788	37	3,533
University of Iowa College of Medicine	Iowa	25	11,117	1.3	20	13,396	26	8,502	28	6,615	34	3,826
Vanderbilt University School of Medicine	Tenn	26	10,969	1.3	25	11,026	25	8,709	21	8,782	25	4,577
University of Maryland School of Medicine	Md	27	10,784	1.3	34	9,232	39	4,347	40	4,184	32	3,838
University of Texas Southwestern Medical School	Tex	28	10,760	1.3	27	10,720	31	6,957	32	5,979	29	4,135
University North Carolina School of Medicine	NC	29	10,666	1.3	32	9,448	32	6,683	24	7,722	31	3,896
Cornell University Medical School	NY	30	10,538	1.3	30	9,550	27	7,673	29	6,345	28	4,261

[1]Includes FY 1973 funds released for obligation in FY 1974.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table 4-5. Federal Health R&D Support to the 30 Institutions of Higher Education Receiving the Largest Amounts, Ranked by Institution for Selected Years, FY 1968-1975[1]

(Dollars in thousands)

Institutions of higher education (listed in order of FY 1975 obligations)	State	FY 1975			FY 1974		FY 1973		FY 1972		FY 1968	
		Rank	Amount	Percent of total	Rank	Amount	Rank	Amount	Rank	Amount	Rank	Amount
Total, all academic institutions			$1,321,191	100.0		$1,305,398		$1,004,351		$894,154		$727,228
Total, top 30 institutions in FY 1975			731,631	55.4		707,975		552,955		543,210		388,771
University of California - Los Angeles	Cal	1	38,887	2.9	1	40,160	2	30,124	3	29,345	2	22,667
University of Washington	Wash	2	37,287	2.8	3	36,101	4	27,462	4	29,087	8	15,987
Johns Hopkins University	Md	3	36,605	2.8	4	35,741	3	29,792	2	30,805	4	17,889
Harvard University	Mass	4	34,371	2.6	2	37,493	1	30,149	1	31,477	1	24,249
U. of California-San Francisco Medical Center	Cal	5	34,239	2.6	8	29,525	7	22,661	9	20,997	14	13,742
Stanford University	Cal	6	32,894	2.5	5	31,475	5	24,033	5	23,751	10	15,272
University of Pennsylvania	Pa	7	32,531	2.5	7	29,630	10	21,320	10	20,630	11	14,882
University of Wisconsin - Madison	Wis	8	30,234	2.3	6	29,679	6	23,808	8	21,668[2]	5	17,615[2]
Yale University	Conn	9	29,364	2.2	9	29,495	9	21,804	12	18,774	16	12,640
Columbia University	NY	10	28,439	2.1	10	28,132	8	21,971	6	23,470	3	18,236
University of Minnesota	Minn	11	27,397	2.1	12	27,641	11	21,082	7	23,486	7	16,426
University of Chicago	Ill	12	27,262	2.1	13	23,914	13	19,967	16	15,974	12	14,627
Washington University	Mo	13	26,784	2.0	11	27,930	14	19,764	14	18,222	15	12,841
Yeshiva University	NY	14	24,414	1.9	17	20,634	15	18,083	13	18,509	17	12,464
University of Michigan	Mich	15	24,121	1.8	14	23,755	12	20,060	11	20,328	6	17,222
New York University	NY	16	21,978	1.7	16	20,826	16	18,012	17	15,702	9	15,793
University of Rochester	NY	17	20,888	1.6	22	16,933	21	14,381	24	12,980	22	9,618
Duke University	NC	18	20,793	1.6	15	20,830	17	16,625	20	14,303	21	11,122
University of California - San Diego	Cal	19	20,311	1.5	19	19,582	20	14,730	21	13,651	42	5,831
Baylor College of Medicine	Tex	20	18,766	1.4	20	19,529	19	14,756	29	11,444	19	11,516[2]
Cornell University	NY	21	18,256	1.4	23	16,875	22	14,047	19	14,344	18	12,002
University of California - Berkeley	Cal	22	18,017	1.4	21	17,550	18	16,497	15	17,316	13	14,173
Massachusetts Institute of Technology	Mass	23	17,773	1.4	24	16,745	26	12,839	25	12,808	23	9,596
University of Southern California	Cal	24	17,045	1.3	27	15,401	23	13,658	23	13,340	26	9,018
University of North Carolina - Chapel Hill	NC	25	16,369	1.2	18	19,710	27	12,548	18	15,566[2]	29	7,771[2]
CUNY Mount Sinai School of Medicine	NY	26	15,755	1.2	31	14,110	41	7,503	35	9,297	38	6,042
University of Utah	Utah	27	15,339	1.2	26	15,436	28	11,474	30	10,555	33	7,011
University of California - Davis	Cal	28	15,128	1.2	30	14,288	31	10,223	26	12,689	28	8,850
University of Miami	Fla	29	15,094	1.1	35	12,376	29	10,701	36	9,098	31	7,645
University of Alabama - Birmingham	Ala	30	15,072	1.1	25	16,479	25	12,881	22	13,634[2]	39	6,024[2]

[1]Includes medical school obligations separately shown on Table 4-3.

[2]Includes all campuses, plus systems offices where applicable. Comparable FY 1975 figures would have been: University of Wisconsin, $31.1 million; Baylor University, $19.0 million; University of Alabama, $15.4 million; University of North Carolina, $16.9 million.

Note: Detail may not add to totals because of rounding.

Source: National Institutes of Health.

Table 4-6. Federal and NIH Obligations for Health R&D to the 50 Institutions of Higher Education Receiving the Largest Amounts, Their Medical School Components and Total Federal R&D Support, FY 1975

(Dollars in thousands)

Institutions (ranked in order of academic health R&D support)	State	Health R&D								Total R&D[1]	
		Federal				NIH					
						Academic institutions		Medical schools			
		Rank	Academic institutions, total	Medical school component	Medical as percent of academic	Amount	Percent of academic health R&D	Amount	Percent of medical school R&D	Rank	Academic institutions, total
Total, all institutions			$1,321,191	$837,469	63.4	$1,063,103	80.5	$750,685	70.6		$2,259,824
Total, top 50 institutions			954,213	685,681	71.9	789,159	82.7	611,299	77.5		1,389,623
U. of California - Los Angeles	Cal	1	38,887	25,017	64.3	28,536	73.4	22,056	88.2	4	54,429
University of Washington	Wash	2	37,287	26,406	70.8	31,076	83.3	23,876	90.4	2	60,323
Johns Hopkins University	Md	3	36,605	23,033	62.9	29,389	80.3	20,820	90.4	10	41,434
Harvard University	Mass	4	34,371	20,199	58.8	28,543	83.0	17,546	86.9	5	49,193
U. of California-San Francisco Med. Center	Cal	5	34,239	30,218	88.3	29,731	86.8	27,319	90.4	18	34,038
Stanford University	Cal	6	32,894	25,631	77.9	26,214	79.7	22,140	86.4	3	53,621
University of Pennsylvania	Pa	7	32,531	21,989	67.6	27,664	85.0	20,092	91.4	9	44,016
University of Wisconsin-Madison	Wis	8	30,234	17,048	56.4	26,130	86.4	16,412	96.3	8	46,797
Yale University	Conn	9	29,364	21,669	73.8	24,330	82.9	18,511	85.4	16	36,976
Columbia University	NY	10	28,439	22,163	77.9	24,239	85.2	20,466	92.3	7	48,690
University of Minnesota	Minn	11	27,597	19,699	71.4	24,076	87.2	18,248	92.6	12	40,188
University of Chicago	Ill	12	27,262	24,412	89.6	20,378	74.8	19,057	78.1	15	38,379
Washington University	Mo	13	26,784	23,604	88.2	23,064	86.1	20,866	88.4	19	30,997
Yeshiva University	NY	14	24,414	23,767	97.4	23,213	95.1	22,984	96.7	23	25,065
University of Michigan	Mich	15	24,121	12,889	53.4	17,374	72.0	10,666	82.8	14	38,876
New York University	NY	16	21,978	19,534	88.9	17,102	77.8	16,092	82.4	21	27,939
University of Rochester	NY	17	20,888	17,641	84.5	14,654	70.2	13,052	74.0	22	25,517
Duke University	NC	18	20,793	19,086	91.8	18,774	90.3	17,953	94.1	24	24,475
U. of California - San Diego	Cal	19	20,311	13,343	65.7	16,811	82.8	12,046	90.3	6	49,009
Baylor College of Medicine	Tex	20	18,766	18,766	100.0	16,080	85.7	16,080	85.7	37	18,855
Cornell University	NY	21	18,254	10,538	57.7	15,732	86.2	9,823	93.2	13	39,894
U. of California - Berkeley	Cal	22	18,017	--	--	12,645	70.2	--	--	11	40,626
Mass. Institute of Technology	Mass	23	17,773	--	--	13,216	74.4	--	--	1	68,820
University of Southern California	Cal	24	17,045	13,429	78.8	14,938	87.6	13,039	97.1	20	28,547
U. of North Carolina - Chapel Hill	NC	25	16,369	10,666	65.2	13,649	83.4	9,610	90.1	34	19,618

Table 4-6 (continued). Federal and NIH Obligations for Health R&D to the 50 Institutions of Higher Education Receiving the Largest Amounts, Their Medical School Components and Total Federal R&D Support, FY 1975

(Dollars in thousands)

Institutions (ranked in order of academic health R&D support)	State	Health R&D								Total R&D[1]	
		Federal				NIH					
						Academic institutions		Medical schools			
		Rank	Academic institutions, total	Medical school component	Medical as percent of academic	Amount	Percent of academic health R&D	Amount	Percent of medical school R&D	Rank	Academic institutions, total
CUNY Mount Sinai School of Medicine	NY	26	$ 15,755	$ 15,755	100.0	$ 13,598	86.3	$ 13,598	86.3	45	$ 15,762
University of Utah	Utah	27	15,339	9,065	59.1	10,954	71.4	7,223	79.7	33	20,048
University of California - Davis	Cal	28	15,128	5,861	38.7	11,559	76.4	5,117	87.3	32	20,173
University of Miami	Fla	29	15,094	13,299	88.1	12,840	85.1	12,542	94.3	26	22,861
University of Alabama - Birmingham	Ala	30	15,072	12,228	81.1	13,237	87.8	11,180	91.4	47	14,878
U. of Texas - M.D. Anderson Hospital	Tex	31	14,360	--	--	14,296	99.6	--	--	49	14,449
University of Colorado	Col	32	13,789	10,441	75.7	11,117	80.6	9,189	88.0	27	22,469
Case-Western Reserve University	Ohio	33	13,613	10,106	74.2	11,390	83.7	8,875	87.8	35	19,148
University of Iowa	Iowa	34	13,154	11,117	84.5	11,570	88.0	10,253	92.2	40	16,876
Vanderbilt University	Tenn	35	12,506	10,969	87.7	11,337	90.7	10,505	95.8	52	13,841
Boston University	Mass	36	12,085	10,509	87.0	10,317	85.4	9,470	90.1	53	13,432
University of Pittsburgh	Pa	37	11,831	6,912	58.4	9,435	79.8	6,353	91.9	39	18,122
University of Maryland - Baltimore	Md	38	11,812	10,784	91.3	10,739	90.9	10,512	97.5	57	12,145
Rockefeller University	NY	39	11,379	--	--	10,066	86.9	--	--	56	12,084
Northwestern University	Ill	40	11,268	6,372	56.6	9,109	80.8	6,030	94.6	36	18,957
U. Texas Health Science Center - Dallas	Tex	41	10,915	--	--	10,291	94.3	--	--	60	10,784
Emory University	Ga	42	10,615	7,893	74.4	9,212	86.8	6,788	86.0	59	10,952
Michigan State University	Mich	43	9,839	3,728	37.9	6,003	61.0	3,671	98.5	38	18,192
Pennsylvania State University	Pa	44	9,810	5,719	58.3	7,943	81.0	5,601	97.9	31	20,455
Temple University	Pa	45	9,725	8,511	87.5	8,530	87.7	7,607	89.4	64	10,578
SUNY at Buffalo	NY	46	9,590	5,249	54.7	8,524	88.9	5,047	96.2	58	11,437
Ohio State University	Ohio	47	9,350	4,267	45.6	7,691	82.3	4,198	98.5	30	21,030
University of Florida	Fla	48	9,197	5,409	58.8	6,945	75.5	4,998	92.4	41	16,313
University of Kansas	Kans	49	8,817	4,161	47.2	7,194	81.7	4,101	98.6	63	10,756
University of Virginia	Va	50	8,762	5,897	67.3	7,704	87.9	5,557	94.2	55	12,319

[1]Discrepancies between health R&D and total R&D may occur because of difference in time reports are made. Includes NIH General Research Support shown separately by NSF.

Sources: Total Federal R&D: National Science Foundation, "Federal Obligations to Universities, Colleges, and Selected Nonprofit Institutions," (NSF77-303, Appendix B); Health R&D: National Institutes of Health.

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HEALTH PROBLEMS AND RESEARCH

Mr. FLOOD. This committee is constantly hearing, and I mean constantly, from people telling us that the NIH should reexamine its funding priorities. We get that all the time. We are told if one compares the NIH funding priorities with lost productivity because of illness, disability, premature deaths, you would find that these priorities are in reverse order.

What is your reaction to that kind of statement or complaint that we are getting all the time?

What I mean is, for example, we have more deaths and disability from heart disease than we have from cancer, and yet cancer gets twice the money. That is also true in a lot of other areas: strokes, arthritis, et cetera. What about that?

Dr. FREDRICKSON. We have compared our activities with the cost of illness and with various tables of morbidity and mortality, Mr. Chairman. Actually, we are not so far off from a fairly congruent distribution of our resources with a number of these factors, but, of course, they are not exactly identical, and I think they can never be, primarily because part of the movement of research must depend on scientific opportunities.

There are many serious chronic problems that plague many people for which we still must seek the basic kind of information that allows us to break through and move to practical developments, and I am afraid that is the way nature moves. When we get certain opportunities, we adjust our priorities to the opportunity that we have in order to make the most of our funds in gaining useful new knowledge, and that is not always a one-to-one match with the health problems in the population.

Mr. FLOOD. You are talking about the methods you are working under right now. Are you reexamining these methods you are talking about for assigning the funding priorities to all the categorical programs?

Dr. FREDRICKSON. Yes, we are. We are constantly reexamining those priorities. We have just completed a review of each institute and division in which this was a major topic of discussion. We examined how the institutes assign their own assessments and ambitions to move in certain areas and how they match the scientific opportunities and the public need. So we do constantly do this.

Mr. FLOOD. On the categorical programs.

Dr. FREDRICKSON. On all categorical programs.

Mr. FLOOD. Mr. Early?

REAPPOINTMENT OF DR. FREDRICKSON

Mr. EARLY. Thank you, Mr. Chairman.

Doctor, it is a pleasure to have you back, and I would like to say at the outset that I have never seen a reappointment meet with more approval than yours. In my area, which is well-known in the health profession with our four medical schools, the University of Massachusetts, Harvard, et cetera, all the professional people I spoke with thought yours was a tremendous reappointment.

Dr. FREDRICKSON. Thank you, Mr. Early.

Mr. EARLY. The other day, Secretary Califano suggested that there would not be too many reappointments, but I think that really shows the type of job you have done.

In your statement I was impresed with a sentence where you say, "Our main mission, and our expertise, lies in providing the substance of what must be communicated and used to provide the best standard of care."

There are too many Federal agencies that are rhetoric substance and not the substance that I think you refer to. I don't think the country can afford that rhetorical luxury any longer. We have to produce results and that is your approach to performance, by production, by effectiveness, and not merely one of a standard of complacency and keeping the ball in the middle of the road. I think you are to be commended for that, too.

BIOMEDICAL RESEARCH SUPPORT GRANTS

It seems that the new administration is proposing to eliminate the biomedical research support grant program. As I recall, the previous administration also proposed to do this.

Has this program served its purpose and therefore is ready to be phased out?

Three things: Should it be phased out and do you think the funds should be made available for this program and is it essential that it at least be at the same level as 1977 or less?

Dr. FREDRICKSON. I think its disappearance from the budget represents the priorities which the administration has addressed. Within the overall level under which we have to operate, we must elect to support grants and contracts rather than these more general support mechanisms, Mr. Early.

You asked for my personal opinion. I would say that biomedical research support grants have provided an extraordinarily important part of the support of research in the United States. It is sometimes looked upon as unnecesary because we have stopped growing at the rate that was characteristic of the last decade. I look on biomedical research support grants as being more like an antirust compound that must be put into an expensive engine to insure its continuing effective function.

AWARDS TO NEW INVESTIGATORS

Mr. EARLY. I do suggest, though, Doctor, in the case of these ongoing grants, that it is going to call for tough priority decisions. You will be forced to discontinue some grants even though there is always the threat that there would be something there. It is just a judgment call, and I think we have to discard some of them, so that we can establish new ones and keep the process of research for development going. I don't think we can enjoy what we have in the past, just renewing to renew.

Dr. FREDRICKSON. I quite agree with you. About 32 percent of our awards each year are new and 10 percent of all awards involve investigators entering the system for the first time. That means, in a steady state, that a certain fraction of people are dropping out, that they are not coming up to the competitive standards. I think that is the only

appropriate way in an area like biomedical research, where vigor and creativity are essential criteria, for meeting the requirements of programs being supported by public funds.

Mr. EARLY. I think that is where your substance is not always popular until it gets down the road. It is us elected people, not you scientists, who have to be popular and can't always take the right road.

SUPPORT FOR ARTHRITIS RESEARCH

You say that NIH will increase the support for arthritis from $33 million in 1977 to $34 million in 1978. How does this compare with what the arthritis commission recommends?

Dr. FREDRICKSON. The total support for arthritis in 1977, adding up the contributions of all the institutes, is about $30.4 million. In the budget that you have before you, the 1978 budget, we expect the total of institute support to be about $34.5 million. This is based on the allocations made by the several institutes, in their best judgments, to the requirements of the plan.

Now the recommendation of the Arthritis Commission, of course, is for a much larger sum. In 1977, the Arthritis Commission recommended that $97 million should be spent as opposed to the $30.5 million which was actually available in all the institutes participating in arthritis research. For 1978, the Commission recommends $120.7 million, and this is to be compared with the $34.5 million which the institutes feel they will be able to allocate to the support of this kind of research in 1978 in their respective budgets.

Mr. EARLY. Why such a big shortfall?

Dr. FREDRICKSON. I think for several reasons, Mr. Early. First of all, last year, which saw the beginning of the initiative in arthritis, the Commission report came several months after the appropriation hearings. Only $2.5 million was introduced into the budget specifically for the creation of arthritis centers as against the very large increase thought necessary in the Commission's judgment.

The second reason, of course, is that it is impossible for us to come up to the ambitions of the Arthritis Commission, with its very large increases, or project them against the budgets available to the participating institutes. There simply are nowhere near the funds that would make possible——

Mr. EARLY. Can this committee interpret, Doctor, if what we are going to get from the $34 million is worth what we would get with the $120 million? Are you going to cut out the bureaucratic part of their request, and are you going to try to really get, as the people like to think, a dollar's worth for dollar spent in research.

Dr. FREDRICKSON. We try to provide that at any budget level. We feel very responsible that that be done. No; one cannot buy the same amount of knowledge for $34 million that you might be able to get at an expenditure three or four times that.

Mr. EARLY. But there is a critical point. As we spend more money in research programs, we get more opinion and less decisions. We in the Federal Government, in my opinion, are funding more programs and putting more people aboard who all have to justify their existence and justify their jobs. So I am going to suggest to you that sometimes a smaller budget can be more productive.

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What is the Arthritis Institute going to do for arthritis research in 1978, cut back or do more?

Dr. FREDRICKSON. It will add approximately $4 million—that is, the Arthritis Institute itself—to the allocation for support of arthritis research in 1978 as compared to its figure in 1977.

Mr. EARLY. Not in dollars, in program.

Dr. FREDRICKSON. It will primarily attempt to move toward the development of the centers that were a prominent part of the recommendation of the Commission. The principal increase will actually be for centers. They will also attempt to put somewhat more money into the training of research manpower, because one of the problems in this area has been that, while one has an ambition to increase the amount of research relative to this disease, it is necesary to have more trained people to do this research.

Mr. EARLY. Doctor, do you consult with the Arthritis Board in developing your budget; do they have any role in determining the priorities in arthritis research when there isn't enough money to do what you want to do?

Dr. FREDRICKSON. Yes, they will have that opportunity. They are going to have their first organizational meeting this March, and they will be given full access to all the information, and they will be asked for advice at a very hard level and particularly with regard to their opinions on priorities.

Mr. EARLY. I hope we have the togetherness because we are both trying to serve the same people out there, and we can eliminate the duplication as much as we can, so it is all productive, and we get away from this prime concern of authorship, which can't be as important as achieving what we want to do.

STATUS OF ARTHRITIS RESEARCH

Finally, Doctor, what is the status of arthritis research? A lot of people suffer from it and would like to have more help than be told to take an aspirin. Do you think you have any good ideas or leads with regard to arthritis?

Dr. FREDRICKSON. Yes, progressively more inroads are beginning to be made on this problem. I think, Mr. Early, when we talk about arthritis, we are talking about a whole span of not only joint but muscular and skeletal diseases.

The more common forms of arthritis, particularly rheumatoid arthritis, like a number of other diseases, seems to fall into an area of diseases that may be due to errors in the immune system. This is one of the most exciting areas in all biomedical research; that is, the expansion of knowledge about how our bodies react to foreign proteins, and the extraordinary manifestations that can occur with abnormalities in the system. It is an area that touches not only arthritis but may be related to multiple sclerosis and other neurological problems. For this reason, I think that expanding our basic science knowledge in this particular area can be extraordinarily important to a better understanding of arthritis.

ARTHRITIS COMMISSION RECOMMENDATIONS

Mr. EARLY. Doctor, finally, would you provide for the record whether you think the Commission's recommendations are reasonable and if you had the money, could you get as much good research going as they would like you to?

Dr. FREDRICKSON. I will be glad to provide it for the record.

[The information follows:]

REASONABELNESS OF ARTHRITIS COMMITTEE REPORT

The National Arthritis Commission has submitted an ambitious plan for conquering a painful and debilitating disease. I support their programmatic recommendations and the statements of their ideals. Were funds available in the amount recommended the quality of research performed would not be compromised.

Mr. FLOOD. Mr. O'Brien?

ALLERGY

Mr. O'BRIEN. I have a parochial interest in the allergy and infectious diseases. I don't think the family will quarrel over the estate, but they will remember me by coughs and sneezes. My daughters have it, and my grandchildren, so I take a little personal interest in it, and I gather that your appropriation for that Institute is up about $12 million over last year, and I subscribe to that, but I think there were about 43 million visits to doctors' offices for allergy problems last year, and I think over $325 million was spent for allergy problems, so it is nothing to be taken lightly, and I wonder what your views were budgetwise. Are we adequately funding you for that?

Dr. FREDRICKSON. I think that allergy is coming into its own, Mr. O'Brien. You problem is maturing. There are some very encouraging things about it. We are getting away from the school book science of sensitization test. Perhaps you had to go through that. We are understanding more about the basic aspects of allergy, doing it better, and applying the use of drugs more selectively to stop allergic reactions.

Finally, the relationship of the immune system and certain other blood factors—the things that make a reaction between foreign proteins and their manifestations in itching and sneezing—and those things that relate to allergy are becoming much clearer.

The increase in the budget for the Allergy Institute this year includes about $4 million for more research on the immune system. It also includes some increase in funding for the encouragement of more and somewhat larger allergy centers. The Institute is taking seriously the need to put its resources into areas of research that also have a practical interface with the needs of the community and the practicing physicians. In fact, they even want to set up, on an experimental basis, a dial-in telephone system so that your neighborhood physician can get to the Allergy Center and ask practical questions about what is the latest stage of knowledge in this area.

I think we do have an opportunity for a modest increase in that activity, and I think it is time for it. I am encouraged about what the Institute describes to us as opportunities to use their funds wisely.

ASTHMA

Mr. O'BRIEN. I suppose the most serious aspect, at least in my judgment of the allergy problems, concerns the asthmatic, and I think there were 2,000 or 3,000 deaths from asthma last year, which startled me when I checked it out.

Do you look out for the asthmatic in a kind of general way, or does he get special attention?

Dr. FREDRICKSON. He gets special attention as well as general. Both the Allergy and Infectious Disease Institute and the National Heart, Lung, and Blood Institute have a real interest in improving research and the support of centers where asthma patients are cared for. These two Institutes work closely in this area. They are also aware of other service organizations throughout the Federal Government that have clinics where they are attempting to upgrade and support research that can be profitably used there. Asthma is an important problem. Again, there are more research opportunities here.

Mr. O'BRIEN. Do you think you are getting enough money in this area presently?

Dr. FREDERICKSON. I think we can very profitably use the amount that we have.

Mr. O'BRIEN. Thank you, Doctor. Good luck to you.

Mr. FLOOD. Mr. Natcher?

CANCER BUDGET REQUEST

Mr. NATCHER. Doctor, according to the amounts that we have before our committee, I believe, for the National Cancer Institute it is $818,-936,000 and at the proper time, of course, we will have the Cancer Institute testify before the committee. That amount is correct?

Dr. FREDRICKSON. That is the correct amount for this year.

Mr. NATCHER. Is that an adequate amount, Doctor?

Dr. FREDERICKSON. It will mean a decline in the actual purchasing power of the Cancer Institute to continue the activities it now has.

Mr. NATCHER. Moneywise, what do we have, $40 million or $50 million?

Dr. FREDRICKSON. The increase, sir?

Mr. NATCHER. No, you say a decline; what do you have in mind?

Dr. FREDRICKSON. If it were to maintain its purchasing power against an inflation rate of approximately 6.5 percent, it would require an additional $40 to $50 million in the budget for that purpose.

CONSULTATION WITH PRACTITIONERS

Mr. NATCHER. Doctor, in arriving at the amounts that are placed in the budget for the different institutes, such as cancer, do you or the members of your staff or your associates from time to time talk to the doctors in this country as to the amounts for research, as to the followup on the discoveries and as to the projects. Also as to splitting of the funds.

You know, I hear complaints from time to time that the amount approved, for instance, for the National Cancer Institute, cancer research, the amount is adequate, but it is the splitting of the funds and failure to really get this research together.

Doctor, do you talk to them from time to time about it? Is there any validity to the complaints I hear as to the use of this money?

Dr. FREDRICKSON. Mr. Natcher, we talk to them all the time.

Mr. NATCHER. Which, I think, is good.

Dr. FREDRICKSON. We do it informally—we get lots of messages from that community—but more than that, we involve them in a structural way in setting the priorities through the National Advisory Councils, on which there must be both practicing people and lay people. We find more and more our advisory councils providing a meaningful public sector of opinion to bear upon the Institute's priority setting.

I am encouraged by the increase in this kind of interchange. I think it is absolutely critical.

Mr. NATCHER. Now, as a result of this interchange and the information that you obtain from time to time as a result of these meetings, and so forth, do you make changes in the operation, Doctor, as far as the Institutes are concerned, and as to the type of research, and as to your grants that you are making?

Dr. FREDRICKSON. Yes. The Institutes, themselves, operate very sensibly in regard to the advice that they are getting. The practice of a program manager sitting in isolation and deciding by himself, without this kind of exchange, simply doesn't go on anymore. When the Institutes defend their programs to me—as we go through our annual reviews, which are lengthy and stringent and very useful exchanges—they also provide me with information about the kinds and the quality of the arguments about their programs, from various sources, and what their advisory councils feel. I think we have a continuing process where we meld and blend advice from as wide a range sources as we can—including, certainly, this committee—in regard to setting priorities. And we do change them. Every year priorities are rearranged, new decisions are made as to where to put what fraction of the resources available to us. That, I think, is a natural and important part of this annual appropriation process which we go through with you.

Mr. NATCHER. Thank you, Doctor. Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Patten?

Mr. PATTEN. Doctor, it is a pleasure to be able to sit here in front of you. I think a lot of Americans appreciate your service.

Dr. FREDRICKSON. Thank you very much.

SALARY INCREASES

Mr. PATTEN. Just 1 year ago, Dr. Rauscher sat before us, and I think it is in the record, but he said to me, "As a matter of pride, if I don't receive a raise this year of at least 5 percent, I am going to leave you." That was the way he put it. He has left us; right?

Dr. FREDRICKSON. Yes.

Mr. PATTEN. Has our action here in the Congress providing raises at the higher levels helped you a little?

Dr. FREDRICKSON. Yes, it has. This last pay raise, which for many of our higher level officials was the first they had in about 6 years, was an extraordinary important move from the point of view of the Federal service. Perhaps not uniquely, but in the health professions the income differential is so enormous between the private sector and the Government that this was a very welcome, and indeed timely

improvement, Mr. Patten. We still have tremendous problems in competing with those differences, but this was a great help.

TOP LEVEL POSITIONS

Mr. PATTEN. How many of your Assistant Secretaries are confirmed? Are you in a hangup?

Dr. FREDRICKSON. Within the agency, we are in good shape. We have only one vacant Institute Director position. I still lack a deputy, but in the main our agency is well off.

Heads have been appointed for two of the six Public Health Service agencies. And we await the appointment of the Assistant Secretary for Health.

MEDICAL LIBRARIES

Mr. PATTEN. One last thing about that medical library at Rutgers, how do you feel now? We funded that money some years back. You mentioned it in your statement. On the medical libraries that you are supporting, are you still as satisfied as you were when we first decided to go ahead?

Dr. FREDRICKSON. I think this is a tremendous thing that has been done through the extramural program of the National Library of Medicine—this opportunity to set up regional library systems that can offer service to hospitals even in very small communities. I think we still have a long way to go. We want to increase that network and those channels, but the Library is working hard and effectively with the resources it has had to improve the opportunities for every physician to get the information he needs. I believe that extramural program of the libraries, the regional library system, is incredibly important and a great achievement.

Mr. PATTEN. I can only confirm from talking to practitioners and others I meet, who know the medical library that it is beautiful.

NIH ACCOMPLISHMENTS

Mr. PATTEN. I am glad you are here, Doctor.

Now, the $64 question. When I say a good word for NIH, people say to me, "Ed, what have they done; document it"; I am not that type. I don't document things. Have you something that will fortify me, so if someone says to me, you are spending $2 billion at NIH, what did they do up there, I can document?

Dr. FREDRICKSON. Yes; we will give you that kind of ammunition. We have a lot of achievements we can show you. I will get it for you.

RESEARCH TRAINING

Mr. FLOOD. Doctor, the report on the National Research Council, the one on the research manpower, has made a number of recommendations, and one was to boost the research training on clinical science. Does this NIH training budget for 1978 reflect an increase in this area in the budget?

Dr. FREDRICKSON. It does not reflect an increase in the budget for training, Mr. Chairman.

Mr. FLOOD. The National Research Council also called for a reduction of biomedical science of predoctoral candidates. Do you agree with that recommendation, and does this budget before us reflect that kind of a shift?

Dr. FREDRICKSON. This budget does reflect that kind of a shift in that moneys are allocated in new programs, under the National Research Service award, only for post-doctoral fellowships.

Mr. FLOOD. Let me ask you this: Is your training budget adequate enough for you to begin to carry out the recommendations of the National Research Council?

Dr. FREDRICKSON. I think we are doing an extremely critical amount of training. The National Research Council preliminary report refers to an increase in certain clinical or clinically related specialties.

Mr. FLOOD. Can you carry out the recommendations?

Dr. FREDRICKSON. We cannot through this budget provide as much training for certain critical clinical specialties as they suggest.

Mr. FLOOD. What are the inadequacies?

Dr. FREDRICKSON. Well, I think that some of the inadequacies lie in very special areas which they have partially identified. We expect to be more explicit, in their September report, in setting out critical categories. They have referred to clinical researchers which are always in short supply, if you want good ones, because here you must have an M.D. who is capable of doing both basic research and clinical research which is a hybrid product that takes a long time to develop.

It is also true that they point out that we are very short—and everyone knows it—in certain other categories that relate to pressing modern problems, such as environmental health specialists, epidemiologists and toxicologists. If we are to carry out the mandates of the Toxic Substances Control Act, there will be a tremendous shortage.

Mr. FLOOD. If you had a free hand to do as you pleased with the NIH spending programs, how would you restructure them and in what areas would you give the high priorities to?

Dr. FREDRICKSON. That is a very open invitation, Mr. Chairman.

I would—and I think that we will attempt to do so, as best we can—look at it in several ways. For example, I would like to see much of the predoctoral training concentrated in one or two institutes. But more than that, I would like to see us support more training that will provide multidisciplinary opportunities to allow the best kinds of people to get their doctoral degree in basic disciplines from which they can then move into critical areas.

Third, I would like to increase, if I could, the medical research training program which now has about 500 trainees; the academy recommends 600. This is a program to provide, for a certain number of very highly qualified and highly motivated medical students, part of the support for their education provided they combine training leading to the M.D. with the equivalent of getting a Ph. D. Such people, who will interpret research developed in the laboratory at the practical level at the bedside, make the difference between superlative and mediocre application of all the research knowledge that we have.

Mr. FLOOD. How many of your Institutes, and which ones, are carrying out or supporting the recombinant DNA research at this time?

By the way, you better translate recombinant DNA research.

Dr. FREDRICKSON. DNA, as we discussed earlier, and as you know, is the substance of the gene, deoxyribonucleic acid. Recombination means, literally, splicing together genes from different organisms. If one takes the bacterial gene, which is a simple one—not in a nucleus like ours are in chromosomes but which moves in the cell substance as a ring—one can extract the ring from a bacterium, one can open it up like a set of beads, take out a piece with some enzymes that leave sticky ends; then one can get a piece of foreign gene and stick it back in the ring and close it up and put the ring back into the bacterium. What you have done is created in the laboratory a recombinant DNA, which means genes from two different or several different species that are put back into a host organism.

At the present time, I think it is important to stress, that this is a technique more than a specific research problem. It is a fantastic new technique which allows people working in many areas to use it for their purposes.

[The information follows:]

At the National Institutes of Health, practically every Institute supports some DNA research—These are the National Cancer Institute, the National Heart, Lung and Blood Institute, the National Institute of Dental Research, the National Institute of Arthritis, Metabolism and Digestive Diseases, the National Institute of Allergy and Infectious Diseases, the National Institute of General Medical Sciences, the National Institute of Child Health and Human Development, the Division of Research Resources, and the John E. Fogarty International Center for Advanced Study in the Health Sciences.

Mr. FLOOD. What is the total funding at NIH for this area?

Dr. FREDRICKSON. At the present time, research involving the use of recombinant DNA totals $18.3 million.

Mr. FLOOD. How much of this entire recombinant DNA research is being conducted in the private sector?

Dr. FREDRICKSON. Very little. Ninety percent of the recombinant DNA research, according to our present estimate, is being conducted with Federal money and NIH is the principal supporter. The National Science Foundation is the only other one.

Mr. FLOOD. Whatever they are doing in the private industry, are they complying with your guidelines and safeguards?

Dr. FREDRICKSON. The Pharmaceutical Manufacturers Association, among whose members clearly lies most of the industrial activity, has adopted those guidelines as a standard for the industry.

Mr. FLOOD. Who should we have monitoring the responsibility, the commercial and non-NIH-funded recombinant DNA research, your organization, or some kind of organization such as OSHA?

Dr. FREDRICKSON. That, Mr. Chairman, is a very important question and the subject of the Interagency Committee about which I spoke earlier, a committee which is bringing in its recommendations on that point.

I do want to say one thing, and that is that NIH is not a regulatory agency, and we think it very unwise for it to become one. Therefore it will be necessary for NIH to work as a standard setter, in cooperation with at least one other regulatory agency, to carry out this important responsibilitity.

Mr. FLOOD. Does the budget have sufficient dollars for the NIH Institute to comply even with your own guidelines and safeguards on recombinant DNA research?

Dr. FREDRICKSON. We are going to attempt to find, Mr. Chairman, enough money and positions to continue to fund these activities.

Mr. FLOOD. All right.

RENOVATION OF FREDERICK FACILITY

Dr. FREDRICKSON. We have, in addition, a requirement for certain new containment facilities. We are going to have to renovate certain laboratories were we do high containment research and try to renovate our mobile P–4 laboratory for maximum containment. That is going to represent a cost of nearly $1 million in this fiscal year or over into the next.

Finally, we are going to have to create, we have decided after a hard analysis, a permanent P–4 facility at the Frederick Cancer Research Center at Fort Detrick, which will also be available to outside investigators.

Mr. FLOOD. Are you planning to move any work out to Fort Detrick?

Dr. FREDRICKSON. Yes.

Mr. FLOOD. Do you have money in this budget to make such a move?

Dr. FREDRICKSON. We do not have sufficient funds earmarked in this budget to begin to create that permanent facility. While funds are available in one or two appropriations, authority for major renovations is in the buildings and facilities appropriation and cannot be shifted. We will start it, however, with a cooperative effort supported by funds from three Institutes.

Mr. FLOOD. How much will it cost to set up facilities out at Fort Detrick?

Dr. FREDRICKSON. It would cost us about $1.8 million to renovate the existing complex; about $1.2 million for equipment. That is, a total of about $3 million over 2 years to do this. In addition, a number of positions will be needed to run the facility.

INFORMATION DISSEMINATION

Mr. FLOOD. Now we have all heard a great deal about, and this committee, itself, on several occasions expressed concern about the result of biomedical research not being adequately translated into health care and health disease prevention.

What is the current status of your information dissemination program? What are you developing at NIH on the overall strategy of disseminating and evaluating research results?

Dr. FREDRICKSON. We are following several lines. There are several stages, as you have identified, yourself. When Mr. Early and I were talking earlier, I mentioned that we feel a very real responsibility for what gets into the doctors' bag, what he has to use, the substance of

care. Part of that substance—most of it in this country—rises out of research findings. We are examining the processes whereby we can track research developments and at appropriate times, long before it is too late, anticipate the need to bring experts together for review and validation of research results and to arrive at a technical consensus on what is it that we know so that we can provide the best authority not only to practicing physicans but also, importantly, to other Government agencies who have to make decisions about funding and allocations and the use and the transfer of this knowledge.

This is a very important process which goes on. It is rather informal and not much structured at the present time, and we want to add some further structure to it to make sure that we don't fail to provide the best quality information to those who have to make many decisions about it, including using it for patients.

Mr. FLOOD. You are communicating with the practicing physicians now?

Dr. FREDRICKSON. Indeed we are. The report I have submitted to you lists a number of particular ways that have been developed in the last few years.

Mr. FLOOD. What we are concerned about here is in your statement that you made, the written statement, and the statement you made to us, you said that you had made a great deal of progress now in providing communications with the health professionals that are engaged in primary care. That is what we are concerned about.

Dr. FREDRICKSON. Here is the Journal of the American Medical Association. In it now, each month, is a page from the NIH which provides an analysis of the latest research developments for the practicing physician. That is one particular activity. We have developed a number of cassettes on practical problems like breast cancer and diabetes, and we are also developing television-taped programs which are used widely in closed circuit systems by local hospitals to update their practitioners.

We are now surveying the members of the American Academy of Family Practice to determine how they get their information. We may do the same for the osteopathic physicians. We are talking to them. We would also like to do the same project with the American College of Physicians. We are opening up joint symposia. We launched the first effort last year in cooperation with the District Medical Society. We had over 400 practicing physicians from 22 States who came to be brought up-to-date on the latest research findings and how they can be used in practice. We are providing assistance to a publisher of a reference manual for physicians. We are also doing NIH grand round by satellite. It is an experimental way of satelliting local communities in closed circuit television.

We have, in addition to the items I have indicated, developed a series of other tapes for use by practicing physicians, and it may be interesting, Mr. Chairman, to—if you remember the old-time current events test that used to be so popular—to know that we have, in connection with the educational testing system at Princeton, been working out a possible new annual self-examination for physicians that could be sent to them, all around the country, where, by doing their own grading, they could test their own knowledge of what is new in research as it applies to the practice of medicine.

Mr. FLOOD. I would like to say that we are pleased with your efforts so far in this area, and we are encouraged by the remarks you made in your opening statement. This process is an ongoing thing as far as you are concerned, an expanding one?

Dr. FREDRICKSON. Yes, it is.

Mr. FLOOD. We are going to be watching your efforts very closely.

DIABETES RESEARCH

Doctor, again in your opening statement, you said that $76 million is being spent for the diabetes research, slightly more than the amount recommended by the Diabetes Commission. How much more?

Dr. FREDRICKSON. It is approximately $3 million more in 1977 than the Commission recommendation.

Mr. FLOOD. How much more do you plan to spend in 1978, and how does that compare with the committee's recommendation?

Dr. FREDRICKSON. The total amount in 1978 will remain, Mr. Chairman, at approximately $76 million as compared with a Commission recommendation of $111 million.

Mr. FLOOD. Why aren't you funding the diabetes at the same level recommended by the Commission?

Dr. FREDERICKSON. The problem, Mr. Chairman, is that there simply are not enough resources in the several Institutes and, most particularly, in the National Institute for Arthritis, Metabolism and Digestive Diseases.

Mr. FLOOD. Do you think the committee's recommendation is too high? Is there enough high-quality research waiting in the wings to be supported?

Dr. FREDRICKSON. Mr. Chairman, the Commission's recommendation is too high relative to the amount of money available to the several Institutes, particularly the Arthritis Institute, to fund those diabetes projects against a whole variety of other competing problems they have.

Diabetes is an extremely important problem and an important effort is required. But there are other areas that will be even less well funded if any more money is removed from the present Arthritis Institute budget to shift to diabetes.

Mr. FLOOD. Have you discussed with the Diabetes Commission the problem you have and seem to have in meeting this recommendation?

Dr. FREDRICKSON. This will be discussed with the Board when it meets for the first time this month, Mr. Chairman.

Mr. FLOOD. Is the Diabetes Board giving you help in determining these priorities?

Dr. FREDRICKSON. Of course they have not yet convened for the first time, but it will be expected that they will be a help. That is their role.

Mr. FLOOD. What are the other Institutes going to do so far as diabetes is concerned in 1978? What I mean, if they plan to spend more, how much more? You can put that on a list in the record, showing the current funding and the 1978 proposed funding.

Dr. FREDRICKSON. We have that and will be glad to provide it, Mr. Chairman.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH—DIABETES

[In thousands of dollars]

	1977		1978	
	Commission recommendation	Appropriation	Commission recommendation	Budget request
NIAMDD:				
Total	42,071	39,826	65,684	37,907
Research grants and contracts		28,682	41,031	25,350
Centers	(8,000)	6,000	12,000	6,480
Training		1,635	6,635	2,365
Special activities		625	1,431	625
Intramural research (positions)	(15)	2,884	3,837	3,087
Program implementation (positions)	(17)		750	
NHLBI:				
Total	7,450	11,900	12,350	12,400
Research grants		8,851		8,412
Contracts				1,295
Centers		3,049		2,693
Positions	(2)			
NEI:				
Total	8,207	9,065	11,500	9,065
Research grants		5,141		5,141
Contracts		3,122		3,122
Training		400		400
Intramural research		402		402
Positions	(14)			
NICHHD:				
Total	4,016	4,618	6,166	4,746
Research grants		3,766	5,097	3,877
Contracts		500	700	500
Training		75	75	75
Intramural research		277	294	294
Positions	(2)			
NINCDS:				
Total	1,792	1,860	2,400	2,088
Research grants		984		1,107
Centers		400		459
Training		200		230
Special activities		276		292
Positions	(2)			
RR:				
Total	6,750	6,355	9,186	7,378
Other	2,970	2,413	4,128	2,425
Positions	(5)			
Total	73,256	76,038	111,414	76,009

Note: Commission did not consistently recommend distribution of the funds for each institute. Commission did not recommend positions in 1978. Commission recommendation for 1977 was contained in the report prepared in 1975. The 1978 recommendations were prepared in 1976.

PEER REVIEW SYSTEM

Mr. FLOOD. I understand that you recently examined your peer review process for approving grants to determine if any improvements can be made. You know we keep hearing a great deal from people about this, that the process is really an old boys' club, you know, and also there is no provision for appeals.

What do you have to say; what kind of improvements, if any, are you going to make in this peer review process?

Dr. FREDRICKSON. That system has been the subject of intensive review over the last year involving an extensive questionnaire, a number of hearings, and a tremendous input from the community of

researchers. The committee has just finished its report, and it has been submitted to me. It is now being reviewed in my office by a number of people because it contains a large number of important and interesting recommendations. These have to do with the question of appointment to study sessions to avoid the old boy problems, conflict of interest, and they have recommended an appeals system, an ombudsman, in the process, in addition to a number of other important changes.

I am proud of the committee—headed by Dr. Ruth Kirschstein, the Director of the Institute for General Medical Science—and the tremendous amount of work they did, in addition to their regular load, to do this job carefully and, I think, thoughtfully. I will have a full copy of that report for you, Mr. Chairman, just as soon as it is printed.

GAO REPORT

Mr. FLOOD. GAO, the General Accounting Office, has issued a report on the need for better controls over biomedical research, supported by NIH. One of the recommendations calls for the development of a system to identify noncompeting grants with significantly less scientific merit and the unfunded competing grants applications. What, if anything, have you done to implement that recommendations?

Dr. FREDRICKSON. We have responded to that GAO report.

Mr. FLOOD. What I means, in effect, is that GAO seems to be saying stop funding low quality ongoing work, and use that money to fund a higher quality of research projects.

Dr. FREDRICKSON. Basically, Mr. Chairman, we have disagreed with the GAO and the administration has supported our opinion. We have provided a detailed answer. Our position is simply that this is not an efficient way to run a scientific system, that once you chose a scientist, on the basis of very competitive analysis—which does not allow, at any current funding levels, the choice of a bad scientist—you must allow him a sufficient time to proceed with the project for which you have supported him. You cannot possibly, in the first year of such support, make an analysis that would allow you to drop out people in any kind of an efficient way, so that new grants might be substituted for them. It is simply not possible in the scientific process.

Mr. FLOOD. Also, that GAO report recommended the establishment of a formal system for approving all intramural research projects. Have you established or set up such a system?

Dr. FREDRICKSON. No, we have not, Mr. Chairman. We disagreed, also, with the GAO in that recommendation although we understand their sensitivities to an important problem about which we are always concerned. That is, to make sure that the quality of our in-house work is every bit as good as the outside work we support—and we hope, in the main, better, but——

Mr. FLOOD. You have not set up such a system?

Dr. FREDRICKSON. No, sir, we cannot. We think it would be unwise to attempt to do this within the intramural system.

Mr. FLOOD. You couldn't give us a detailed description about how such a system would work, or anything? Can you do it for the record?

Dr. FREDRICKSON. We can do it for the record, and we would like to add what we are doing and why we think it is a better system.

[The information follows:]

SYSTEM FOR APPROVING INTRAMURAL RESEARCH PROJECTS

Appendix I of the GAO Report dated July 22, 1976, entitled, "Better Controls Needed Over Biomedical Research Supported by the National Institutes of Health" contains the comments of the Department of Health, Education, and Welfare in response to the GAO Draft Report; in the section responding to the GAO recommendation concerning intramural research it says, "We do not concur in the recommendation that intramural research projects be reviewed and approved by a peer review group prior to the initiation of research projects. We believe that the present internal system of control over intramural research is more economical, efficient, and timely than a peer review system similar to or duplicative of the system used for awarding grants would be. The quality of the work of NIH intramural scientists as well as the priority of their ongoing research projects is already routinely reviewed and evaluated at several levels within the NIH system.

Operating the type of formalized peer review system used for awarding NIH grant funds is very costly in several ways. NIH spends considerable money in consultant fees and travel costs for the hundreds of outside experts it uses to review and evaluate grant applications. Much high-level scientific manpower is spent in reviewing and evaluating applications, making needed site visits to prospective grantees, and meeting three times yearly to decide on the acceptability of grant applications and set priorities on those judged acceptable.

However, a system had to be established to assure that only meritorious science is supported under the NIH grants mechanism. To meet this need the peer review system has evolved as the best mechanism for defining and administering a quality extramural biomedical research program which is spread over a wide geographic area. However, it is not the best mechanism for administering an ongoing intramural scientific program. The intramural research program of NIH is largely self-contained in the geographic sense and can avail itself of a highly appropriate but different mechanism for defining and administering a quality in-house research program, namely, continuing review and evaluation, carried out both formally and informally by the scientists' colleagues and superiors.

Only if the operating NIH intramural system were not providing highly productive, high level research results would it appear desirable to consider imposing on it such a costly mechanism as outside peer review. The NIH intramural program, however, by any method of measurement yet devised, has produced extremely well resulting in very high quality scientific endeavors.

Intramural NIH scientists are under the control and supervision of carefully selected section and laboratory or branch chiefs who continually review and evaluate their work. The laboratory or branch chiefs report to and are under the control of their Institutes' Scientific Directors who report to the Institute Directors and also to the NIH Deputy Director for Science, both individually and collectively, at semimonthly scientific directors meetings.

Every time a technician is assigned or a piece of equipment purchased a decision is made on the quality and priority of the research. The real reviews and decisions are made within the area of allocating scarce resources. When projects do not measure up, such resources are withheld or negotiated downward.

Each Institute has a Board of Scientific Conselors, comprised of scientists from outside NIH, which reviews in an advisory capacity the Institute's intramural research programs. These Boards were created to bring to bear on the various intramural programs the direct views of experts from outside NIH. The Boards, in essence boards of visitors, were intended to (1) advise Institute Directors and their Scientific Directors on research program designs, emphases, and directions and (2) review and generally evaluate scientific work under the research programs.

The continuing review and evaluation mechanism, such as used at NIH, has gained long-standing acceptance in industry, commerce, and academic because it is: (1) Continuous rather than episodic; (2) immediately responsive in allocating resources in the continuous competition for the limited budget and space available; and (3) dynamic and produces viable and effective feedback.

An important contrast can be made between the extramural peer review process and the intramural review and evaluation process. In the former, there is only periodic opportunity for assessment of the value of research work being proposed. In the latter, there is close supervision and continuous assessment by superiors, colleagues, and associates during the conduct of the research itself.

Therefore, we believe that the continuing review and evaluation mechanism is the best method for supporting and maintaining the quality of the NIH intramural program.

We do not believe that approval of a written protocol prior to initiation of an intramural research project would be a desirable procedure to impose upon NIH intramural projects. Such a procedure would impose an unnecessary degree of formality and rigidity to the ongoing internal management of the intramural research program. It would possibly, by stifling work in particular areas, actually diminish the uniqueness and quality of the intramural program.

In response to the final GAO report, HEW gave the following comments in regard to the GAO recommendation concerning intramural research.

"As we stated in our comments on the GAO draft report, 'The administrative practices of almost any enterprise can be strengthened or improved. NIH is no exception. However, while it is frequently easy to design apparently appropriate improvements, particular care must be taken that instituting such improvements does not irreversibly alter the integrity of the involved organization.

"In our previous comments we discussed the high cost in dollars and manpower that would be involved in instituting formal preaward reviews of intramural projects by panels of outside experts. The final [GAO] report states that 'a peer review group of NIH scientists could be used for such a purpose.' We agree that in terms of lower costs, primarily dollar costs, such in-house reviews would be preferable to reviews by outside consultants. However, we still disagree with the recommendation 'that written plans for all intramural research be reviewed and approved by peer review groups before research projects are initiated.'

"In the ongoing work of any scientist it is very difficult to define when one project ends and another begins. It is the nature of science that the process of answering one question generally creates a whole array of new questions, resulting in new priorities that could not have been originally anticipated. Often, a junior staff member initially works on a project of his supervisor, but later branches off on his own project. However, it is often difficult to define exactly when the new project begins.

"When an extramural NIH grant is given to a university, the scientists doing the work are university employees. NIH intramural scientists are NIH employees. The relationships NIH has with grantee university employees and those it has with its own employees are very different and require different mechanisms of administration, supervision, and review."

In summary we believe that the present system of control over intramural research is more economical and efficient than a prereview system similar to the system used for awarding extramural grants. The NIH intramural program has produced extremely well, resulting in very high quality scientific results. The extensive intramural review and evaluation process already in place is functioning very well. We disagree with GAO, "that written plans for all intramural research be reviewed and approved by peer review groups before research projects are initiated." However we agree with GAO that if such a system were to begin, a peer review group of NIH scientists could be used for such a purpose.

It should be noted that while we reject the concept of formal prereview for all intramural projects, NIH does now require and will continue to require formal prereview for certain types of projects, including any experiment involving human subjects and any experiment involving hazardous or potentially hazardous microbiological agents, including research involving recombinant DNA molecules. In these cases, no such project may begin until the formal prereview is completed and the project approved. As an example of the process, in the case of research involving recombinant DNA experiments, the investigator proposing to initiate such a project must prepare a memorandum of understanding and agreement describing the proposed experiment, the potential risks, and the proposed safety measures. This must be approved by the investigator's laboratory or branch chief, the Scientific Director of the Institute, and the Director of the Office of Recombinant DNA Activities. It must also be approved by the NIH Biohazards Committee. This committee consists of scientists from each of the NIH Institutes. It also consists of a representative from the Montgomery County Health Department (currently the representative is Chief of the Bureau of Community Health Services and Epidemiology), a representative from the Montgomery County Department of Environmental Protection (currently the representative is Chief of the Water Quality Control Section), and a representative of the

Maryland State Department of Health (currently the representative is also Secretary of the American Society for Microbiology).

In addition, the laboratory where the proposed recombinant DNA experiment will be conducted must be inspected and certified by the NIH Associate Director for Environmental Health and Safety. Only after these preliminary approvals and certificatons are given is the final approval given by the NIH Deputy Director for Science, and then that particular recombinant DNA experiment may begin.

Mr. FLOOD. One of the findings of the GAO was that NIH is not receiving certain reports from grantees required by a condition to the grant. Have you corrected that deficiency?

Dr. FREDRICKSON. We have begun to bring more pressure on the grantees to get their final reports in. The main reason, Mr. Chairman, why this is of less importance than it might otherwise be is that the final report of a grant is, in effect, the usual request for renewal of that grant, and it is impossible for an investigator to continue to receive support if he cannot justify the use of his previous funds in terms of further achievements. We therefore have an excellent tracking system for determining how well our advisors are doing because the vast majority are returning for repeats and their activities are fully——

Mr. FLOOD. GAO says there is a deficiency. The minute we get something like that we want to know are these grantees meeting this condition precedent to a grant?

Dr. FREDRICKSON. We regard this as a technical deficiency but not a substantive one in the appropriate management of our funds in regard to our public accountability.

Mr. FLOOD. Mr. Natcher?

Mr. NATCHER. No further questions, Mr. Chairman.

Mr. FLOOD. Thank you very much.

Dr. FREDRICKSON. Thank you, Mr. Chairman.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record:]

RECOMBINANT DNA RESEARCH

Mr. ROYBAL. As your statement indicates, there has been much concern over the possible dangers that could result from recombinant DNA.

Would you briefly outline how you developed your guidelines?

Answer. Stimulus for the development of guidelines for recombinant DNA research came from those most knowledgeable about its potential risks and promise—scientists (predominantly academic) actually engaged in that research. NIH—the principal supporter of research in relevant areas—took the lead in guideline development because a special committee of the National Academy of Sciences, representing the research community, specifically asked it to. From the beginning, NIH viewed this task as having several phases. In the initial or "technical" phase, the principal concern was to bring together the most knowledgeable scientists to achieve a "technical consensus" on the nature and extent of risks involved, and what could be done to minimize them. With technical aspects of the problem pinned down as well as possible, the next phase would subject resultant draft guidelines to review and modification in terms of a wide range of public policy concerns, including environmental, ethical, et cetera. Beyond this, there were problems of securing compliance with these or similar guidelines by researchers not dependent on NIH support (that is, those in industry, in foreign countries, et cetera.)

In October 1974, the Director, NIH established the NIH Recombinant DNA Molecule Program Advisory Committee (made up of leading scientists, but with consultants in several other areas) to propose draft guidelines. Based on recommendations that came out of an international conference concerned with this

research (the Asilomar Conference, held in February 1975), the committee wrote a series of guideline drafts that incorporated the basic principles of physical and biological containment as safety features. Proposed guidelines were recommended to the Director, NIH in December 1975, and a special open meeting of the Advisory Committee to the Director, NIH was convened in February 1976 to review them.

The comments received from committee members and public witnesses (representing a wide range of viewpoints) were considered by the NIH Recombinant DNA Molecule Program Advisory Committee at a meeting in April. Concurrently, meetings with representatives from other Federal agencies and private industry, as well as with congressional staffs were held to exchange information on the proposed guidelines. On July 7, 1976, the NIH guidelines, including a document indicating the basis of decisions by the Director, NIH, were published in the Federal Register for public comment. The guidelines establish stringent safeguards for experiments utilizing this technology and prohibit experiments considered to be too risky. In addition, a draft environmental impact statement was published in the Federal Register on September 9, 1976, to afford additional review and comment on environmental effects, if any, of the research permissible under the guidelines. Comments received are being analyzed and will be responded to in the final environmental impact statement to be published soon.

There are provisions for modifying the NIH guidelines as new knowledge concerning the technology becomes available.

Mr. ROYBAL. Did those persons who are vocally opposed to this type of research have an input into the drafting of these guidelines? If so, how? If not, why not?

Answer. Procedures for developing the NIH guidelines made provision at a number of points for a wide range of policy perspectives, including those of individuals vocally opposed to recombinant DNA research. Provision is also made for continuous revision and updating of the guidelines as better information becomes available.

Divergent public and scientific comment clearly was possible at the several open meetings of the NIH Recombinant DNA Molecule Program Advisory Committee and the February 1976 meeting of the Advisory Committee to the Director, NIH. Many changes in the guidelines resulted from comments made in the open meetings, or as a result of written comments, solicited in followup to these meetings. Much of the documentation on these comments will be found in the NIH publication, Recombinant DNA Research, Volume I. Of course, not every criticism of the guidelines could be accepted, since many directly contradicted each other. In any case, it probably won't be possible to satisfy the relatively small number of commentators who oppose this type of research irrespective of efforts to minimize risks.

A further airing of issues over the next several months is expected at congressional hearings in the House and Senate on several bills that have been introduced on Recombinant DNA Molecules.

Mr. ROYBAL. Would you briefly outline the problems that could develop as a result of this research?

Answer. The principal concern which has been raised regarding the actual conduct of this research has to do with the possibility that organisms containing recombined DNA may be altered in a way which would cause them to become harmful to other life forms or to the environment. In the research under discussion, the recipient cells are generally single-cell microorganisms such as bacteria, or animal or plant cells that were originally obtained from living tissue but are grown as single cells under special laboratory conditions.

Current knowledge does not permit accurate assessment of whether or how the insertion of DNA derived from one microorganism into another may change the properties of the recipient organism. Such changes may be advantageous, detrimental, or neutral with regard to the recipient organism's ability to survive outside of controlled laboratory conditions. Whether the organism would be able to affect other forms of life that come into contact with it also isn't clear. While it should be emphasized that there is no known instance in which a hazardous agent has been created by recombinant DNA technology, it is not possible at this time to outline the problems that could develop as a result of this research because all discussions of harmfulness or harmlessness are speculative in the absence of more knowledge. In the meantime, scientists have felt that it is possible to advance certain assessments regarding probabilities of risk and it is these categories of probabilities on which current NIH guidelines for recombinant DNA molecules are based.

Mr. ROYBAL. Do you believe that we should allow private companies to engage in this kind of research? Why?

Answer. Provided that private companies conduct recombinant DNA research under the same carefully controlled conditions required of others engaged in this work, there is no reason to deny them the opportunity to do so. Indeed, the range of potential practical applications of this research is so vast that considerable interest on the part of the private sector is to be expected, and (given adequate controls) should be encouraged.

Mr. ROYBAL. In Cambridge, Mass., the city council did not allow Harvard to engage in this type of research until after it held a hearing and voted on the matter.

Do you believe that local units of government should have the power to halt this type of research?

Answer. Local units of government, such as Cambridge, derive their powers from the State. State authority to regulate health and safety matters derives from the U.S. Constitution, the common term for this authority being "police power." Accordingly, the Cambridge City Council acted entirely within its authority in temporarily halting moderate to high risk. Low risk research was allowed to continue. In specific circumstances, the Federal Government may, by statute, preempt State and local authority, and has done so in a number of instances.

In the NIH view, the regulation of recombinant DNA molecules is an area in which the adoption of a single national standard makes best sense. In no other way will it be possible to achieve maximum research gain in an area of unusual promise, with minimum risk to health or the environment. Federal preemption of State and local authority therefore becomes the recommended course of action. The potential hazards posed by the use of recombinant DNA techniques extends well beyond the local to the national and international levels. The complex and sophisticated scientific techniques involved require that the judgments on what is safe be made by the best informed individuals. At the same time, this complexity makes it unlikely that local jurisdictions would have the resources to interpret, inspect, and enforce regulations in a uniform and meaningful way.

If a single national standard for this research were mandated, this would not mean that local research institutions could or should ignore the community within which they are located. On the contrary, effective interaction with the community, including full information exchange, would become most important. In the current NIH guidelines for the conduct of recombinant DNA research, the local biohazards committees specified are designed to allow for strong community representation.

DISSEMINATION OF RESEARCH RESULTS

Mr. ROYBAL. In your statement, you spoke about dissemination of information. Would you indicate what sort of liaison you have established with professional association to help disseminate the results of your studies?

Answer. Our initial effort to improve the dissemination of research results has been carried out through the Journal of the American Medical Association (JAMA). The format and general content of the "From the NIH" series published monthly in JAMA were developed in discussions with the AMA officials responsible for the journal.

We are preparing materials for a survey of the patterns of communications used by a 2,500-member panel of the American Academy of Family Practice (AAFP) through a contract awarded by the NIH to the AAFP. The purpose of this study is to identify the most effective channels of communication with family physicians.

We have opened discussions with the AAFP and the American Osteopathic Association to plan surveys of their total memberships regarding the means they use for keeping current and to evaluate our dissemination projects, particularly the video cassettes to be distributed shortly.

The NIH and the Medical Society of the District of Columbia jointly sponsored a bicentennial symposium on research related to clinical problems on September 16–18, 1976, to which American Medical Association members from all eastern States were invited.

Thus far we have given priority to communication with organizations of frontline physicians. However as our programs develop we will deal with other specialty groups concerning the communication of subject matter of special interest to the various specialties.

PEER REVIEW SYSTEM

Mr. ROYBAL. Last year you indicated that you would be completing your study on the peer review system in fiscal year 1977. Did you complete it? What did it show? Will you be making any changes as a result of the study?

Answer. The study has been completed and the report has been submitted to me. It is in the process of being reviewed in our office by a number of people, because it contains many important and interesting recommendations. These have to do with the question of appointments to study sections, conflict of interest, an appeals system, the appointment of an ombudsman in the process, and other important changes. After these recommendations have been reviewed, we will be making decisions as to any changes we will make in the process. I will be happy to provide a copy of the report for you as soon as it is printed.

MINORITY EMPLOYMENT

Mr. ROYBAL. Last year you told us that Spanish-surnamed employment at NIH was six-tenths of 1 percent. Has it improved since last year?

Answer. As of December 1976, Spanish-surnamed employment remains at six-tenths of 1 percent. However, NIH has hired a Spanish-speaking program coordinator with the intent of substantially increasing the number and percentage of Hispanics in the work force.

INSTANT CONSULTATION SYSTEM

Mr. ROYBAL. Last year you told us that you were setting up a system in cooperation with the University of Wisconsin, which would expand your instant consultation system. Would you bring us up to date with what has occurred in this regard in the last fiscal year?

Answer. The Wisconsin project is still considered to be feasible and promising. However during the past year the limited staff of the NIH Task Force on Communications has concentrated on the activities listed in the report which I filed with the committee at the opening of these hearings. Several of the activities reported were one-time efforts (the DC–NIH seminar, two 1-hour videotape productions, preparation of videotapes from the International Breast Cancer Conference) and their completion will make it possible for the task force to resume efforts this spring to establish the Wisconsin project.

CONSENSUS DEVELOPMENT

Mr. ROYBAL. I understand that extensive discussions are taking place in NIH concerning the need for a new approach in monitoring and evaluating research results and their impact on health practice. Could you please inform us what is the nature and scope of this approach?

Answer. The NIH has had extensive discussions concerning the role and responsibilities of the NIH in promoting the effective introduction into the health care delivery system of new knowledge pertinent to health care. The key element in the concept we are considering lies in the requirement that each institute create a formal mechanism whereby new knowledge pertinent to health care is subjected to a technical consensus process participated in by all the relevant and interested parties. In this process, emphasis would be placed on such key questions as the adequacy of validation for safety and efficacy; identification of gaps in the knowledge base; the need for control/demonstration programs, and the need for impact assessment as to cost, ethical aspects, legal, et cetera. Recommendations emerging from this process would be packaged in a form for ready understanding and acceptance by the practicing community. It is anticipated that academic medical centers, the professional societies, and other groups in the professional and voluntary medical sectors will play a major role in the dissemination process. An important derivative benefit would lie in the fact that recommendations evolving from the consensus process could provide a basis for standard setting and criteria for third-party payers.

This concept is now being circulated in the Department for review and comment.

Mr. ROYBAL. Would you explain how this approach would benefit health care in our communities? Would it involve impact assessment and recommended safeguards?

Answer. The approach we are considering represents an effort to improve and enhance the dissemination of new research results pertinent to health care

and to provide guidelines to the practicing community concerning optimal intervention as they emerge from the consensus development process. Although this process will not solve all the problems of the Nation's health care delivery system, it should help to ameliorate the unevenness in the quality of care delivery.

As indicated above, the technical consensus process would undertake some degree of impact assessment and as such, would make recommendation concerning precautions and safeguards. Frequently, the technical consensus process might indicate the need for a full impact assessment and in such cases, organizations in the health care sector with its diverse components would be in a better position and have the necessary expertise to assess economic, cost, legal, or other potential social effects.

Mr. ROYBAL. What biomedical or health consensus would be necessary in establishing guidelines? Would the consumer be able to participate in the development of such a consensus?

Answer. Certainly. In many of the consensus processes, consumer or public participation would be essential.

Mr. ROYBAL. Would you furnish us with a list of important research subjects which would undergo this approach and perhaps require guidelines? Would you please explain how, for example, you would specifically deal with the definition of brain death? Or with the control of genetic diseases?

Answer. A definition of brain death provides an excellent example whereby consensus development could be utilized. As a first step there would be a compilation by the NIH of the available knowledge base on this subject. Next, a group of neurological experts in the field, scientific staff from NINCDS, representatives of professional neurology societies, members of the legal profession, ethicists, theologians, public representatives, et cetera, would be brought together and asked to attempt to develop guidelines delineating criteria for cessation of brain function. Such guidelines would then be widely disseminated as previously described: Updating would occur as indicated utilizing the same mechanism.

[Following is a list of research subjects.]

Possible NIH topics for consensus development

Mental retardation—detection, diagnosis, and intervention.
Role of mammography in detection and diagnosis of breast cancer.
Coronary artery disease and behavior patterns.
Hypertension and diet.
Specific combined modality treatment for breast cancer.
Control of genetic diseases—prevention of disease and disability through application of knowledge concerning human genetics—role of diet, amniocentesis, enzyme replacement, tissue transplantation.
Definition of brain death.
Treatment of diabetic retinopathy.
Diabetic acidosis—use of low-dose insulin.
Diabetes in the elderly—diagnosis and therapy.
Screening for glaucoma.
Perinatal intensive care—fetal monitoring, nutrition, phototherapy modification of sensory input.
New contraceptive measures.
Hemodialysis—utilization, funding.
Gastrointestinal endoscopy—indications; who should perform it and under what circumstances.
Advisability of breast feeding in presence of toxic environmental pollutants.
Cholestyramine in management of PCB, PBB, et cetera, "poisoning."
Utility of certain new antitumor drugs (for example, adriamycin).
Chenodeoxycholic acid for dissolution of gallstones.
Artificial pancreas.
Weight reduction—appropriate diet.
Insect sting, allergy—skin testing, desensitization, and treatment.
Asthma—diagnostic classification and appropriate treatment.
Asthma and allergic rhinitis—treatment.
Penicillin "allergy"—appropriate diagnostic tests.
Schistosomiasis—conditions of treatment and appropriate drugs.
Viral hepatitis—use of hyperimmune serum; testing of inactivated vaccine.
Thromboembolism—use of low-dose heparin.

Estrogen replacement in the postmenopause.
Osteroporosis—prevention and therapy.
Bromocriptine in the treatment of Parkinsonism.
Treatment of epilepsy—measurement of blood levels of anticonvulsant drugs.
Deafness—implantation of electrodes as treatment.

Mr. ROYBAL. Could this effort begin in fiscal year 1978? What kind of budget and positions would be necessary?

Answer. As an initial step the NIH has begun to structure a small office of five people in the Office of the Director which will have responsibility for providing guidance and central support to the Institutes in this process as well as evaluating the progress of their activities. We anticipate that the program can be initiated this year at an estimated cost of $134,000.

The total cost and personnel requirements for all of the National Institutes of Health for the first year startup are estimated to be approximately $670,000 and 15 positions.

NUMBER OF DISEASES

Mr. MICHEL. How many diseases is NIH currently investigating or are affected by your research? Can you provide a number in this regard so we can get a general idea?

Answer. This is a very difficult question to answer due to the problem of defining the word "diseases". I will place in the record an excerpt from the "Report of the U.S. Delegation to the International Conference for the Eighth Revision of the International Classification of Diseases," which lists over 1,000 different disease areas and each of these having from three to nine subcategories. The National Institutes of Health has interests in and performs research on practically every one of these; not necessarily all at one time, but at different times.

Mr. MICHEL. What I would like to have you do is to list all these diseases by disease grouping and provide the amount of funds being spent by NIH directly and indirectly (two columns) on these diseases. In other words, as an example, "skin diseases" should be listed as a general heading, with all the various skin diseases and their dollar amounts listed below it, and then a total for skin diseases listed.

Answer. Cost data for each and every one of these diseases is not available. I will be happy to supply for the record a table which members of your committee have found useful in providing cost data for various disease areas. This table reflects specific areas in which the Congress has shown special interest and for which cost data is available, or for which reliable cost estimates can be made. In addition, we have some cost data on trans-NIH issues, such as diabetes, arthritis, nutrition, and genetic diseases. I will also place these in the record.

A COLLATION OF NIH INSTITUTE EXPRESSIONS OF INTEREST IN DISEASE CATEGORIES

Prepared Feb. 18, 1977 from memoranda supplied by 6 institutes (NIAMDD, NIDR, NIEHS, NHLBI, NINCDS & NICHD) and respecting other institutes, the judgment of DRG Staff.

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INSTITUTE CODES
AM = NIAMDD
DE = NIDR
ES = NIEHS
HE = NHLBI
NS = NINCDS
AG = NIA
AI = NIAID
CA = NCI
EI = NEI
GM = NIGMS
HD = NICHD

VITAL and HEALTH STATISTICS

DOCUMENTS AND COMMITTEE REPORTS

Report of the United States Delegation to the International Conference for the Eighth Revision of the International Classification of Diseases, Geneva, 1965.

Geneva, Switzerland - July 6-12, 1965

Discussion and recommendations at the Conference that was concerned primarily with Eighth Revision of the International Classification of Diseases and gave some consideration to multiple-cause tabulation and analysis and to hospital statistics.

Washington, D.C. September 1966

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
John W. Gardner
Secretary

Public Health Service
William H. Stewart
Surgeon General

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APPENDIX III

INTERNATIONAL CLASSIFICATION OF DISEASES
EIGHTH REVISION

1. Three- and four-digit titles

The following three- and four-digit categories constitute The Detailed List referred to in the Report of the Conference under item 1.2. They are based on the revision proposals submitted to the Conference (WHO/HS/ICD/74.65 Add. 1-17) and on the amendments adopted by the Conference (WHO/HS/8 Rev. Conf./10.65). Editorial changes suggested during the Conference and not appearing in the amendments were incorporated as far as appropriate. A few changes of substance became advisable in the detailed review of the revised classification.

2. Other indications

Apart from the three- and four-digit titles there are various references and notes, in order to enable countries to start work on national adaptations in languages other than those of the international versions.

2.1 References to ICD numbers

New titles were related to the numbers of the current ICD whenever the content was the same or changed in a way which could be expressed in a relatively simple form. Such references were omitted in the Nature-of-injury classification (N-code), the larger part of which corresponds to the three-digit categories of the ICD (Nos. N800-N959). No attempt was made in respect of ICD references for sections which underwent a complete revision, e.g. mental disorders.

2.2 Exclusion notes

Although not exhaustive, exclusion notes were provided for titles that would raise doubts regarding their content.

2.3 Inclusion terms

Inclusion terms are as a rule not stated, although inclusion notes appear in some places. This particularly applies to diseases of the circulatory system, in view of the complexity of the classification.

Fourth digits .8/.9

As recommended by the Conference, fourth digits .8 and .9 were respectively reserved for "Other" and "Unspecified" where both titles conveyed a real meaning. Otherwise .9 was used for "Other and unspecified" or "Other" only in order to save fourth digits for further sub-division. For the same reason absence of an associated condition ("without mention of . . .") was given the fourth digit .9. It should be pointed out that the arrangement may still undergo some changes during the compilation of the full tabular list in the light of the inclusions to be accommodated.

I. INFECTIVE AND PARASITIC DISEASES

This section includes diseases generally recognized as communicable or transmissible. It excludes acute respiratory infections, influenza and pneumonia and certain localized infections.

Intestinal infectious diseases (000-009)
Excludes helminthiasis (120-129)

000 Cholera AM AI

.0 Classical
.1 El Tor
.9 Unspecified

001 Typhoid fever AM AI

002 Paratyphoid fever AM AI

.0 Paratyphoid fever A
.1 Paratyphoid fever B
.2 Paratyphoid fever C
.9 Unspecified

003 Other Salmonella infections AM AI
As ICD 042

.0 Without mention of food as vehicle of infection
.1 With food as vehicle of infection

004 Bacillary dysentery AI

.0 Shiga
.1 Flexner
.2 Boyd
.3 Sonne
.4 Schmitz-Stutzer
.8 Other
.9 Unspecified

005 Food poisoning (bacterial) AM AI
Excludes Salmonella food poisoning (003.1)

.0 Staphylococcal
.1 Botulism
.2 Due to other clostridia
.8 Other bacterial food poisoning
.9 Unspecified

006 Amoebiasis AM AI

.0 With liver abscess AM
.8 With other manifestations
.9 Unqualified

007 Other protozoal intestinal diseases AM AI

.0 Balantidiasis
.1 Giardiasis
.2 Coccidiosis
.9 Other and unspecified

008 Enteritis due to other specified organism AM AI

.0 Escherichia coli
.1 Arizona
.2 Other bacteria
.3 Bacterial enteritis NOS
.9 Other organism, not elsewhere classified

009 Diarrhoeal disease AM AI

.0 Dysentery NOS AM
.1 Diarrhoea AM
.2 Gastro-enteritis and colitis AM
.9 Other AM

} Without mention of non-infectious aetiology or infecting organism

Tuberculosis (010-019)

010 Silicotuberculosis AI ES

011 Pulmonary tuberculosis HE AI

012 Other respiratory tuberculosis
Excludes respiratory tuberculosis, unqualified (011)

.0 Primary
.1 Pleurisy specified as tuberculous
.2 Pleurisy with effusion without mention of cause
.3 Tuberculous laryngitis
.9 Other

013 Tuberculosis of meninges and central nervous system AI NS

.0 Tuberculous meningitis
.9 Other

014 Tuberculosis of intestines, peritoneum and mesenteric glands AM AI

015 Tuberculosis of bones and joints AI

.0 Vertebral column AM *
.1 Hip AM
.2 Knee AM
.8 Other AM
.9 Unspecified AM

016 Tuberculosis of genito-urinary system AM AI

017 Tuberculosis of other organs AM AI

.0 Skin and subcutaneous cellular tissue AM
.1 Peripheral lymphatic glands
.2 Eye
.3 Ear
.9 Other

018 Disseminated tuberculosis AI

.0 Acute miliary tuberculosis specified as non-pulmonary
.1 Acute miliary tuberculosis unspecified
.9 Other forms of disseminated tuberculosis

019 Late effects of tuberculosis AM

.0 Respiratory tuberculosis HE
.1 Central nervous system
.2 Bones and joints
.3 Genito-urinary system
.9 Other specified organs

Zoonotic bacterial diseases (020-027)

020 Plague AI

.0 Bubonic
.1 Pulmonic
.9 Unspecified

021 Tularaemia AI

022 Anthrax AI

023 Brucellosis AI

.0 Br. melitensis
.1 Br. abortus
.2 Br. suis
.9 Unspecified

024 Glanders AI

025 Melioidosis AI

026 Rat-bite fever
- .0 Spirillum minus
- .1 Streptobacillus moniliformis
- .9 Unspecified

027 Other zoonotic bacterial diseases AI
- .0 Listeriosis
- .1 Erysipelothrix infection
- .9 Other

Other bacterial diseases (030-039)
Excludes bacterial venereal diseases (098, 099) and bartonellosis (089.0)

030 Leprosy AI
- .0 Lepromatous
- .1 Tuberculoid
- .2 Indeterminate
- .3 Borderline
- .8 Other
- .9 Unspecified

031 Other diseases due to mycobacteria AI

032 Diphtheria AI

033 Whooping cough AI
- .0 B. pertussis
- .1 B. parapertussis
- .9 Unspecified

034 Streptococcal sore throat and scarlet fever AM, HE, NS AI
- .0 Streptococcal sore throat AM
- .1 Scarlet fever

035 Erysipelas AM AI

036 Meningococcal infection
- .0 Meningococcal meningitis NS
- .1 Meningococcaemia without mention of meningitis
- .8 Other forms of meningococcal infection
- .9 Unspecified

037 Tetanus AI

038 Septicaemia AI
- .0 Streptococcal
- .1 Staphylococcal
- .2 Pneumococcal
- .8 Other bacterial
- .9 Unspecified

039 Other bacterial diseases AI
- .0 Gas gangrene
- .1 Rhinoscleroma
- .9 Other

Poliomyelitis and other enterovirus diseases of central nervous system (040-045) NS

040 Acute paralytic poliomyelitis specified as bulbar NS AI

041 Acute poliomyelitis with other paralysis AI NS

042 Acute non-paralytic poliomyelitis AI NS

043 Acute poliomyelitis, unspecified AI NS

044 Late effects of acute poliomyelitis AI NS

045 Aseptic meningitis due to enterovirus NS AI
Excludes aseptic meningitis due to: Poliovirus (042); virus of herpes zoster (053); herpes simplex (054); mumps (072); lymphocytic choriomeningitis (079.2)
- .0 Coxsackie virus NS
- .1 ECHO virus NS
- .9 Aseptic meningitis, NOS NS

046 Other enterovirus diseases of central nervous system AI NS

Viral diseases accompanied by exanthem (050-057)
Excludes arthropod-borne viral diseases (060-068)

050 Smallpox AI
- .0 Variola major
- .1 Variola minor (alastrim)
- .9 Unspecified

051 Cowpox AI

052 Chickenpox AI

053 Herpes zoster AI

054 Herpes simplex AI

055 Measles AI

056 Rubella (German measles) AI

057 Other viral exanthem AI
- .0 Erythema infectiosum (fifth disease)
- .1 Exanthema subitum (Roseola infantum) (sixth disease)
- .8 Other
- .9 Unspecified

Arthropod-borne viral diseases (060-069)

060 Yellow fever AI

.0 Sylvatic
.1 Urban
.9 Unspecified

061 Dengue AI
Excludes haemorrhagic fever caused by dengue virus (067.8)

062 Mosquito-borne viral encephalitis AI NS

.0 Japanese encephalitis NS
.1 Western equine encephalitis NS
.2 Eastern equine encephalitis NS
.3 St. Louis encephalitis NS
.4 Murray Valley encephalitis NS
.9 Other and unspecified NS

063 Tick-borne viral encephalitis AI NS

.0 Russian spring-summer ("Taiga") NS
.1 Louping-ill encephalitis NS
.2 Central-European encephalitis NS
.9 Other and unspecified NS

064 Viral encephalitis transmitted by other arthropods AI NS

065 Viral encephalitis, unspecified AI NS

066 Late effects of viral encephalitis AI NS

067 Arthropod-borne haemorrhagic fever AM AI

.0 Crimean haemorrhagic fever
.1 Omsk haemorrhagic fever
.2 Kyasanur Forest disease
.3 Other tick-borne haemorrhagic fever
.4 Mosquito-borne haemorrhagic fever
.5 Haemorrhagic nephroso-nephritis AM
.9 Other and unspecified

068 Other arthropod-borne viral diseases AI

.0 Phlebotomus fever
.1 Tick-borne fever
.2 Mosquito-borne fever
.9 Other

Other viral diseases (070-079)

070 Infectious hepatitis AM, HE AI
Excludes serum hepatitis (N999.2)

071 Rabies AI NS

072 Mumps AI

073 Psittacosis (ornithosis) AI

074 Specific diseases due to Cocksackie virus AI: C.
Excludes aseptic meningitis (045)

.0 Herpangina
.1 Epidemic pleurodynia (Bornholm disease)
.2 Epidemic myocarditis of newborn HE
.9 Other

075 Infectious mononucleosis AM, HE

076 Trachoma, active AI

077 Late effects of trachoma AI EY

078 Other viral diseases of the conjunctiva AI EY

.0 Inclusion conjunctivitis
.1 Epidemic kerato-conjunctivitis
.2 Acute adeno-viral follicular conjunctivitis
.8 Other
.9 Viral conjunctivitis NOS

079 Other viral diseases AI

.0 Molluscum contagiosum
.1 Viral warts
.2 Lymphocytic choriomeningitis
.3 Cat-scratch disease
.4 Foot and mouth disease
.5 Cytomegalic inclusion disease
.8 Other
.9 Viral infection NOS

Rickettsioses and other arthropod-borne infectious diseases (080-089)
Excludes arthropod-borne viral diseases (060-068)

080 Epidemic louse-borne typhus AI

081 Other typhus AI

.0 Endemic flea-borne (murine)
.1 Brill's disease
.2 Mite-borne (scrub)
.9 Unspecified

082 Tick-borne rickettsiosis AI

.0 Spotted fevers
.1 Fièvre boutonneuse
.2 North-Asian tick-borne typhus fever
.9 Other

083 Other rickettsioses AI

.0 Rickettsialpox
.1 Q fever
.2 Wolhynian fever (trench fever)
.8 Other
.9 Rickettsiosis NOS

084 Malaria [1] AM AI

- .0 Falciparum malaria (malignant tertian)
- .1 Vivax malaria (benign tertian)
- .2 Malariae malaria (quartan)
- .3 Ovale malaria
- .4 Blackwater fever AM
- .5 Recurrent induced malaria
- .8 Other forms of malaria
- .9 Unspecified

085 Leishmaniasis AM AI

- .0 Visceral (Kala-azar and Mediterranean type) AM
- .1 Cutaneous AM
- .2 Mucocutaneous (American)
- .9 Unspecified

086 American trypanosomiasis (Chagas' disease) AI

- .0 With heart involvement
- .8 With other organ involvement
- .9 Without mention of organ involvement

087 Other trypanosomiasis AI

- .0 Gambian
- .1 Rhodesian
- .8 African trypanosomiasis NOS
- .9 Trypanosomiasis NOS

088 Relapsing fever AI

- .0 Louse-borne
- .1 Tick-borne
- .9 Unspecified

089 Other arthropod-borne diseases AI

- .0 Bartonellosis
- .9 Other

Syphilis and other venereal diseases (090-099)
Excludes non-venereal syphilis (104.0)

090 Congenital syphilis AI HD

- .0 Early congenital syphilis, symptomatic (less than five years)
- .1 Early congenital syphilis, latent (less than five years)
- .2 Early congenital syphilis, NOS
- .3 Interstitial keratitis
- .4 Juvenile neurosyphilis
- .5 Other late congenital syphilis, symptomatic (five years and over)
- .6 Late congenital syphilis, latent (five years and over)
- .7 Late congenital syphilis NOS
- .9 Congenital syphilis NOS

091 Early syphilis, symptomatic AM AI

- .0 Primary syphilis, except extragenital chancre
- .1 Extragenital chancre
- .2 Secondary syphilis of skin and mucous membranes AM
- .3 Secondary syphilis, relapse (treated, untreated)
- .8 Other recently acquired syphilis, symptomatic
- .9 Early syphilis NOS

092 Early syphilis, latent AI

- .0 Early syphilis, latent, serological relapse after treatment
- .9 Early syphilis, latent NOS

093 Cardiovascular syphilis AE AI

- .0 Aneurysm of aorta, specified as syphilitic
- .9 Other cardiovascular syphilis

094 Syphilis of central nervous system AI NS

- .0 Tabes dorsalis NS
- .1 General paresis NS
- .9 Other syphilis of central nervous system NS

095 Other forms of late syphilis, with symptoms ~~AI~~ NS

096 Late syphilis latent (duration two years and over) ~~AI~~ NS

097 Other syphilis, and not specified NS

- .0 Late syphilis NOS
- .1 Latent syphilis NOS
- .2 Syphilis NOS

098 Gonococcal infections AM AI EY

- .0 Acute gonococcal infection of genito-urinary system AM
- .1 Chronic gonococcal infection of genito-urinary system (over two months' duration)
- .2 Gonococcal infection of eye
- .3 Gonococcal infection of joint
- .8 Gonococcal infection of other sites
- .9 Gonorrhoea, unspecified

099 Other venereal diseases AI AM

- .0 Chancroid
- .1 Lymphogranuloma venereum (Nicolas Favre)
- .2 Granuloma inguinale (Donovan)
- .8 Other
- .9 Unspecified

[1] When more than one type is mentioned, priority in classification follows the order of listing of numbers in fourth digit.

Other spirochaetal diseases (100-104)

100 Leptospirosis AM A1

.0 Leptospirosis ictero-haemorrhagica (Weil's disease) A1
.8 Other A1
.9 Unspecified A1

101 Vincent's angina A1

102 Yaws AM A1

.0 Initial lesions
.1 Multiple papillomata and "wet crab" yaws
.2 Other early skin lesions
.3 Hyperkeratosis
.4 Gummata, ulcers
.5 Gangosa
.6 Bone and joint lesions AM
.7 Other manifestations
.8 Latent yaws
.9 Yaws NOS

103 Pinta (carate) A1

.0 Primary lesions
.1 Intermediate lesions
.2 Late lesions
.3 Mixed lesions
.9 Unspecified

104 Other spirochaetal infections A1

.0 Non-venereal endemic syphilis
.9 Other

Mycoses (110-117)

110 Dermatophytosis AM A1

111 Dermatomycosis, other and unspecified AM A1

.0 Pityriasis versicolor AM
.1 Tinea nigra A1
.2 Tinea blanca A1
.8 Other A1
.9 NOS A1

112 Candidiasis (moniliasis) A1

113 Actinomycosis A1

114 Coccidioidomycosis A1

115 Histoplasmosis A1 HL

116 Blastomycosis A1

.0 European
.1 North American
.2 South American
.9 Unspecified

117 Other systemic mycosis A1

.0 Rhinosporidiosis
.1 Sporotrichosis
.2 Chromomycosis
.3 Aspergillosis
.4 Maduromycosis
.8 Other
.9 Unspecified

Helminthiases (120-128)

120 Schistosomiasis (bilharziasis) AM, ES A1

.0 S. haematobium
.1 S. mansoni AM
.2 S. japonicum
.3 Cutaneous
.8 Other
.9 Unspecified

121 Other trematode infestation A1

.0 Opisthorchiasis
.1 Clonorchiasis
.2 Paragonimiasis
.3 Fasciolisasis
.4 Fasciolopsiasis
.9 Other

122 Hydatidosis AM A1

.0 Liver AM
.1 Lung
.8 Other sites
.9 Unspecified

123 Other cestode infestation AM A1

.0 Taenia solium infestation, intestinal form
.1 Cysticercosis (larval form, Taenia solium)
.2 Taenia saginata infestation
.3 Taeniasis NOS
.4 Diphyllobothriasis intestinal
.5 Sparganosis (larval diphyllobothriasis)
.6 Hymenolepiasis
.9 Other

124 Trichiniasis AM A1

125 Filarial infestation A1

.0 Wuchereriasis
.1 Brugia filariasis
.2 Loiasis
.3 Onchocercosis
.4 Acanthocheilonemiasis

.5 Mansonelliasis
.8 Other filariasis
.9 Unspecified

126 Ancylostomiasis AM AI

.0 Ancylostoma duodenale
.1 Necator americanus
.8 Other ancylostoma
.9 Unspecified

127 Other intestinal helminthiasis AM AI

.0 Ascariasis
.1 Strongyloidiasis
.2 Trichuriasis
.3 Enterobiasis
.4 Other intestinal nematode infestation
.5 Mixed intestinal helminthiasis
.9 Intestinal helminthiasis NOS

128 Other and unspecified helminthiasis AM AI

.0 Larva migrans, visceralis
.7 Other
.8 Mixed
.9 Unspecified

129 Intestinal parasitism, NOS AM AI

Other infective and parasitic diseases (130-136

130 Toxoplasmosis AI

.0 Acquired
.1 Congenital active
.2 Late effects of intra-uterine infection
.9 Unspecified

131 Trichomoniasis urogenitalis AI

132 Pediculosis AI

133 Acariasis AM AI

.0 Scabies
.9 Other

134 Other infestation AI

.0 Myiasis
.1 Phthirus infestation
.2 Other arthropod infestation
.3 Hirudiniasis
.9 Other

135 Sarcoidosis AM, HE, AI

136 Other infective and parasitic diseases

II. NEOPLASMS

Malignant neoplasm of buccal cavity and pharynx (140-149) DE

140 Malignant neoplasm of lip DE, NS CA
Excludes malignant neoplasm of skin of lip (172.0, 173.0)

.0 Upper lip NS
.1 Lower lip NS
.2 Both lips NS
.9 Lip unspecified (including commissure) NS

141 Malignant neoplasm of tongue DE, NS CA

.0 Base of tongue NS
.1 Dorsal surface NS
.2 Borders and tip NS
.3 Ventral surface NS
.9 Part unspecified NS

142 Malignant neoplasm of salivary gland DE, NS CA

.0 Parotid gland NS
.8 Other specified salivary gland NS
.9 Unspecified salivary gland NS

143 Malignant neoplasm of gum DE, NS CA

.0 Upper gum NS
.1 Lower gum NS
.9 Gum unspecified NS

144 Malignant neoplasm of floor of mouth DE, NS CA

145 Malignant neoplasm of other and unspecified parts of mouth DE, NS CA

.0 Buccal mucosa NS
.1 Palate (hard) (soft) NS
.8 Other specified parts NS
.9 Part unspecified NS

146 Malignant neoplasm of oropharynx DE NS CA

.0 Tonsil NS
.8 Other specified parts NS
.9 Part unspecified NS

147 Malignant neoplasm of nasopharynx DE NS CA

148 Malignant neoplasm of hypopharynx DE NS CA

.0 Postcricoid region NS
.1 Pyriform fossa NS
.8 Other specified parts NS
.9 Part unspecified NS

149 Malignant neoplasm of pharynx, unspecified DE NS CA

Malignant neoplasm of digestive organs and peritoneum (150-159 ES CA

150 Malignant neoplasm of oesophagus AM CA

151 Malignant neoplasm of stomach AM, ES CA
- .0 Cardia AM
- .1 Pylorus AM
- .8 Other specified parts
- .9 Part unspecified

152 Malignant neoplasm of small intestine, including duodenum AM, ES CA
- .0 Duodenum AM
- .8 Other specified parts AM
- .9 Part unspecified AM

153 Malignant neoplasm of large intestine, except rectum AM, ES CA
- .0 Caecum, appendix and ascending colon AM
- .1 Transverse colon, including hepatic and splenic flexures AM
- .2 Descending colon AM
- .3 Sigmoid colon AM
- .8 Large intestine (including colon), part unspecified AM
- .9 Intestinal tract, part unspecified AM

154 Malignant neoplasm of rectum and rectosigmoid junction AM, ES CA
- .0 Rectosigmoid junction AM
- .1 Rectum AM
- .2 Anal canal AM

155 Malignant neoplasm of liver and intrahepatic bile ducts, specified as primary AM, ES CA
- .0 Liver AM
- .1 Intrahepatic bile ducts AM

156 Malignant neoplasm of gall-bladder and bile ducts AM, ES CA
- .0 Gall-bladder AM
- .1 Extrahepatic bile ducts AM
- .2 Ampulla of Vater AM
- .9 Biliary tract NOS AM

157 Malignant neoplasm of pancreas AM, ES CA
- .0 Head AM
- .8 Other specified parts
- .9 Unspecified AM

158 Malignant neoplasm of peritoneum and retroperitoneal tissue AM, ES CA
- .0 Retroperitoneal tissue AM
- .9 Other and unspecified parts AM

159 Malignant neoplasm of unspecified digestive organs AM CA

Malignant neoplasm of respiratory system (160-163) ES

160 Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses ES, NS CA
- .0 Nose (internal) and nasal cavities NS
- .1 Eustachian tube and middle ear NS
- .2 Maxillary sinus NS
- .8 Other sinus NS
- .9 Unspecified sinus (accessory) NS

161 Malignant neoplasm of larynx NS CA
- .0 Glottis, true vocal cords NS
- .8 Other specified parts NS
- .9 Part unspecified NS

CA NS

162 Malignant neoplasm of trachea bronchus and lung ES, HE
- .0 Trachea NS
- .1 Bronchus and lung NS

163 Malignant neoplasm of other and unspecified respiratory organs ES, HE CA
- .0 Pleura
- .1 Mediastinum
- .9 Site unspecified

Malignant neoplasm of bone, connective tissue, skin and breast (170-174) ES

170 Malignant neoplasm of bone AM, ES CA
- .0 Bones of skull and face
- .1 Lower jaw bone
- .2 Vertebral column (excluding sacrum and coccyx) NS
- .3 Ribs, sternum and clavicle
- .4 Long bones of upper limb and scapula
- .5 Upper limb, short bones
- .6 Pelvic bones, sacrum, coccyx
- .7 Lower limb, long bones
- .8 Lower limb, short bones
- .9 Site unspecified

171 Malignant neoplasm of connective and other soft tissue ES, CA AM
- .0 Head, face and neck NS
- .1 Trunk
- .2 Upper limb (including shoulder)
- .3 Lower limb (including hip)
- .9 Site unspecified

172 Malignant melanoma of skin AM, ES CA
- .0 Lips
- .1 Eyelids, including canthi
- .2 Ear and external auricular canal NS
- .3 Other and unspecified parts of face

.4 Scalp and neck NS CA
.5 Scrotum
.6 Trunk, except scrotum
.7 Upper limb
.8 Lower limb
.9 Site unspecified

173 Other malignant neoplasm of skin AM CA
.0 Lips
.1 Eyelids, including canthi
.2 Ear and external auricular canal NS
.3 Other and unspecified parts of face NS
.4 Scalp and neck
.5 Scrotum
.6 Trunk, except scrotum
.7 Upper limb
.8 Lower limb
.9 Site unspecified

174 Malignant neoplasm of breast HD CA

Malignant neoplasm of genito-urinary organs (180-189) ES

180 Malignant neoplasm of cervix uteri ES CA

181 Chorionepithelioma CA

182 Other malignant neoplasm of uterus HD CA
.0 Corpus uteri
.9 Uterus unspecified

183 Malignant neoplasm of ovary, Fallopian tube, and broad ligament ES CA
.0 Ovary 183.7 HD
.1 Fallopian tube and broad ligament
.9 Part unspecified

184 Malignant neoplasm of other and unspecified female genital organs ES CA HD
.0 Vagina
.1 Vulva
.8 Other specified sites
.9 Site unspecified

185 Malignant neoplasm of prostate AM CA HD

186 Malignant neoplasm of testis ES CA HD

187 Malignant neoplasm of other and unspecified male genital organs CA HD
.0 Penis
.8 Other specified sites
.9 Site unspecified

188 Malignant neoplasm of bladder AM, ES CA

189 Malignant neoplasm of other and unspecified urinary organs AM, ES CA HD
.0 Kidney, except pelvis
.1 Pelvis of kidney
.2 Ureter
.9 Other and unspecified

Malignant neoplasm of other and unspecified sites (190-199)

190 Malignant neoplasm of eye ES, CA EY

191 Malignant neoplasm of brain ES, NS CA

192 Malignant neoplasm of other parts of nervous system NS CA
.0 Spinal cord NS
.1 Meninges NS
.2 Peripheral nerves NS
.3 Sympathetic nervous system NS
.9 Site unspecified NS

193 Malignant neoplasm of thyroid gland AM, ES CA

194 Malignant neoplasm of other endocrine glands AM CA
.0 Suprarenal gland AM
.1 Parathyroid gland AM
.2 Thymus AM
.3 Pituitary gland and craniopharyngeal duct AM, NS
.4 Pineal gland AM, NS
.8 Other
.9 Unspecified endocrine gland AM

195 Malignant neoplasm of ill-defined sites CA
.0 Abdomen, intra-abdominal cancer
.1 Pelvis, pelvic viscera, rectovaginal septum
.9 Other

196 Secondary and unspecified malignant neoplasm of lymph nodes HE CA
.0 Head, face and neck NS
.1 Intrathoracic
.2 Intra-abdominal
.3 Axillary and upper limb
.4 Inguinal and lower limb
.7 Other specified sites
.8 Multiple sites
.9 Site unspecified

197 Other secondary malignant neoplasm, primary site unspecified CA
.0 Lung, specified as secondary HE
.1 Liver, specified as secondary AM
.2 Liver, unspecified as primary or secondary AM
.3 Brain, specified as secondary NS

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.4 Bone, specified as secondary AM
.9 Other sites, specified as secondary

198 Malignant neoplasm without specification of site CA
.0 Multiple
.1 Other

199 Secondary malignant neoplasm, primary site known
Not to be used for primary mortality classification CA
.0 Lymph nodes
.1 Thoracic organs HE
.2 Liver
.3 Brain NS
.4 Bone
.9 Other

Neoplasms of lymphatic and haematopoietic tissue (200-209) ES

200 Lymphosarcoma and reticulosarcoma CA, HE, ES
.0 Reticulum-cell sarcoma
.1 Lymphosarcoma

201 Hodgkin's disease HE CA

202 Other neoplasms of lymphoid tissue HE, ES CA
.0 Giant follicular lymphoma (Brill-Symmers' disease)
.1 Mycosis fungoides
.2 Other primary malignant neoplasms of lymphoid tissue
.9 Other forms of lymphoma (reticulosis)

203 Multiple myeloma (plasmacytoma) AM, HE CA

204 Lymphatic leukaemia HE CA
.0 Acute
.1 Chronic
.9 Unspecified

205 Myeloid leukaemia HE CA
.0 Acute
.1 Chronic
.9 Unspecified

206 Monocytic leukaemia HE CA
.0 Acute
.1 Chronic
.9 Unspecified

207 Other and unspecified leukaemia HE CA
.0 Leukaemia, acute
.1 Leukaemia, chronic
.2 Acute erythraemia (Di Guglielmo's disease)
.9 Leukaemia, unspecified

208 Polycythaemia vera AM, HE CA
Excludes secondary polycythaemia (289.0) and acute erythraemia (207.2)

209 Myelofibrosis HE CA

Benign neoplasm (210-229) ES CA

210 Benign neoplasm of buccal cavity and pharynx
Excludes cyst of jaw (526) and oral soft tissues (528) CA DE, NS
.0 Lip DE, NS
.1 Tongue DE NS
.2 Salivary gland DE NS
.3 Floor of mouth DE NS
.4 Other and unspecified parts of mouth DE NS
.5 Tonsil NS
.6 Other parts of oropharynx NS
.7 Nasopharynx NS
.8 Hypopharynx NS
.9 Pharynx unspecified NS

211 Benign neoplasm of other parts of digestive system AM CA
.0 Oesophagus AM
.1 Stomach AM
.2 Small intestine AM
.3 Large intestine, except rectum AM
.4 Rectum AM
.5 Liver and biliary passages AM
.6 Pancreas AM
.7 Peritoneum and retroperitoneal tissue AM
.9 Unspecified site AM

212 Benign neoplasm of respiratory system HE CA
.0 Nose, nasal cavities, middle ear and accessory sinuses NS
.1 Larynx NS
.2 Trachea NS
.3 Bronchus and lung
.4 Pleura
.5 Mediastinum
.9 Unspecified site

213 Benign neoplasm of bone and cartilage AM CA

214 Lipoma AM CA

215 Other benign neoplasm of muscular and connective tissue AM CA

216 Benign neoplasm of skin AM CA
.0 Epidermis AM
.1 Hair follicles and sebaceous glands AM
.2 Sweat glands and sweat ducts AM

.8 Other
Excludes benign melanoma (757.1) AM
.9 Unspecified AM

217 Benign neoplasm of breast HD CA

218 Uterine fibromyoma HD CA

219 Other benign neoplasm of uterus HD CA
.0 Endometriosis, endometrioma
.1 Adenomyosis, adenomyoma
.2 Papilloma, polyp
.3 Benign cyst
.9 Other and unspecified

220 Benign neoplasm of ovary HD CA
Excludes the listed conditions with ovarian hyperfunction (256.0)

221 Benign neoplasm of other female genital organs HD CA
.0 Fallopian tube and broad ligament
.1 Vagina
.2 Vulva
.8 Other specified sites
.9 Unspecified site

222 Benign neoplasm of male genital organs HD CA
.0 Testis
Excludes the listed conditions with testicular hyperfunction (257.0)
.1 Penis
.8 Other specified sites
.9 Unspecified site

223 Benign neoplasm of kidney and other urinary organs AM CA
.0 Kidney, except pelvis AM
.1 Pelvis of kidney AM
.2 Ureter AM
.3 Bladder AM
.8 Other specified sites AM
.9 Unspecified site AM

224 Benign neoplasm of eye CA EY

225 Benign neoplasm of brain and other parts of nervous system CA
Excludes neurofibromatosis (743.3) NS
.0 Brain NS
.1 Spinal cord NS
.2 Meninges NS
.3 Peripheral nerves NS
.4 Sympathetic nervous system NS
.9 Unspecified site NS

226 Benign neoplasm of endocrine glands
Excludes the listed conditions with endocrine hyperfunction (253, 254, 255, 258) AM CA
.0 Suprarenal gland AM
.1 Thymus AM
.2 Pituitary gland and craniopharyngeal duct AM, NS
.3 Pineal gland AM, NS
.8 Other specified endocrine glands AM
.9 Unspecified site AM

227 Haemangioma and lymphangioma CA

228 Benign neoplasm of other and unspecified organs and tissues CA

Neoplasm of unspecified nature (230-239)

230 Neoplasm of unspecified nature of digestive organs AM CA
.0 Oesophagus AM
.1 Stomach AM
.2 Small intestine AM
.3 Large intestine AM
.4 Rectum AM
.5 Liver and biliary passages AM
.6 Pancreas AM
.7 Peritoneum AM
.9 Unspecified site AM

231 Neoplasm of unspecified nature of respiratory organs HE CA
.0 Nose, nasal cavities, middle ear and accessory sinuses NS
.1 Larynx NS
.2 Trachea NS
.3 Bronchus and lung
.4 Pleura
.5 Mediastinum
.9 Unspecified site

232 Neoplasm of unspecified nature of skin and musculo-skeletal system AM CA
.0 Bone and cartilage AM
.1 Muscular and connective tissue AM
.2 Skin AM

233 Neoplasm of unspecified nature of breast CA HD

234 Neoplasm of unspecified nature of uterus CA HD
.0 Carcinoma *in situ* of cervix uteri
.1 Cervix uteri, other
.9 Other and unspecified parts

235 Neoplasm of unspecified nature of ovary CA HD

236 Neoplasm of unspecified nature of other female genital organs CA HD

.0 Fallopian tube and broad ligament
.1 Vagina
.2 Vulva
.8 Other specified sites
.9 Unspecified site

237 Neoplasm of unspecified nature of other genito-urinary organs AM CA HD

.0 Testis AM
.1 Penis AM
.2 Other and unspecified male genital organs AM
.3 Kidney, except pelvis AM
.4 Pelvis of kidney AM
.5 Ureter AM
.6 Bladder AM
.9 Other and unspecified urinary organs AM

238 Neoplasm of unspecified nature of eye, brain and other parts of nervous system CA, EY, NS

.0 Eye
.1 Brain
.2 Spinal cord NS
.3 Meninges NS
.4 Peripheral nerves NS
.5 Sympathetic nervous system NS
.9 Unspecified site NS

239 Neoplasm of unspecified nature of other and unspecified organs CA

.0 Buccal cavity and pharynx DE, NS
.1 Endocrine glands
.9 Other and unspecified sites

III. ENDOCRINE, NUTRITIONAL AND METABOLIC DISEASES

Diseases of thyroid gland (240-246) ES

240 Simple goitre AM, ES
As ICD 250 with sub-divisions:

.0 Endemic AM
.1 Sporadic AM
.9 Unspecified AM

241 Non-toxic nodular goitre AM
As ICD 251 with sub-divisions:

.0 Endemic AM
.1 Sporadic AM
.9 Unspecified AM

242 Thyrotoxicosis with or without goitre AM

.0 Toxic diffuse goitre AM
As ICD 252.0 except for 242.2 below

.1 Toxic nodular goitre AM
As ICD 252.1

.2 Thyrotoxicosis without mention of goitre AM

243 Cretinism of congenital origin AM

244 Myxoedema AM

245 Thyroiditis AM

246 Other diseases of thyroid gland
As ICD 254 except thyroiditis (245)

Diseases of other endocrine glands (250-258) ES

250 Diabetes mellitus AM AE EY
As ICD 260

251 Disorders of pancreatic internal secretion other than diabetes mellitus AM
As ICD 270

252 Diseases of parathyroid gland AM
As ICD 271

.0 Hyperparathyroidism AM
.1 Hypoparathyroidism AM
.9 Other and unspecified AM

253 Diseases of pituitary gland AM HD
As ICD 272 with sub-divisions:

.0 Anterior pituitary hyperfunction AM
.1 Anterior pituitary hypofunction AM
.2 Chromophobe adenoma, pituitary AM, NS
.9 Other and unspecified AM
Remainder of ICD 272

254 Diseases of thymus gland AM AI
As ICD 273

255 Diseases of adrenal glands AM

.0 Adrenal cortical hyperfunction AM
Excludes congenital hyperadrenocorticism (272.0)

.1 Adrenal cortical hypofunction AM
.2 Pheochromocytoma AM
.9 Other and unspecified AM

256 Ovarian dysfunction AM, ES HD HD
As ICD 275 with sub-divisions:

.0 Hyperfunction AM
.1 Hypofunction AM
.9 Ovarian dysfunction NOS AM

257 Testicular dysfunction AM, ES HD HD
As ICD 276 with sub-divisions:

.0 Hyperfunction AM

.1 Hypofunction AM
.9 Testicular dysfunction NOS

258 Polyglandular dysfunction and other diseases of endocrine glands HD
.0 Pituitary basophilism
.1 Polyglandular dysfunction
.9 Other and unspecified diseases of endocrine system
Remainder of ICD 277 except:
Congenital dwarfism (756.6)
Cushing's syndrome (255.0)

Avitaminoses and other nutritional deficiency (260-269)
Excludes deficiency anaemias (280, 281).

260 Vitamin A deficiency AM HD EY TD
.0 Night blindness
.1 Xerophthalmia, keratomalacia
.8 Other manifestation
.9 Unspecified

261 Thiamine deficiency (including beriberi) HD

262 Niacin deficiency (including pellagra) AM HD

263 Other vitamin B deficiency HD
.0 Ariboflavinosis
.1 Vitamin B6 deficiency
.8 Other
.9 Unspecified

264 Ascorbic acid deficiency (including scurvy) HD

265 Vitamin D deficiency HD
.0 Rickets, active
.1 Rickets, late effect
.2 Osteomalacia
.9 Unspecified

266 Other vitamin deficiency states HD
.0 Vitamin K deficiency
.8 Other
.9 Unspecified

267 Protein malnutrition HD

268 Nutritional marasmus HD

269 Other nutritional deficiency HD
.0 Sprue and steatorrhoea
.1 Malabsorption syndrome NOS
.9 Other and unspecified

Other metabolic diseases (270-279)

270 Congenital disorder of amino-acid metabolism
.0 Phenylketonuria
.1 Cystinuria
.2 Other disorders of amino-acid renal transport
.3 Cystinosis
.4 Maple syrup disease
.5 Disorders of purine and pyrimidine metabolism
.6 Alcaptonuria
.8 Other
.9 Unspecified

271 Congenital disorders of carbohydrate metabolism HD
.0 Glycogen storage disease
.1 Galactosaemia
.2 Von Gierke's disease
.8 Other
.9 Unspecified

272 Congenital disorders of lipid metabolism HD
Excludes amaurotic familial idiocy (342.0) and leukodystrophy (342.1)
.0 Disorders of steroid metabolism
.1 Xanthomatosis
.8 Other
.9 Unspecified

273 Other and unspecified congenital disorders of metabolism H
.0 Cystic fibrosis (mucoviscidosis)
.1 Disorders of porphyrin metabolism
.2 Haemochromatosis
.3 Hepatolenticular degeneration
.4 Other disorders involving metabolism of minerals
.5 Defective bilirubin excretion
.8 Other
.9 Unspecified

274 Gout
As ICD 288

275 Plasma protein abnormalities
.0 Agammaglobulinaemia
.1 Hypogammaglobulinaemia
.2 Analbuminaemia
.3 Bisalbuminaemia
.4 Cryoglobulinaemia
.5 Macroglobulinaemia
.9 Other and unspecified

276 Amyloidosis
As ICD 289.1

... usually not specified as of endocrine origin
As ICD 287 AM

278 Other hyperalimentation AM
Excludes conditions due to excess administration of drugs (N963.6)
.0 Hypervitaminosis A AM
.1 Carotinaemia
.2 Hypervitaminosis D } of dietary origin
.9 Other and unspecified

279 Other and unspecified metabolic diseases
Excludes congenital metabolic defects (270-273) AM

IV. DISEASES OF BLOOD AND BLOOD-FORMING ORGANS

280 Iron deficiency anaemias
As ICD 291 AM, HE

281 Other deficiency anaemias AM, HE
.0 Pernicious anaemia AM
.1 Other vitamin B12 deficiency anaemia
.2 Folic acid deficiency anaemia AM
.3 Vitamin B6 deficiency anaemia
.4 Protein deficiency anaemia
.9 Other and unspecified deficiency anaemia

282 Hereditary haemolytic anaemias AM, HE
.0 Familial acholuric jaundice
.1 Hereditary non-spherocytic haemolytic anaemia AM
.2 Hereditary elliptocytosis
.3 Mediterranean anaemia
.4 Haemoglobinopathies
.5 Anaemia due to glucose-6-phosphate dehydrogenase deficiency
.9 Other AM

283 Acquired haemolytic anaemias AM, HE
.0 Acute AM
.9 Other AM
Acquired acholuric jaundice

284 Aplastic anaemias AM, ES, HE

285 Other and unspecified anaemias AM, HE
.0 Hypochromic anaemia with iron loading
.8 Other specified anaemias
.9 Anaemia unspecified AM
As ICD 293

286 Coagulation defects AM, HE
.0 Haemophilia AM
.1 Christmas disease AM
.2 PTA deficiency AM
.3 Vascular haemophilia
.4 Haemorrhagic fibrinolysis (fibrinogenolysis)
.5 Circulating anticoagulants
.9 Other AM

287 Purpura and other haemorrhagic conditions HE AM
.0 Allergic purpura
.1 Thrombocytopenia
.2 Haemorrhagic thrombocythaemia
.9 Other

288 Agranulocytosis HE
As ICD 297

289 Other diseases of blood and blood-forming organs
.0 Polycythaemia, secondary
.1 Diseases of spleen
As ICD 298 except hepatolienal fibrosis (571)
.2 Chronic lymphadenitis AM
As ICD 468.0
.3 Non-specific mesenteric lymphadenitis
As ICD 468.1
.4 Lymphadenitis, unspecified AM
As ICD 468.2
.8 Other AM
.9 Unspecified AM

V. MENTAL DISORDERS

This section is intended primarily for the classification of admissions to mental hospitals, psychiatric clinics, mental deficiency institutions, etc. For this reason, all forms of mental disorder are classified here, even though associated with or secondary to physical conditions as in categories 290-294, 309, 310-315. For primary mortality classification and for morbidity classification where the main interest is not in the mental state, these categories should not be used but assignment made to the underlying cause.

Psychoses (290-299)

290 Senile and pre-senile dementia NS AG
.0 Senile dementia NS
.1 Pre-senile dementia NS

291 Alcoholic psychosis NS
.0 Delirium tremens NS
.1 Korsakoff's psychosis (alcoholic) NS
.2 Other alcoholic hallucinosis NS
.3 Alcoholic paranoia NS
.9 Other and unspecified NS

292 Psychosis associated with intracranial infection NS
.0 With general paralysis NS

.1 With other syphilis of central nervous system NS
.2 With epidemic encephalitis NS
.3 With other and unspecified encephalitis NS
.9 With other and unspecified intracranial infection NS

293 Psychosis associated with other cerebral condition NS

.0 With cerebral arteriosclerosis HE NS
.1 With other cerebrovascular disturbances NS
.2 With epilepsy NS
.3 With intracranial neoplasm NS
.4 With degenerative diseases of central nervous system NS
.5 With brain trauma NS
.9 With other and unspecified cerebral condition NS

294 Psychosis associated with other physical condition AT, AM, HD

.0 With endocrine disorders
.1 With metabolic and nutritional disorders
.2 With systemic infections
.3 With drug or poison intoxication
Excludes alcoholic psychosis (291)
.4 With childbirth
Excludes psychosis of specified type arising during the puerperium (295-298)
.8 With other physical conditions
.9 With physical condition, NOS

295 Schizophrenia

.0 Simple type
.1 Hebephrenic type
.2 Catatonic type
.3 Paranoid type
.4 Acute schizophrenic episode
Excludes acute schizophrenia of the types listed above
.5 Latent schizophrenia
.6 Residual schizophrenia
.7 Schizo-affective type
.8 Other
.9 Unspecified type

296 Affective psychoses

.0 Involutional melancholia
.1 Manic-depressive psychosis, manic type
.2 Manic-depressive psychosis, depressed type
Includes endogenous depression
.3 Manic-depressive psychosis, circular type
.8 Other
.9 Unspecified

297 Paranoid states
Excludes acute paranoid reaction (298.3)

.0 Paranoia
.1 Involutional paraphrenia
.9 Other

298 Other psychoses

.0 Reactive depressive psychosis
.1 Reactive excitation
.2 Reactive confusion
.3 Acute paranoid reaction
.9 Reactive psychosis unspecified

299 Unspecified psychosis

Neurosis, personality disorders and other non-psychotic mental disorders (300-309)

300 Neuroses

.0 Anxiety neurosis
.1 Hysterical neurosis
.2 Phobic neurosis
.3 Obsessive compulsive neurosis
.4 Depressive neurosis
.5 Neurasthenia
.6 Depersonalization syndrome
.7 Hypochondriacal neurosis
.8 Other
.9 Unspecified neurosis

301 Personality disorders

.0 Paranoid
.1 Affective (cyclothymic)
.2 Schizoid
.3 Explosive
.4 Anancastic (obsessive-compulsive)
.5 Hysterical
.6 Asthenic
.7 Antisocial
.8 Other
.9 Unspecified

302 Sexual deviation HD

.0 Homosexuality
.1 Fetishism
.2 Pedophilia
.3 Transvestitism
.4 Exhibitionism
.8 Other
.9 Unspecified

303 Alcoholism
Excludes alcoholic psychosis (291); acute poisoning by alcohol (E860, N980). For primary cause classification it excludes alcoholic cirrhosis of the liver (571.0)

.0 Episodic excessive drinking
.1 Habitual excessive drinking
.2 Alcoholic addiction
.9 Other and unspecified alcoholism

304 Drug dependence
- .0 Opium, opium alkaloids and their derivatives
- .1 Synthetic analgesics with morphine-like effects
- .2 Barbiturates
- .3 Other hypnotics and sedatives or "tranquilizers"
- .4 Cocaine
- .5 Cannabis sativa (hashish, marihuana)
- .6 Other psycho-stimulants
- .7 Hallucinogenics
- .8 Other
- .9 Unspecified

305 Physical disorders of presumably psychogenic origin AM HD
- .0 Skin
- .1 Musculo-skeletal NS
- .2 Respiratory AE
- .3 Cardiovascular AE
- .4 Haemic and lymphatic AE
- .5 Gastro-intestinal
- .6 Genito-urinary
- .7 Endocrine
- .8 Organs of special sense NS
- .9 Other

306 Special symptoms not elsewhere classified HD
- .0 Speech disturbance NS
- .1 Specific learning disturbance NS
- .2 Tics
- .3 Other psychomotor disorders NS
- .4 Disorders of sleep NS
- .5 Feeding disturbances NS
- .6 Enuresis
- .7 Encopresis
- .8 Cephalalgia NS
- .9 Other

307 Transient situational disturbances

308 Behaviour disorders of childhood

309 Mental disorders not specified as psychotic associated with physical conditions HD ES, NS
- .0 With intracranial infections NS AI
- .1 With drug, poison of systemic intoxication Excludes alcoholism (303) and drug dependence (304) ES, NS
- .2 With brain trauma NS
- .3 With circulatory disturbance NS
- .4 With epilepsy NS
- .5 With disturbance of metabolism, growth or nutrition HD
- .6 With senile or pre-senile brain disease NS AG
- .7 With intracranial neoplasm CA NS
- .8 With degenerative diseases of central nervous system NS
- .9 With other and unspecified physical conditions

Mental retardation (310-315) NS (except

310 Borderline mental retardation HD HD
IQ 68-85 ES, NS (except 2.2+0.7-0.9)

311 Mild mental retardation HD
IQ 52-67 NS (except 1.2+1.7-1.9)

312 Moderate mental retardation HD
IQ 36-51 NS (except 2.2+2.7-2.9)

313 Severe mental retardation HD
IQ 20-35 NS (except 2.2+2.7-3.9)

314 Profound mental retardation HD
IQ under 20 NS (except 4.2+4.7-4.9)

315 Unspecified mental retardation HD NS (except 5.2 +5.7-5.9)

The following fourth-digit sub-divisions should be used with each of the above categories:
- .0 Following infections and intoxications
- .1 Following trauma or physical agents
- .2 With disorders of metabolism, growth or nutrition
- .3 Associated with gross brain disease (postnatal)
- .4 Associated with diseases and conditions due to (unknown) pre-natal influence HE
- .5 With chromosome abnormalities
- .6 Associated with prematurity
- .7 Following major psychiatric disorder
- .8 With psycho-social (environmental) deprivation
- .9 Other and unspecified

VI. DISEASES OF THE NERVOUS SYSTEM AND SENSE ORGANS

Inflammatory diseases of central nervous system (320-324)

320 Meningitis, except meningococcal, tuberculous and viral AI NS
- .0 H. influenzae NS
- .1 Pneumococcus NS
- .8 Due to other specified organism NS
- .9 With no organism specified as cause

321 Phlebitis and thrombophlebitis of intracranial venous sinuses HE, NS
As ICD 341

322 Intracranial and intraspinal abscess NS
As ICD 342

323 Encephalitis, myelitis, and encephalomyelitis (except acute infectious) NS
As ICD 343

324 Late effects of intracranial abscess or pyogenic infection NS AI
As ICD 344

Hereditary and familial diseases of nervous system (330-333)

330 Hereditary neuromuscular disorders NS HD
.0 Neuropathic muscular atrophy NS
.1 Familial progressive spinal muscular atrophy NS
.2 Amyotonia congenita NS
.3 Progressive muscular dystrophy NS
.9 Other NS

331 Hereditary diseases of the striato-pallidal system NS HD
Excludes hepatolenticular degeneration (273.3)
.0 Hereditary chorea NS
.1 Dystonia musculorum deformans NS
.2 Progressive familial myoclonic epilepsy (Unverricht-Lundborg) NS
.9 Other NS

332 Hereditary ataxia NS HD
.0 Hereditary spinal ataxia NS
.1 Hereditary cerebellar ataxia NS
.9 Other and unspecified NS

333 Other hereditary and familial diseases of nervous system NS HD
.0 Amaurotic familial idiocy NS
.1 Progressive cerebral leukodystrophy NS
.9 Other and unspecified NS

Other diseases of central nervous system (340-349)

340 Multiple sclerosis NS
Excludes diffuse cerebral sclerosis (341)
As ICD 345

341 Other demyelinating diseases of central nervous system NS

342 Paralysis agitans NS
As ICD 350

343 Cerebral spastic infantile paralysis NS HD
As ICD 351

344 Other cerebral paralysis NS
As ICD 352

345 Epilepsy NS
.0 Generalized non-convulsive NS
.1 Generalized convulsive NS
.2 Partial (focalized) NS
.3 Status epilepticus NS
.9 Other and unspecified NS

346 Migraine NS
As ICD 354

347 Other diseases of brain NS
.0 Cataplexy and narcolepsy NS
.9 Other NS

348 Motor neurone disease NS
.0 Amyotrophic lateral sclerosis NS
As ICD 356.1
.1 Progressive bulbar palsy NS
.2 Other progressive muscular atrophy NS
.9 Other and unspecified manifestations NS
As ICD 356.3 except primary muscular atrophy (733.1) NS

349 Other diseases of spinal cord NS
.0 Syringomyelia and syringobulbia NS
.9 Other
Excludes Landry's paralysis (354) NS

Diseases of nerves and peripheral ganglia (350-359) ES, NS

350 Facial paralysis NS
As ICD 360

351 Trigeminal neuralgia NS
As ICD 361

352 Brachial neuritis NS
As ICD 362 except brachial radiculitis (728-3)

353 Sciatica NS
As ICD 363 except lumbosacral radiculitis (728-8)

354 Polyneuritis and polyradiculitis NS

355 Other and unspecified forms of neuralgia and neuritis NS
As ICD 366

356 Other diseases of cranial nerves NS
As ICD 367

357 Other diseases of peripheral nerves except autonomic NS
As ICD 368 except vertebrogenic conditions (728)

358 Diseases of peripheral autonomic nervous system
As ICD 369 except vertebrogenic conditions (728) NS

Inflammatory diseases of the eye (360-369)

360 Conjunctivitis and ophthalmia EY
Excludes viral conjunctivitis (078) and gonococcic (098.2)

361 Blepharitis EY
As ICD 371

362 Hordeolum (sty) EY
As ICD 372

363 Iritis EY

364 Keratitis EY
.0 With ulceration
As ICD 381
.9 Without mention of ulcer
As ICD 374

365 Choroiditis EY
As ICD 375

366 Other inflammation of uveal tract EY
As ICD 376 except cyclitis and iridocyclitis (363)

367 Inflammation of optic nerve and retina EY
As ICD 377

368 Inflammation of lachrymal glands and ducts EY
As ICD 378

369 Other inflammatory diseases of eye EY
As ICD 379

Other diseases and conditions of eye (370-379)

370 Refractive errors EY
As ICD 380

371 Corneal opacity EY
As ICD 382

372 Pterygium EY
As ICD 383

373 Strabismus EY
As ICD 384

374 Cataract EY
As ICD 385

375 Glaucoma EY
As ICD 387 with sub-divisions:
.0 Primary acute
.1 Chronic (primary)
.2 Secondary
.9 Unspecified

376 Detachment of retina EY
As ICD 386

377 Other diseases of retina and optic nerve AIII EY
.0 Vascular lesions of retina AIII
.1 Degeneration of retina AIII
.2 Amblyopia
.3 Colour blindness
.8 Other
.9 Unspecified

378 Other diseases of eye EY
.0 Chalazion
.9 Other

379 Blindness AIII EY
As ICD 389
.0 Blindness, both eyes, specifically defined
.1 Blindness, both eyes, not specifically defined
.2 Blindness, one eye, specifically defined
.3 Blindness, one eye, not specifically defined

Diseases of the ear and mastoid process (380-389)

380 Otitis externa NS
As ICD 390

381 Otitis media without mention of mastoiditis AI NS
As ICD 391
.0 Acute NS
.1 Chronic NS
.2 Unspecified NS

382 Otitis media with mastoiditis AI NS
As ICD 392
.0 Acute NS
.1 Chronic NS
.2 Unspecified NS

383 Mastoiditis without mention of otitis media NS
As ICD 393
.0 Acute NS
.1 Chronic NS
.2 Unspecified NS

384 Other inflammatory diseases of ear
As ICD 394 NS

385 Ménière's disease
As ICD 395 NS

386 Otosclerosis NS

387 Other diseases of ear and mastoid process NS
.0 Cholesteatoma of ear NS
.1 Wax in ear NS
.9 Other and unspecified NS

388 Deaf mutism
As ICD 397 NS

389 Other deafness NS
As ICD 398
.0 Deafness, both ears NS
.1 Deafness, one ear, and partial deafness in other NS
.2 Deafness, one ear NS
.3 Impairment of hearing, one or both ears NS

VII. DISEASES OF THE CIRCULATORY SYSTEM

Active rheumatic fever (390-392) HE AI

390 Rheumatic fever without mention of heart involvement AI
As ICD 400

391 Rheumatic fever with heart involvement HL
Excludes chronic heart diseases of rheumatic origin (393-398) unless rheumatic fever is also present or there is evidence of recrudescence or activity of the rheumatic process. In cases where there is doubt as to rheumatic activity at the time of death, see Rules for Classification
.0 Active rheumatic pericarditis
.1 Active rheumatic endocarditis
.2 Active rheumatic myocarditis
.9 Other active rheumatic heart disease

392 Chorea NS
.0 With heart involvement NS HL
As ICD 402.1
.9 Without mention of heart involvement NS
As ICD 402.0

Chronic rheumatic heart disease (393-398) HE

393 Diseases of pericardium, specified as rheumatic HL

394 Diseases of mitral valve HL
Includes the listed conditions with disease of pulmonary or tricuspid valves
.0 Specified as rheumatic
.9 Not specified as rheumatic

395 Diseases of aortic valve, specified as rheumatic HL
Includes the listed conditions with disease of pulmonary or tricuspid valves
As ICD 411

396 Diseases of mitral and aortic valves HL
Includes the listed conditions with disease of pulmonary or tricuspid valves
.0 Specified as rheumatic
.9 Not specified as rheumatic

397 Diseases of other endocardial structures, specified as rheumatic HL
As ICD 412-414, specified as rheumatic

398 Other heart disease, specified as rheumatic HL

Hypertensive disease (400-404) AM, HE
Categories 400-404 include the listed conditions with arteriosclerosis; they exclude them with ischaemic heart disease (410-414)

400 Malignant hypertension AM HL
Includes any condition in 401-404 if specified as malignant or associated with malignant hypertension
.0 Without mention of organ damage AM
.1 With heart involvement (any condition in 427-429) AM
.2 With cerebrovascular involvement (any condition in 430-438) NS
.3 With renal involvement (any condition in 580-584, 593.2, 792) AM
.9 With multiple organ involvement AM

401 Essential benign hypertension HL
As ICD 444, 447
Excludes the listed conditions with cerebrovascular disease (430-438)

402 Hypertensive heart disease AM HL
Includes any condition in 427-429 with hypertension (benign)
Excludes the listed conditions with any conditions in 403, 584 (404)

403 Hypertensive renal disease AM HL
As ICD 446
Excludes the listed conditions with any condition in 402, 427-429 (404)

404 Hypertensive heart and renal disease AM HL
Includes any condition in 402 with any condition in 403

Ischaemic heart disease (410-414) AM, HE
Categories 410-414 include the listed conditions with arteriosclerosis, hypertension (benign) (malignant), or any condition in 427-429. The

following fourth-digit sub-divisions should be used with these categories:

.0 With hypertension (benign) (malignant)
.9 Without mention of hypertension

410 Acute myocardial infarction AM HL
Includes any condition in 412 specified as acute or with a stated duration of eight weeks or less. Excludes the listed conditions specified as chronic or with a stated duration of over eight weeks (412). Includes them with conditions in 411-413

411 Other acute and sub-acute forms of ischaemic heart disease AM HL

412 Chronic ischaemic heart disease AM HL
Includes any condition in 410 specified as chronic or with a stated duration of over eight weeks. Excludes the listed conditions specified as acute or with a stated duration of eight weeks or less (410). Includes them with conditions in 413

413 Angina pectoris AM HL

414 Asymptomatic ischaemic heart disease AM HL

Other forms of heart disease (420-429) HE

420 Acute pericarditis HE

421 Acute and sub-acute endocarditis HE
.0 Acute and sub-acute bacterial endocarditis
As ICD 430.0 HE
.9 Other acute endocarditis
As ICD 430.1 HE

422 Acute myocarditis HE
As ICD 431

423 Chronic disease of pericardium AM, HE

424 Chronic disease of endocardium, not specified as rheumatic HE,
Includes the listed conditions when specified as due to hypertension (benign) or arteriosclerosis. When more than one valve is mentioned, priority in classification is in the order mitral valve, aortic valve, other
.0 Mitral valve, specified as non-rheumatic
.1 Aortic valve
.9 Other endocardial structures

425 Cardiomyopathy HE

426 Pulmonary heart disease HE
For primary mortality classification, excludes the listed conditions when the underlying pulmonary condition is known

427 Symptomatic heart disease HE
Excludes the listed conditions with malignant hypertension (400.1), other hypertension (402) and ischaemic heart disease (410-414)
.0 Congestive heart failure
.1 Left ventricular failure
.2 Heart block
.9 Other disorders of heart rhythm

428 Other myocardial insufficiency HE
Excludes the listed conditions with malignant hypertension (400.1), other hypertension (402) and ischaemic heart disease (410-414)
.0 With arteriosclerosis
.9 Other
Excludes the listed conditions with arteriosclerosis (428.0)

429 Ill-defined heart disease HE
Excludes the listed conditions with malignant hypertension (400.1), other hypertension (402) and ischaemic heart disease (410-414)

Cerebrovascular disease (430-438) AM, HE, NS
Categories 430-438 include the listed conditions with arteriosclerosis or hypertension (benign). They exclude them with malignant hypertension (400.2). The following fourth-digit sub-divisions should be used with these categories:
.0 With hypertension (benign)
.9 Without mention of hypertension

430 Subarachnoid haemorrhage HL, NS
As ICD 330

431 Cerebral haemorrhage HL, NS
As ICD 331

432 Occlusion of pre-cerebral arteries HL, NS

433 Cerebral thrombosis HL, NS

434 Cerebral embolism HL, NS
Includes cerebral infarction NOS, cerebral (artery) occlusion NOS

435 Transient cerebral ischaemia HL, NS

436 Acute but ill-defined cerebrovascular disease NS, HL

437 Generalized ischaemic cerebrovascular disease NS HL

438 Other and ill-defined cerebrovascular disease NS, HL
Excludes hemiplegia (old or long-standing) of uncertain origin (344) but
Includes hemiplegia specified as due to hypertension or arteriosclerosis

Diseases of arteries, arterioles and capillaries (440-447) HE

440 Arteriosclerosis AM, HE
Excludes the listed conditions with any condition in 400-404, 410-414, 430-438 (assign to these conditions), 428.9 (428.0) and 445.9 (445.0), and when reported as the underlying cause of any condition in 342, 424, 427, 441-444 (assign to these conditions) or of the terms nephritis (chronic) (interstitial) and Bright's disease (chronic) (403)
.0 Of aorta AM
.1 Of renal artery AM
.2 Of peripheral arteries
.3 Of other specified arteries
Excludes arteriosclerosis, coronary (412) and cerebral (437)
.9 Generalized and unspecified AM

441 Aortic aneurysm (non-syphilitic) HE
Includes the listed conditions when specified as due to hypertension or arteriosclerosis
.0 Dissecting aneurysm of aorta (any part) AM
.1 Aneurysm of aorta, thoracic or unspecified
.2 Aneurysm of aorta, abdominal AM
.9 Other

442 Other aneurysm HE
As ICD 452

443 Other peripheral vascular disease
As ICD 453 HE
.0 Raynaud's syndrome
.1 Thrombo-angiitis obliterans (Buerger's disease)
.2 Chilblains
.9 Other

444 Arterial embolism and thrombosis AM, HE
.0 Mesenteric
.1 Renal AM
.2 Peripheral arteries
.9 Other arteries, not elsewhere classified

445 Gangrene AM, HE, AI
Excludes diabetic gangrene (250), gas gangrene (039.0), and gangrene of certain sites (see Alphabetical Index)
.0 Arteriosclerotic gangrene
.9 Gangrene not elsewhere classified

446 Other diseases of arteries and arterioles AM, HE
.0 Polyarteritis nodosa AM
.1 Hypersensitivity angiitis AM
.2 Rheumatic arteritis
.3 Wegener's granulomatosis AM
.4 Cranial arteritis NS
.5 Thrombotic microangiopathy
.9 Other

447 Diseases of capillaries AM, HE
As ICD 467.1

Diseases of veins and lymphatics, and other diseases of circulatory system (450-459) HE

450 Pulmonary embolism and infarction HE
As ICD 465

451 Phlebitis and thrombophlebitis AM, HE
.0 Of lower extremities
As ICD 463
.9 Of other sites AM
As ICD 464

452 Portal vein thrombosis HE

453 Other venous embolism and thrombosis
As ICD 466 HE

454 Varicose veins of lower extremities HE
.0 With ulcer
.9 Without mention of ulcer

455 Haemorrhoids AM, HE
As ICD 461

456 Varicose veins of other sites
As ICD 462 HE
.0 Of oesophagus
.1 Of scrotum
.9 Of other sites

457 Non-infective disease of lymphatic channels
As ICD 468.3 HE
Excludes lymphangitis with cellulitis (682) and lymphadenitis, acute (683), chronic (289.2), mesenteric (289.3), unqualified (289.4)

458 Other diseases of circulatory system HE
As ICD 467 except diseases of capillaries (447)
.0 Hypotension
.9 Other and unspecified circulatory diseases

VIII. DISEASES OF THE RESPIRATORY SYSTEM

Acute respiratory infections (except influenza) (460-466)

Excludes pneumonia and influenza (470-474)

460 Acute nasopharyngitis (common cold) HE, NS AI
As ICD 470

461 Acute sinusitis HE, NS, AI
As ICD 471

462 Acute pharyngitis HE, NS, AI
As ICD 472 without sub-divisions

463 Acute tonsillitis AM HE, NS, AI
As ICD 473

464 Acute laryngitis and tracheitis HE, NS AI
As ICD 474

465 Acute upper respiratory infection of multiple or unspecified sites AM, HE, NS, AI
As ICD 475

466 Acute bronchitis and bronchiolitis AM, HE, NS, AI
As ICD 500 and bronchiolitis

Influenza (470-474)

470 Influenza unqualified AM AI

471 Influenza with pneumonia AI HL
As ICD 480

472 Influenza with other respiratory manifestations AI HL

473 Influenza with digestive manifestations AI AM
As ICD 482

474 Influenza with nervous manifestations
As ICD 483 AI NS

Pneumonia (480-486)

Excludes lipid pneumonias and eosinophilic pneumonitis (519.2)

480 Viral pneumonia AI HL
Excludes influenza virus pneumonia (471); measles pneumonia (055); psittacotic pneumonia (073)

481 Pneumococcal pneumonia AI HL

482 Other bacterial pneumonia
.0 Friedländer's bacillus
.1 Hemophilus influenzae
.2 Streptococcus
.3 Staphylococcus
.9 Other

483 Pneumonia due to other specified organism AM AI
Excludes pneumonia in coccidioidomycosis (114); histoplasmosis (115); Q-fever (083.1); and other diseases classified as infectious (000-136)

484 Acute interstitial pneumonia AM AI

485 Bronchopneumonia, unspecified AM AI
Excludes bronchiolitis (466) and lipoid pneumonia (519.2)

486 Pneumonia, unspecified AM, HE AI

Bronchitis, emphysema and asthma (490-493)

Excludes acute bronchitis (466) ES

490 Bronchitis, unqualified HE, NS, AI
As ICD 501
Excludes the listed conditions with emphysema (491)

491 Chronic bronchitis HE, ES, NS AI
As ICD 502 without sub-divisions

492 Emphysema HE, ES
As ICD 527.1
Excludes the listed conditions with bronchitis, chronic or unqualified (491)

493 Asthma HE, ES, AI
As ICD 241
Excludes the listed conditions with bronchitis: acute (466), chronic (491), unqualified (490) and emphysema (492)

Other diseases of upper respiratory tract (500-508)

500 Hypertrophy of tonsils and adenoids
As ICD 510.0

501 Peritonsillar abscess (quinsy) NS
As ICD 511

502 Chronic pharyngitis and nasopharyngitis
As ICD 512 HE, NS
.0 Chronic pharyngitis NS
.1 Chronic nasopharyngitis NS

503 Chronic sinusitis
As ICD 513 HE, NS AI

504 Deflected nasal septum HE, NS
As ICD 514

505 Nasal polyp HE, NS
As ICD 515

506 Chronic laryngitis HE, NS
As ICD 516

507 Hay fever AI
As ICD 240

508 Other diseases of upper respiratory tract HE, NS AI
As ICD 517

Other diseases of respiratory system (510-519)

510 Empyema HE AI
As ICD 518

511 Pleurisy HE AI
As ICD 519

.0 Without mention of effusion or tuberculosis
.1 With effusion, with mention of a bacterial cause other than tuberculosis
.2 Other specified forms of effusion, except tuberculous

512 Spontaneous pneumothorax HE
As ICD 520

513 Abscess of lung HE
As ICD 521

514 Pulmonary congestion and hypostasis HE
As ICD 522

515 Pneumoconiosis due to silica and silicates ES, HE
Excludes silicotuberculosis (010)

.0 Silicosis
.1 Anthracosilicosis
.2 Asbestosis
.9 Other, including pneumoconiosis unspecified

516 Other pneumoconioses and related diseases ES, HE

.0 Due to inhalation of other inorganic dust
.1 Due to inhalation of other dust
.2 Due to inhalation of fumes

517 Other chronic interstitial pneumonia HE
As ICD 525 (with deletion of note)

518 Bronchiectasis HE
As ICD 526

519 Other diseases of respiratory system ES, HE

.0 Pulmonary collapse
As ICD 527.0
.1 Acute oedema of lung without mention of heart
.2 Other diseases of lung
.9 Other
As ICD 527.2, except acute oedema of lung (519.1)

IX. DISEASES OF THE DIGESTIVE SYSTEM

Diseases of oral cavity, salivary glands and jaws (520-529) DE

520 Disorders of tooth development and eruption DE

.0 Anodontia
Excludes missing tooth with abnormal spacing (524.3)
.1 Supernumerary teeth
Excludes supernumerary teeth causing crowding (524.3)
.2 Abnormalities of size and form
.3 Mottled teeth
.4 Enamel hypoplasia
.5 Hereditary disturbances in tooth structure NEC
.6 Disturbances in tooth eruption
Excludes impacted, embedded teeth with abnormal position of such teeth or adjacent teeth (524.3)
.7 Teething syndrome
.9 Other and unspecified

521 Diseases of hard tissues of the teeth DE

.0 Dental caries
.1 Attrition
.2 Abrasion
.3 Erosion
.4 Resorption
.5 Hypercementosis
.6 Ankylosis
.7 Posteruptive colour changes
.8 Irradiated enamel
.9 Other and unspecified

522 Diseases of pulp and periapical tissues DE

.0 Pulpitis
.1 Necrosis of the pulp
.2 Pulp degenerations
.3 Abnormal hard tissue formation in pulp
.4 Acute apical periodontitis
.5 Periapical abscess
.6 Chronic apical periodontitis (granuloma)
.7 Fistula from periapical lesions
.8 Radicular cyst
.9 Other and unspecified

523 Periodontal diseases AM, DE

.0 Acute gingivitis
.1 Chronic gingivitis

.2 Gingival recession
.3 Acute periodontitis
.4 Chronic periodontitis
.5 Periodontosis
.6 Accretions on teeth
.9 Other and unspecified

524 Dento-facial anomalies including malocclusion DE

.0 Major anomalies of jaw size
.1 Anomalies of jaw-cranial base relationship
.2 Anomalies of dental arch relationship
.3 Anomalies of tooth position
.4 Malocclusion NOS
.5 Dento-facial functional abnormalities
.9 Other and unspecified

525 Other diseases and conditions of the teeth and supporting structures DE

.0 Acquired absence of teeth
Excludes missing teeth causing malocclusion (524.3)
.1 Atrophy of edentulous alveolar ridge
.9 Other and unspecified

526 Diseases of the jaws DE

.0 Developmental dental cysts
Excludes radicular cyst (522.8)
.1 Fissural cysts
.2 Other cysts
.3 Reparative giant cell granuloma
.4 Inflammatory conditions
.5 Alveolitis (dry socket)
.9 Other and unspecified

527 Diseases of the salivary glands AM, DE, NS

.0 Atrophy NS
.1 Hypertrophy NS
.2 Sialoadenitis NS
.3 Abscess NS
.4 Fistula NS
.5 Sialolithiasis NS
.6 Mucocele (ranula) NS
.7 Disturbances of salivary secretion AM NS
.8 Sialosis NS
.9 Other and unspecified NS

528 Diseases of the oral soft tissues, excluding gingiva and tongue DE NS

.0 Stomatitis NS
Excludes Vincent's stomatitis (101)
.1 Cancrum oris (noma) NS
.2 Oral aphthous ulceration NS
.3 Cellulitis and abscess NS
.4 Cysts NS

.5 Diseases of lips
Excludes angular cheilosis in vitamin deficiency (262, 263) NS
.6 Leukoplakia NS
.7 Other disturbances of keratinisation NS
.8 Oral submucous fibrosis NS
.9 Other and unspecified NS

529 Diseases of the tongue and other oral conditions DE, NS

.0 Median rhomboid glossitis NS
.1 Geographical tongue (benign, migratory glossitis) NS
.2 Other glossitis NS
.3 Hypertrophy of tongue papillae NS
.4 Atrophy of tongue papillae NS
.5 Plicated tongue NS
.6 Glossodynia (glossopyrosis) NS
.9 Other and unspecified NS

Diseases of oesophagus, stomach and duodenum (530-537)

530 Diseases of oesophagus AM
As ICD 539

.0 Functional disorders of oesophagus AM
.9 Other AM

531 Ulcer of stomach AM
As ICD 540 except peptic ulcer NOS (533)

.0 With perforation AM
.9 Without mention of perforation AM

532 Ulcer of duodenum AM
As ICD 541

.0 With perforation AM
.9 Without mention of perforation AM

533 Peptic ulcer, site unspecified AM

.0 With perforation AM
.9 Without mention of perforation AM

534 Gastrojejunal ulcer AM
As ICD 542

.0 With perforation AM
.9 Without mention of perforation AM

535 Gastritis and duodenitis AM
As ICD 543

536 Disorders of function of stomach AM
As ICD 544

.0 Disorders of gastric secretion AM
.1 Disorders of gastric motility AM
.9 Other AM

537 Other diseases of stomach and duodenum
As ICD 545

Appendicitis (540-543)

540 Acute appendicitis
As ICD 550

.0 With peritonitis
.9 Without mention of peritonitis

541 Appendicitis, unqualified
As ICD 551

542 Other appendicitis
As ICD 552

543 Other diseases of appendix
As ICD 553

Hernia of abdominal cavity (550-553)

550 Inguinal hernia without mention of obstruction
As ICD 560.0

551 Other hernias of abdominal cavity without mention of obstruction
.0 Femoral
As ICD 560.1
.1 Umbilical
As ICD 560.2
.2 Ventral (incisional)
As ICD 560.3
.3 Diaphragmatic
Excludes hernias due to gross congenital defect of diaphragm (756.8)
.8 Of other specified sites
As ICD 560.4 except diaphragmatic hernia above
.9 Of unspecified site
As ICD 560.5

552 Inguinal hernias with obstruction
As ICD 561.0

553 Other hernia of abdominal cavity with obstruction
.0 Femoral
As ICD 561.1
.1 Umbilical
As ICD 561.2
.2 Ventral (incisional)
As ICD 561.3
.3 Diaphragmatic
Excludes hernia due to gross congenital defect of diaphragm (756.8)
.8 Of other specified sites
As ICD 561.4 except diaphragmatic hernia above
.9 Of unspecified site
As ICD 561.5

Other diseases of intestine and peritoneum (560-569)

560 Intestinal obstruction without mention of hernia
As ICD 570 except mesenteric infarction (447.0)
.0 Intussusception
.1 Paralytic ileus
.2 Volvulus
.3 Impaction of intestine
.9 Other and unspecified

561 Gastro-enteritis and colitis, except ulcerative, of non-infectious origin
Excludes colitis, diarrhoea, enteritis, gastro-enteritis, infectious or unspecified (009)

562 Diverticula of intestine
.0 Small intestine
.1 Colon

563 Chronic enteritis and ulcerative colitis
.0 Regional enteritis
As ICD 572.0
.1 Ulcerative colitis
As ICD 572.2
.9 Other
As ICD 572.3

564 Functional disorders of intestines
.0 Constipation
As ICD 573.0
.1 Irritable colon
.9 Other
As ICD 573.3 except membranous colitis (564.4)

565 Anal fissure and fistula
.0 Anal fissure
.1 Anal fistula

566 Abscess of anal and rectal regions
As ICD 575

567 Peritonitis
As ICD 576

568 Peritoneal adhesions
As ICD 577

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569 Other diseases of intestines and peritoneum
As ICD 578 AM

Diseases of liver, gallbladder and pancreas (570-577) ES

570 Acute and subacute necrosis of liver
As ICD 580 AM, ES

571 Cirrhosis of liver AM, ES
.0 Alcoholic AM
.9 Other AM

572 Suppurative hepatitis and liver abscess
As ICD 582 AM

573 Other diseases of liver AM
As ICD 583 except portal vein obstruction (452)

574 Cholelithiasis AM
As ICD 584

575 Cholecystitis and cholangitis, without mention of calculi AM
As ICD 585

576 Other diseases of gallbladder and biliary ducts
As ICD 586 AM

577 Diseases of pancreas AM, ES
.0 Acute pancreatitis AM
As ICD 587.0
.1 Chronic pancreatitis AM
As ICD 587.1
.9 Other diseases of pancreas AM
As ICD 587.2 except fibrocystic disease of pancreas (273.0)

X. DISEASES OF GENITO-URINARY SYSTEM

Nephritis and nephrosis (580-584) AM, ES
Categories 580-583 (but not 584) include the listed conditions with hypertension (benign) but exclude them with malignant hypertension (400.3)

580 Acute nephritis AM

581 Nephrotic syndrome AM

582 Chronic nephritis AM
Excludes the terms "chronic Bright's disease," "chronic interstitial nephritis" and "chronic nephritis NOS" when specified as arteriosclerotic or due to any condition in 440(403)

583 Nephritis unqualified AM
Excludes the terms "Bright's disease NOS," "interstitial nephritis NOS" and "nephritis NOS" when specified as arteriosclerotic or due to any condition in 440(403)

584 Renal sclerosis, unqualified AM
Excludes the conditions when specified as arteriosclerotic or due to any condition in 401, 403 (403), 402, (404) or malignant hypertension (400.3). It also excludes contracted kidney, hydronephrotic (591) and pyelonephritic(590.0)

Other diseases of urinary system (590-599) ES

590 Infections of kidney AM AM
.0 Chronic pyelonephritis AM
.1 Other pyelonephritis, pyelitis and pyelocystitis
Remainder of ICD 600.0 AM
.2 Abscess of kidney and perirenal tissue
As ICD 600.1 AM
.9 Other
As ICD 600.2 AM

591 Hydronephrosis
As ICD 601 AM, ES

592 Calculi of kidney and ureter
As ICD 602 AM

593 Other diseases of kidney and ureter AM
.0 Renal dwarfism AM, ES
.1 Acute tubular nephrosis AM, ES
Excludes traumatic anuria (crush syndrome) (N996.7)
.2 Other renal disease AM
.3 Obstruction of ureter, not elsewhere classified AM
.4 Other diseases of ureter
Rest of ICD 603 AM

594 Calculi of other parts of the urinary system
As ICD 604 AM

595 Cystitis
As ICD 605 AM

596 Other diseases of bladder. AM
As ICD 606

597 Urethritis (non-venereal)
As ICD 607 AM

598 Stricture of urethra
As ICD 608 AM

599 Other diseases of urinary tract AM

Diseases of male genital organs (600-607)

600 Hyperplasia of prostate
As ICD 610 AM CA

601 Prostatitis AM CA
As ICD 611

602 Other diseases of prostate AM HD
As ICD 612

603 Hydrocele AM
As ICD 613

604 Orchitis and epididymitis AM HD
As ICD 614

605 Redundant prepuce and phimosis AM HD
As ICD 615

606 Sterility, male AM, ES HD
As ICD 616

607 Other diseases of male genital organs HD
As ICD 617 with sub-divisions: AM

.0 Leukoplakia of penis
.1 Erythroplasia of penis
.2 Chronic ulceration of penis
.3 Balanitis
.4 Seminal vesiculitis
.5 Other inflammatory diseases
.6 Spermatocele
.7 Torsion of testis
.8 Atrophy of testicle
.9 Other
Remainder of ICD 617

Diseases of breast, ovary, Fallopian tube and parametrium (610-616)

610 Chronic cystic disease of breast HD
As ICD 620

611 Other diseases of breast HD

.0 Acute mastitis not associated with lactation
As ICD 621.0
.1 Hypertrophy of breast
As ICD 621.1
.2 Fissure of nipple
.9 Other
Remainder of ICD 621.2

612 Acute salpingitis and oophoritis HD
As ICD 622

613 Chronic salpingitis and oophoritis HD
As ICD 623

614 Salpingitis and oophoritis, unqualified HD
As ICD 624

615 Other diseases of ovary and Fallopian tube HD
As ICD 625 with sub-divisions:

.0 Prolapse of ovary
.1 Hydrosalpinx
.2 Ovarian cyst, retention
.9 Other
Remainder of ICD 625

616 Diseases of parametrium and pelvic peritoneum (female) HD
As ICD 626 with sub-divisions:

.0 Pelvic inflammatory disease
.1 Pelvic peritoneal adhesions, female
.2 Pelvic congestion, female
.9 Other
Remainder of ICD 626 except rectovaginal fistula (629.8)

Diseases of uterus and other female genital organs (620-629)

620 Infective diseases of cervix uteri AI HD
Excludes trichomonal infections (131)

.0 Chronic cervicitis
.1 Other cervicitis

621 Other diseases of cervix HD

.0 Leukoplakia of cervix
.1 Erythroplasia of cervix
.2 Hyperplastic endometritis of cervix
.3 Chronic erosion and ulceration of cervix
.4 Old laceration of cervix
.5 Stricture of cervix
.6 Atrophy of cervix
.9 Other

622 Infective diseases of uterus (except cervix), vagina and vulva AI HD
Excludes trichomonal infections (131)

.0 Infective disease of uterus, except cervix
As ICD 630.1
.1 Vaginitis and vulvitis
As ICD 630.2

623 Uterovaginal prolapse HD

.0 Cystocele
.1 Rectocele
.2 Urethrocele
.3 Vaginal enterocele
.9 Other
Remainder of ICD 631

624 Malposition of uterus HD
As ICD 632 with sub-divisions:

.0 Retroversion and retroflexion
.8 Other
.9 Unspecified
Remainder of ICD 632

625 Other diseases of uterus HD

.0 Hyperplasia of endometrium
.1 Atrophy of uterus
.2 Subinvolution of uterus
.9 Other

626 Disorders of menstruation HD
As ICD 634 with sub-divisions:

.0 Absent
.1 Scanty
.2 Excessive
.3 Painful
.4 Frequent
.5 Irregular
.6 Intermenstrual bleeding
.7 Postmenopausal bleeding
.9 Other
Remainder of ICD 634

627 Menopausal symptoms HD
As ICD 635

628 Sterility, female HD
As ICD 636

629 Other diseases of female genital organs HD

.0 Leukoplakia of vagina
.1 Erythroplasia of vagina and vulva
.2 Kraurosis of vulva
.3 Leukorrhoea
As ICD 637.0
.4 Unspecified infection
.5 Vaginal bleeding
.6 Old laceration
.7 Stricture or atresia of vagina and hymen
.8 Rectovaginal fistula
.9 Other

XI. COMPLICATIONS OF PREGNANCY, CHILD-BIRTH AND THE PUERPERIUM

Complications of pregnancy (630-634)

630 Infections of genital tract during pregnancy
Any condition in 612, 613, 614, 616, 620 or 622 arising during pregnancy

HD

631 Ectopic pregnancy HD

.0 Abdominal pregnancy, without mention of sepsis
.1 Tubal pregnancy, without mention of sepsis
.2 Ovarian pregnancy, without mention of sepsis
.3 Other or unspecified ectopic pregnancy, without mention of sepsis
.4 Abdominal pregnancy, with sepsis
.5 Tubal pregnancy, with sepsis
.6 Ovarian pregnancy, with sepsis
.9 Other or unspecified ectopic pregnancy, with sepsis

632 Haemorrhage of pregnancy HD

.0 Placenta praevia
.1 Premature separation of placenta
.2 Haemorrhage from marginal sinus
.3 Threatened abortion
.4 Due to afibrinogenaemia
.9 Other and unspecified

633 Anaemia of pregnancy AM HD
As ICD 646 with sub-divisions:

.0 Macrocytic anaemia of pregnancy AM
.1 Iron deficiency anaemia of pregnancy
.9 Other and unspecified anaemia of pregnancy

634 Other complications of pregnancy AM HD

.0 Malposition of foetus in uterus
Excludes delivery with abnormal presentation (656)
.1 Rupture of pregnant uterus
.2 Hydatidiform mole
.3 Placental abnormalities not elsewhere classified
.4 Hydramnios
.5 Air embolism during pregnancy
.6 Molar pregnancy, undelivered
.9 Other AM

Urinary infections and toxaemias of pregnancy and the puerperium (635-639)

635 Urinary infections arising during pregnancy and the puerperium AM AM HD

.0 Pyelitis and pyelonephritis AM
.9 Other urinary infection

636 Renal disease arising during pregnancy and the puerperium AM HD
Any condition in 580, 581 or 583 arising during pregnancy and the puerperium. Excludes the listed conditions with pre-eclampsia (637.0) or eclampsia (637.1)

637 Pre-eclampsia, eclampsia and toxaemia, unspecified
.0 Pre-eclampsia
.1 Eclampsia
.9 Toxaemia, unspecified

638 Hyperemesis gravidarum

.0 With neuritis
.9 Without mention of neuritis

639 Other toxaemias of pregnancy and the puerperium
.0 Acute and subacute necrosis of liver
.9 Other

Abortion (640-645)

Categories 640-645 include any interruption of pregnancy before 28 weeks of gestation with a dead foetus. The following fourth-digit sub-divisions should be used with categories 640, 641, 643-645

.0 With sepsis
With mention of sepsis or any condition in 635, 670, 671 or 673.9

(640-645) .1 With toxaemia
With mention of toxaemia or any condition in 636-639

(641/3-645) .2 With sepsis and toxaemia

.9 Without mention of sepsis or toxaemia

640 Abortion induced for medical indications
For primary mortality tabulations, excludes the listed conditions if the complication of pregnancy or other pre-existing disease requiring the induction is known

641 Abortion induced for other legal indications

642 Abortion induced for other reasons

.0 With sepsis
.1 With haemorrhage
.2 With sepsis and haemorrhage
.3 With laceration of pelvic organ (with or without mention of sepsis and haemorrhage)
.9 Without mention of sepsis, haemorrhage or laceration

643 Abortion specified as spontaneous

644 Abortion not specified as induced or spontaneous

645 Other abortion

Delivery (650-662)

The following fourth-digit sub-divisions should be used with these categories:

.0 Spontaneous
.1 Manipulation without instruments
.2 Forceps, mid and high
.3 Forceps, low
.4 Forceps, unspecified
.5 Vacuum extractor
.6 Caesarian section
.8 Other surgical or instrumental
.9 Unspecified type of delivery

650 Delivery without mention of complication
As ICD 660

651 Delivery complicated by placenta praevia or antepartum haemorrhage
As ICD 670

652 Delivery complicated by retained placenta
As ICD 671

653 Delivery complicated by other postpartum haemorrhage
As ICD 672

654 Delivery complicated by abnormality of bony pelvis
As ICD 673

655 Delivery complicated by foetopelvic disproportion
Excludes the conditions with mention of abnormality of bony pelvis (654)

656 Delivery complicated by malpresentation of foetus
Excludes the conditions with mention of disproportion (655)

657 Delivery complicated by prolonged labour of other origin
As ICD 675

658 Delivery with laceration of perineum, without mention of other laceration
As ICD 676

659 Delivery with rupture of uterus

660 Delivery with other obstetrical trauma
As ICD 677 except rupture of uterus (659)

661 Delivery with other complications
As ICD 678

662 Anaesthetic death in uncomplicated delivery
Excludes anaesthetic death in complicated deliveries (651-661)

Complications of the puerperium (670-678)

670 Sepsis of child-birth and the puerperium
As ICD 681

671 Puerperal phlebitis and thrombosis HE HD
As ICD 682

672 Pyrexia of unknown origin during the puerperium HD
As ICD 653

673 Puerperal pulmonary embolism HD
.0 Air embolism
.1 Amniotic fluid embolism
.9 Other and unspecified

674 Cerebral haemorrhage in the puerperium HD
As ICD 687 NS

675 Puerperal blood dyscrasias HD

676 Anaemia of puerperium AM HD
As ICD 658.0

677 Other and unspecified complications of the puerperium AM HD
.0 Sudden death from unknown cause in the puerperium
As ICD 658.2
.9 Other
As ICD 658.3

678 Mastitis and other disorders of lactation HD
As ICD 689

XII. DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE

Infections of skin and subcutaneous tissue (680-686)
Excludes viral warts (079.1) and molluscum contagiosum (079.0) ES

680 Boil and carbuncle ES AI HD AM
As ICD 690
.0 Of face
.1 Of neck
.2 Of trunk
.3 Of upper arm and forearm
.4 Of hand
.5 Of buttock
.6 Of other parts of lower extremity
.8 Of other and multiple sites
.9 Of unspecified site

681 Cellulitis of finger and toe AM HD
As ICD 691

682 Other cellulitis and abscess ES AM HD
As ICD 692 and 693
.0 Of head and neck ES
.1 Of trunk ES
.2 Of upper arm and forearm ES
.3 Of hand, except fingers
.4 Of leg
.5 Of foot, except toes
.9 Of other, multiple, and unspecified sites

683 Acute lymphadenitis AM HD
As ICD 694

684 Impetigo AM HD
As ICD 695

685 Pilonidal cyst AM HD
As ICD 221

686 Other local infections of skin and subcutaneous tissue AI AM HD
As ICD 698 with sub-divisions:
.0 Pyoderma
.1 Pyogenic granuloma
.9 Other

Other inflammatory conditions of skin and subcutaneous tissue (690-698)

690 Seborrhoeic dermatitis AM
As ICD 700

691 Infantile eczema and related conditions AM HD

692 Other eczema and dermatitis AM ES
Includes allergic eczema and contact dermatitis
.0 Due to detergents AM, ES
.1 Due to oils and greases AM, ES
As ICD 703.1
.2 Due to solvents AM, ES
As ICD 703.2
.3 Due to drugs AM
As ICD 703.3
.4 Due to other chemicals AM, ES
As ICD 703.4
.5 Due to food AM
.6 Due to plants (except food) AM
As ICD 703.0
.7 Due to radiation, except sunburn AM
As ICD 703.5
.8 Due to other specified agents AM, ES
As ICD 703.6 plus sunburn
.9 Unspecified cause AM

693 Dermatitis herpetiformis AM
As ICD 704.0

694 Pemphigus AM
As ICD 704.1

695 Erythematous conditions AM
As ICD 705

.0 Toxic erythema AM
.1 Erythema multiforme (erythema iris) AM
.2 Erythema nodosum AM
.3 Rosacea AM
.4 Lupus erythematosus AM
.9 Other and unqualified AM

696 Psoriasis and similar disorders AM CA

.0 Psoriatic arthropathy AM
.1 Other psoriasis AM
As ICD 706.0
.2 Parapsoriasis AM
As ICD 706.1
.3 Pityriasis rosea AM
As ICD 706.2
.4 Pityriasis rubra pilaris AM
.5 Other and unspecified pityriasis AM
Remainder of ICD 706.3
.9 Other AM
As ICD 706.4

697 Lichen AM AI

.0 Lichen planus AM
.1 Lichen nitidus AM
.9 Other and unspecified AM
Remainder of ICD 707

698 Pruritus and related conditions AM

.0 Pruritus ani AM
As ICD 708.0
.1 Pruritus of genital organs AM HD
As ICD 708.1
.2 Prurigo AM
As ICD 708.2
.3 Lichenification and lichen simplex chronicus
As ICD 708.3 except diffuse neurodermatitis (Brocq) and atopic eczema (691) AM
.4 Dermatitis factitia (artefacta) AM
As ICD 708.4
.9 Other pruritic conditions AM
As ICD 708.5

Other diseases of skin and subcutaneous tissue (700-709)

700 Corns and callosities AM
As ICD 709

701 Other hypertrophic and atrophic conditions of skin
Excludes hereditary oedema of legs (757.0); scleroderma (generalized) (737.0); and dermatomyositis (716.0) AM

.0 Circumscribed scleroderma AM
.1 Keratoderma AM
As ICD 710.1
Except congenital conditions (757.1) seborrhoeic warts and seborrhoeic keratosis (216.0)
.2 Striae atrophicae AM
As ICD 710.3
.3 Keloid scar AM
As ICD 710.4
.9 Other hypertrophic and atrophic conditions of skin AM
As ICD 710.5

702 Other dermatoses AM
As ICD 711 except congenital conditions (757.2) and senile wart (216.0)

703 Diseases of nail AM
As ICD 712 except congenital conditions (757.4)

704 Diseases of hair and hair follicles AM
As ICD 713 except congenital conditions (757.3)

705 Diseases of sweat glands AM
.0 Anhidrosis AM
.1 Prickly heat AM
.9 Other AM
Remainder of ICD 714.0 except hidrocystoma (216.2)

706 Diseases of sebaceous glands AM
.1 Acne varioliformis AM
.2 Other acne AM
Remainder of ICD 714.1
.3 Sebaceous cyst AM
.4 Seborrhoea AM
.9 Other AM
Remainder of ICD 714.2

707 Chronic ulcer of skin AM, HE
As ICD 715

708 Urticaria AM
.0 Angioneurotic oedema AM
As ICD 242
.9 Other AM
As ICD 243

709 Other diseases of skin AM
As ICD 716 except congenital conditions (757.2, 757.9)

XIII. DISEASES OF THE MUSCULOSKELETAL SYSTEM AND CONNECTIVE TISSUE

Arthritis and rheumatism, except rheumatic fever (710-718)

710 Acute arthritis due to pyogenic organisms
As ICD 720 AM AI

711 Acute non-pyogenic arthritis
As ICD 721 AM

712 Rheumatoid arthritis and allied conditions AM
.0 Juvenile rheumatoid arthritis AM
.1 Rheumatoid arthritis with spleno-adenomegaly and leukopenia AM
.2 Palindromic rheumatism AM
.3 Other rheumatoid arthritis
Remainder of ICD 722.0 AM
.4 Spondylitis ankylopoietica
As ICD 722.1 AM
.5 Chronic rheumatic nodular fibrositis
As ICD 722.2 AM

713 Osteo-arthritis (arthrosis) and allied conditions AM
.0 Osteo-arthritis (arthrosis)
As ICD 723.0 AM
.1 Spondylitis osteo-arthritica (spondylarthrosis) AM
.2 Traumatic spondylopathy AM

714 Other specified forms of arthritis AM
.0 Traumatic arthritis AM
.9 Other AM
Remainder of ICD 724

715 Arthritis, unspecified AM
As ICD 725

716 Myositis AM, NS
Excludes infective myositis (732)
.0 Dermatomyositis AM, NS
.1 Chronic polymyositis AM, NS
.9 Other AM, NS

717 Other non-articular rheumatism AM
.0 Lumbago AM, NS
As ICD 726.0
.1 Myofibrosis scapulohumeral AM
.2 Torticollis not specified as congenital, psychogenic, or traumatic AM, NS
As ICD 726.2
.9 Other muscular rheumatism, fibrositis, and myalgia AM, NS

718 Rheumatism, unspecified
As ICD 727 AM

Osteomyelitis and other diseases of bone and joint (720-729)

720 Osteomyelitis and periostitis AM
As ICD 730 except osteomyelitis and periostitis of the jaw (526.4)
.0 Acute osteomyelitis
.1 Chronic osteomyelitis
.2 Unspecified osteomyelitis
.3 Periostitis without mention of osteomyelitis

721 Osteitis deformans AM
As ICD 731

722 Osteochondrosis AM
.0 Juvenile osteochondrosis of spine AM
.1 Juvenile osteochondrosis of hip AM
.2 Other juvenile osteochondrosis AM
.8 Other specified forms of osteochondrosis AM
.9 Unspecified AM

723 Other diseases of bone AM
.0 Osteoporosis AM
.1 Hypertrophic pulmonary osteo-arthropathy AM
.9 Other AM
Remainder of 733 except: Polyostotic fibrous dysplasia of bone (756.6); Cyst of jaw (526.0-526.2); Granuloma of jaw (526.3); Prognathism retrognathia (524.1)

724 Internal derangement of joint AM
.0 Elbow AM
.1 Knee AM
.9 Other AM

725 Displacement of intervertebral disc AM, NS
As ICD 735 with sub-divisions:
.0 Cervical AM, NS
.1 Lumbar and lumbosacral AM, NS
.8 Other AM, NS
.9 Unspecified AM, NS

726 Affection of sacroiliac joint AM, NS
As ICD 736

727 Ankylosis of joint AM
As ICD 737 with sub-divisions:
.0 Of spine AM
.1 Of shoulder AM
.2 Of elbow AM
.3 Of wrist AM
.4 Of finger AM
.5 Of hip AM
.6 Of knee AM
.7 Of ankle AM
.8 Of other and multiple sites AM
.9 Of unspecified site AM

728 Vertebrogenic pain syndromes AM, NS
Excludes the conditions stated as due to displacement of intervertebral disc (725); rheumatoid arthritis (712); spondyloarthrosis (713.1); spondylitis (713.2)
.0 Cervicalgia AM, NS
.1 Cervico-cranial syndrome AM, NS
.2 Cervico-brachial diffuse syndrome AM, NS
.3 Radicular syndrome of upper limbs AM, NS
Excludes brachial neuritis NOS (352)
.4 Cervical myelopathy AM, NS
.5 Pain in thoracic spine (with radicular and visceral pain) AM, NS
.6 Thoracic myelopathy AM, NS
.7 Lumbalgia AM, NS
.8 Radicular syndrome of lower limbs NS
Excludes sciatic neuritis NOS (353)
.9 Compression syndrome of cauda equina AM, NS

729 Other diseases of joint AM
As ICD 735 except peri-arthritis (717)

Other diseases of musculoskeletal system (730-739)

730 Bunion AM
As ICD 740

731 Synovitis, bursitis and tenosynovitis AM
As ICD 741 and 742

732 Infective myositis and other inflammatory diseases of tendon and fascia AM, NS
As ICD 743

733 Other diseases of muscle, tendon and fascia
Excludes inborn defects of muscle (310); myositis (716); myofibrosis (717) AM, NS
.0 Myasthenia gravis
As ICD 744.0 NS
.1 Muscular atrophy (idiopathic) NS
.9 Other
Remainder of ICD 744.2 NS

734 Diffuse diseases of connective tissue AM, HE
Excludes polyarteritis nodosa (446.0)
.0 Progressive systemic sclerosis
.1 Systemic lupus erythematosus
.9 Other

735 Curvature of spine AM
As ICD 745 except congenital (756.1)

736 Flat foot AM
As ICD 746 except congenital (755.9)

737 Hallux valgus and varus AM
As ICD 747 except congenital (755.9)

738 Other deformities AM

XIV. CONGENITAL ANOMALIES ES

740 Anencephalus HD NS

741 Spina bifida HD NS
Excludes spina bifida occulta (756.1)
.0 With hydrocephalus NS
.9 Without mention of hydrocephalus NS

742 Congenital hydrocephalus NS
Excludes the listed conditions with spina bifida (741.0)

743 Other congenital anomalies of nervous system ES, NS
.0 Encephalocele NS
.1 Microcephalus NS
.2 Other specified anomalies of brain NS
.3 Other specified anomalies of spinal cord NS
.4 Neurofibromatosis NS
.8 Other anomalies of peripheral nervous system NS
.9 Unspecified anomalies of brain, spinal cord or nervous system NS

744 Congenital anomalies of eye ES HD EY
.0 Anophthalmos
.1 Microphthalmos
.2 Buphthalmos
.3 Congenital cataract
.4 Coloboma
.5 Aniridia
.8 Other specified anomalies of eye
.9 Unspecified anomalies of eye

745 Congenital anomalies of ear, face and neck HD
Excludes: cleft lip (749.1), anomalies of cervical spine (756.1), thyroid gland (758.2), parathyroid gland (758.3) and larynx (748.3) NS
.0 Anomalies of ear causing impairment of hearing NS
.1 Accessory auricle NS
.2 Other specified anomalies of ear NS
.3 Unspecified anomalies of ear NS
.4 Branchial cleft, cyst or fistula; pre-auricular sinus NS
.5 Webbing of neck NS
.8 Other specified anomalies of face and neck DE, NS
.9 Unspecified anomalies of face and neck DE, NS

746 Congenital anomalies of heart HE HD

- .0 Common truncus
- .1 Transposition of great vessels
- .2 Tetralogy of Fallot
- .3 Ventricular septal defect
- .4 Atrial septal defect
- .5 Ostium atrioventriculare commune
- .6 Anomalies of heart valves
- .7 Fibroelastosis cordis
- .8 Other specified anomalies of heart
- .9 Unspecified anomalies of heart

747 Other congenital anomalies of circulatory system HD HE

- .0 Patent ductus arteriosus
- .1 Coarctation of aorta
- .2 Other anomalies of aorta
- .3 Stenosis or stresia of pulmonary artery
- .4 Anomalies of great veins
- .5 Absence or hypoplasia of umbilical artery
- .6 Other anomalies of peripheral vascular system
- .8 Other specified anomalies of circulatory system
- .9 Unspecified anomalies of circulatory system

748 Congenital anomalies of respiratory system HD HE

- .0 Choanal atresia
- .1 Other anomalies of nose NS
- .2 Web of larynx NS
- .3 Other anomalies of larynx, trachea and bronchus NS
- .4 Congenital cystic lung
- .5 Agenesis of lung
- .6 Other anomalies of lung
- .8 Other specified anomalies of respiratory system
- .9 Unspecified anomalies of respiratory system

749 Cleft palate and cleft lip DE, ES, NS HD

- .0 Cleft palate NS
- .1 Cleft lip NS
- .2 Cleft palate with cleft lip NS

750 Other congenital anomalies of upper alimentary tract HD

- .0 Tracheoesophageal fistula, oesophageal atresia and stenosis
- .1 Pyloric stenosis
- .2 Anomalies of tongue DE
- .8 Other specified anomalies of upper alimentary tract DE
- .9 Unspecified anomalies of upper alimentary tract

751 Other congenital anomalies of digestive system HD

- .0 Meckel's diverticulum
- .1 Atresia and stenosis of small intestine
- .2 Atresia and stenosis of rectum and anal canal
- .3 Hirschsprung's disease
- .4 Anomalies of intestinal fixation
- .5 Other anomalies of intestine
- .6 Anomalies of gallbladder, bile ducts and liver
- .7 Anomalies of pancreas
- .8 Other specified anomalies of digestive system
- .9 Unspecified anomalies of digestive system

752 Congenital anomalies of genital organs HD

Excludes: male hypogonadism (Klinefelter's syndrome) (759.5), gonadal agenesis (Turner's syndrome) (759.5) ES

- .0 Indeterminate sex
- .1 Undescended testicle
- .2 Hypospadias
- .3 Epispadias
- .4 Hydrocele
- .5 Anomalies of ovary, Fallopian tube and uterus
- .6 Anomalies of vagina and external female genitalia
- .7 Pseudohermaphroditism
- .8 Other specified anomalies of genital organs
- .9 Unspecified anomalies of genital organs

753 Congenital anomalies of urinary system HD AM, ES

- .0 Renal agenesis
- .1 Cystic kidney disease
- .2 Obstructive defects of urinary tract
- .3 Other specified anomalies of kidney
- .4 Other specified anomalies of ureter
- .5 Extrophy of urinary bladder
- .6 Atresia and stenosis of urethra and bladder neck
- .8 Other specified anomalies of bladder and urethra
- .9 Unspecified anomalies of urinary system

754 Congenital clubfoot HD AM

755 Other congenital anomalies of limbs AM, ES

- .0 Polydactyly
- .1 Syndactyly
- .2 Reduction deformity confined to hand
- .3 Reduction deformity of arm (and hand)
- .4 Reduction deformity of leg and foot
- .5 Reduction deformity, unspecified limb
- .6 Other anomaly of upper limb (including shoulder girdle)
- .7 Dislocation of hip AM
- .8 Other anomaly of lower limb (including pelvic girdle)
- .9 Other and unspecified anomaly of unspecified limb

756 Other congenital anomalies of musculoskeletal system ES HD AM

- .0 Anomalies of skull and face bones
  Excludes anomalies of jaw (524.0) DE

.1 Anomalies of spine
.2 Cervical rib
.3 Other anomalies of ribs and sternum
.4 Chondrodystrophy
.5 Osteogenesis imperfecta AMM
.6 Other generalized anomalies of skeleton AMM
.8 Other specified anomalies of muscle, tendon and fascia
.9 Unspecified anomalies of musculoskeletal system

757 Congenital anomalies of skin, hair and nails HD AMM
.0 Hereditary oedema of legs (Milroy's disease) HE
.1 Pigmented naevus
.2 Other specified anomalies of skin
.3 Specified anomalies of hair
.4 Specified anomalies of nails
.9 Unspecified anomalies of skin, hair and nails

758 Other and unspecified congenital anomalies AMM HD
.0 Anomalies of spleen AMM
.1 Anomalies of adrenal gland
.2 Anomalies of thyroid gland
.3 Anomalies of other endocrine glands
.8 Other specified congenital anomaly
.9 Unspecified congenital anomaly

759 Congenital syndromes affecting multiple systems ES HD
.0 Situs inversus
.1 Conjoined twins
.2 Other forms of monster
Excludes anencephaly (740)
.3 Langdon-Down disease NS
.4 Other syndromes due to autosomal abnormality
.5 Syndromes due to sex chromosome abnormality
.6 Tuberous sclerosis NS
.8 Other specified syndromes
.9 Multiple congenital anomalies NOS

XV. CERTAIN CAUSES OF PERINATAL MORBIDITY AND MORTALITY

760 Chronic circulatory and genito-urinary disease in mother AMM, HE HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant
.0 Chronic rheumatic heart disease
.1 Congenital heart disease
.2 Chronic hypertension AMM
.3 Other chronic disease of circulatory system
.4 Chronic nephritis AMM
.5 Other chronic disease of genito-urinary system AMM

761 Other maternal conditions unrelated to pregnancy
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant AI AMM, ES HD
.0 Syphilis
.1 Diabetes mellitus AMM
.2 Influenza
.3 Rubella
.4 Toxoplasmosis NS
.5 Injury
.6 Operation
.7 Chemical substances transmitted through placenta
.9 Other maternal causes

762 Toxaemias of pregnancy AMM HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant
.0 Renal disease arising during pregnancy AMM, HE
.1 Pre-eclampsia of pregnancy AMM
.2 Eclampsia of pregnancy AMM
.3 Toxaemia unspecified AMM
.4 Hyperemesis gravidarum AMM
.5 Acute and subacute necrosis of liver arising during pregnancy AMM
.9 Other toxaemia of pregnancy AMM

763 Maternal ante- and intra-partum infection HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant AMM
.0 Pyelitis and pyelonephritis of pregnancy AMM
.1 Other infections of genito-urinary tract during pregnancy AMM
.9 Other

764 Difficult labour with abnormality of bones, organs or tissues of pelvis HD NS
.0 With birth injury to brain
.1 With birth injury to spinal cord
.2 With birth injury to bone or nerve NS
.3 With other or unspecified birth injury
.4 With asphyxia, anoxia or hypoxia
.9 Without mention of birth injury, asphyxia, anoxia or hypoxia

765 Difficult labour with disproportion, but no mention of abnormality of pelvis HD
.0 With birth injury to brain NS
.1 With birth injury to spinal cord NS
.2 With birth injury to bone or nerve NS
.3 With other or unspecified birth injury
.4 With asphyxia, anoxia or hypoxia
.9 Without mention of birth injury, asphyxia, anoxia or hypoxia

766 Difficult labour with malposition of foetus HD
Excludes the listed conditions with disproportion (765)

.0 With birth injury to brain NS
.1 With birth injury to spinal cord NS
.2 With birth injury to bone or nerve NS
.3 With other or unspecified birth injury
.4 With asphyxia, anoxia or hypoxia
.9 Without mention of birth injury, asphyxia, anoxia or hypoxia

767 Difficult labour with abnormality of forces of labour HD

.0 With birth injury to brain NS
.1 With birth injury to spinal cord NS
.2 With birth injury to bone or nerve NS
.3 With other or unspecified birth injury
.4 With asphyxia, anoxia or hypoxia
.9 Without mention of birth injury, asphyxia, anoxia or hypoxia

768 Difficult labour with other and unspecified complications HD

.0 With birth injury to brain NS
.1 With birth injury to spinal cord NS
.2 With birth injury to bone or nerve NS
.3 With other or unspecified birth injury
.4 With asphyxia, anoxia or hypoxia
.9 Without mention of birth injury, asphyxia, anoxia or hypoxia

769 Other complications of pregnancy and child-birth HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant

.0 Incompetent cervix
.1 Premature rupture of membranes
.2 Hydramnios
.3 Ectopic pregnancy
.4 Multiple pregnancy
.5 Maternal death unspecified
.9 Other

770 Conditions of placenta HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant

.0 Placenta praevia
.1 Premature separation of placenta
.2 Placental infarction HE
.9 Other

771 Conditions of umbilical cord HD
Includes the listed conditions with asphyxia, anoxia or hypoxia in the foetus or infant

.0 Compression of cord
.1 Prolapse of cord without mention of compression
.9 Other

772 Birth injury without mention of cause HD

.0 To brain NS
.1 To spinal cord NS
.2 To bone or nerve NS
.9 Other and unspecified

773 Termination of pregnancy HD
Not to be used for primary mortality classification if reason for termination is known and is classifiable elsewhere in this section

774 Haemolytic disease of newborn with kernicterus HL HD
.0 With Rh incompatibility
.1 With ABO incompatibility
.2 With other or unspecified blood incompatibility
.9 Without mention of cause NS

775 Haemolytic disease of newborn without mention of kernicterus HL HD AM
.0 With Rh incompatibility AM
.1 With ABO incompatibility
.2 With other or unspecified blood incompatibility
.9 Without mention of cause

776 Anoxic and hypoxic conditions not elsewhere classified HD

.0 Aspiration of content of birth canal HE
.1 Hyaline membrane disease HE
.2 Respiratory distress syndrome HE
.3 Foetal distress
.4 Intra-uterine anoxia
.9 Asphyxia of newborn unspecified

777 Immaturity NOS HD

778 Other conditions of foetus AM HD

.0 Foetal blood loss before birth
.1 Chorio-amnionitis
.2 Post-maturity
.3 Haemorrhagic disease of newborn AM
.4 Cold injury syndrome
.9 Other

779 Foetal death of unknown cause HD

.0 Maceration
.9 Other

XVI. SYMPTOMS AND ILL-DEFINED CONDITIONS

There had not been a document prepared on the revision of the section as its form is dependent to some extent on the final arrangement and content of the disease sections I-XV. A separate three-digit category will be provided for 795.2 sudden death (cause unknown).

Certain transfers may already be considered accepted, either of sub-categories or of inclusion terms. Transfers of sub-categories from Section XVI involve ICD 780.3 Jacksonian epilepsy (to Section VI), ICD 785.6 Diarrhoea, age two years and over (to Section I, without age distinction); ICD 787.5 Pain in back (to Section XIII). In respect of inclusion terms it has been agreed to reclassify "Cerebellar ataxia" (from ICD 780.5 Disturbance of co-ordination, to Section VI); "Narcolepsy" (from ICD 780.7 Disturbance of sleep, to Section VI). Transfers into Section XVI affect ICD 534 Toothache from unspecified cause, and inclusion term "Earache of unknown cause" in ICD 394 Other inflammatory diseases of ear. Other transfers have been suggested such as that of ICD 784.6 Excessive salivation (to Section IX) or of ICD 789.1 Albuminuria orthostatic (to Section X). However, only systematic review of all terms in the present alphabetical index assigned to Section XVI as well as other sections will allow conclusions on the merits of a few additional transfers and facilitate consistent decisions.

E XVII. ACCIDENTS, POISONINGS AND VIOLENCE (EXTERNAL CAUSE)

Railway accidents (E800-E807)

To identify the injured person, the following fourth digits are for use with categories E800-E807:

.0 Railway employee
.1 Passenger on railway
.2 Pedestrian
.3 Pedal cyclist
.8 Other specified person
.9 Unspecified person

E800 Railway accident involving collision with rolling stock

E801 Railway accident involving collision with stationary object

E802 Railway accident involving derailment without antecedent collision

E803 Railway accident involving explosion, fire, burning

E804 Fall in, on, or from train

E805 Hit by rolling stock

E806 Other specified railway accident

E807 Railway accident of unspecified nature

Motor vehicle traffic accidents (E810-E819)

To identify the injured person, the following fourth digits are for use with categories E810-E819:

.0 Driver of motor vehicle other than motorcycle
.1 Passenger in motor vehicle other than motorcycle
.2 Motorcyclist
.3 Passenger on motorcycle
.4 Occupant of streetcar
.5 Rider of animal; occupant of animal-drawn vehicle
.6 Pedal cyclist
.7 Pedestrian
.8 Other specified person
.9 Unspecified person

E810 Motor vehicle traffic accident involving collision with train

E811 Motor vehicle traffic accident involving collision with streetcar

E812 Motor vehicle traffic accident involving collision with another motor vehicle

E813 Motor vehicle traffic accident involving collision with other vehicle

E814 Motor vehicle traffic accident involving collision with pedestrian

E815 Other motor vehicle traffic accident involving collision

E816 Non-collision motor vehicle traffic accident due to loss of control

E817 Non-collision motor vehicle traffic accident while boarding or alighting

E818 Other non-collision motor vehicle traffic accident

E819 Motor vehicle traffic accident of unspecified nature

Motor vehicle non-traffic accidents (E820-E823)

To identify the injured person the following fourth digits are for use with categories E820-E823:

.0 Driver of motor vehicle other than motorcycle
.1 Passenger in motor vehicle other than motorcycle
.2 Motorcyclist
.3 Passenger on motorcycle

Certain transfers may already be considered accepted, either of sub-categories or of inclusion terms. Transfers of sub-categories from Section XVI involve ICD 780.3 Jacksonian epilepsy (to Section VI), ICD 785.6 Diarrhoea, age two years and over (to Section I, without age distinction); ICD 787.5 Pain in back (to Section XIII). In respect of inclusion terms it has been agreed to reclassify "Cerebellar ataxia" (from ICD 780.5 Disturbance of co-ordination, to Section VI); "Narcolepsy" (from ICD 780.7 Disturbance of sleep, to Section VI). Transfers into Section XVI affect ICD 534 Toothache from unspecified cause, and inclusion term "Earache of unknown cause" in ICD 394 Other inflammatory diseases of ear. Other transfers have been suggested such as that of ICD 784.6 Excessive salivation (to Section IX) or of ICD 789.1 Albuminuria orthostatic (to Section X). However, only systematic review of all terms in the present alphabetical index assigned to Section XVI as well as other sections will allow conclusions on the merits of a few additional transfers and facilitate consistent decisions.

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E801 Railway accident involving collision with stationary object

E802 Railway accident involving derailment without antecedent collision

E803 Railway accident involving explosion, fire, burning

E804 Fall in, on, or from train

E805 Hit by rolling stock

E806 Other specified railway accident

E807 Railway accident of unspecified nature

Motor vehicle traffic accidents (E810-E819)

To identify the injured person, the following fourth digits are for use with categories E810-E819:

.0 Driver of motor vehicle other than motorcycle
.1 Passenger in motor vehicle other than motorcycle
.2 Motorcyclist
.3 Passenger on motorcycle
.4 Occupant of streetcar
.5 Rider of animal; occupant of animal-drawn vehicle
.6 Pedal cyclist
.7 Pedestrian
.8 Other specified person
.9 Unspecified person

E810 Motor vehicle traffic accident involving collision with train

E811 Motor vehicle traffic accident involving collision with streetcar

E812 Motor vehicle traffic accident involving collision with another motor vehicle

E813 Motor vehicle traffic accident involving collision with other vehicle

E814 Motor vehicle traffic accident involving collision with pedestrian

E815 Other motor vehicle traffic accident involving collision

E816 Non-collision motor vehicle traffic accident due to loss of control

E817 Non-collision motor vehicle traffic accident while boarding or alighting

E818 Other non-collision motor vehicle traffic accident

E819 Motor vehicle traffic accident of unspecified nature

Motor vehicle non-traffic accidents (E820-E823)

To identify the injured person the following fourth digits are for use with categories E820-E823:

.0 Driver of motor vehicle other than motorcycle
.1 Passenger in motor vehicle other than motorcycle
.2 Motorcyclist
.3 Passenger on motorcycle

.4 Occupant of streetcar
.5 Rider of animal; occupant of animal-drawn vehicle
.6 Pedal cyclist
.7 Pedestrian
.8 Other specified person
.9 Unspecified person

E820 Motor vehicle non-traffic accident involving collision with moving object

E821 Motor vehicle non-traffic accident involving collision with stationary object

E822 Motor vehicle non-traffic accident while boarding or alighting

E823 Motor vehicle non-traffic accident of other and unspecified nature

Other road vehicle accidents (E825-E827)

E825 Streetcar accident, except collision with motor vehicle

.0 Injury to pedestrian
.1 Injury to pedal cyclist
.2 Injury to occupant of streetcar
.8 Injury to other specified person
.9 Injury to unspecified person

E826 Pedal cycle accident, except collision with motor vehicle or streetcar

.0 Injury to pedestrian
.1 Injury to pedal cyclist
.8 Injury to other specified person
.9 Injury to unspecified person

E827 Other non-motor road vehicle accidents

.0 Injury to pedestrian
.8 Injury to other specified person
.9 Injury to unspecified person

Water transport accidents (E830-E838)
To identify the injured person, the following fourth digits are for use with categories E830-E838:

.0 Occupant of small boat
.1 Occupant of other water craft—crew
.2 Occupant of other water craft—other than crew
.3 Dockers, stevedores
.8 Other specified person
.9 Unspecified person

E830 Accident to water craft causing submersion

E831 Accident to water craft causing other injury

E832 Other accidental submersion or drowning in water transport

E833 Fall on stairs or ladders in water transport
As ICD E852

E834 Other fall from one level to another in water transport
As ICD E853

E835 Other and unspecified fall in water transport
As ICD E854 and E855

E836 Machinery accident in water transport
As ICD E856

E837 Explosion, fire, burning, in water transport

E838 Other and unspecified water transport accident

Air and space transport accidents (E840-E845)
To identify the injured person, the following fourth digits are for use with categories E840-E846:

.0 Occupant of space craft
.1 Occupant of military aircraft
.2 Occupant of commercial aircraft, crew
.3 Other occupant of commercial aircraft
.4 Occupant of other and unspecified aircraft
.5 Ground crew, airline employee
.8 Other specified person
.9 Unspecified person

E840 Accident to powered aircraft at take-off or landing

E841 Accident to powered aircraft, other and unspecified

E842 Accident to unpowered aircraft

E843 Fall in, on, or from aircraft

E844 Other specified air transport accidents

E845 Accident involving spacecraft

Accidental poisoning by drugs and medicaments (E850-E859)
Excludes (contact) dermatitis due to drugs and medicaments (692.3), complications and misadventures in administration of anaesthetics for purposes of medical care (E930-E936), and idiosyncratic and hypersensitive reactions to drugs (E930-E936)

E850 Accidental poisoning by antibiotics and other anti-infectives AM CM

.0 Penicillin, any AM
.1 Antifungal antibiotics
.2 Chloramphenicol
.3 Erythromycins, streptomycins, tetracyclines
.4 Other antibiotics
.5 Sulfonamides AM
.6 Arsenic anti-infectives
.7 Silver and its compounds
.8 Quinoline and hydroxyquinoline derivatives
.9 Other anti-infectives

E851 Accidental poisoning by hormones and synthetic substitutes AM CM HD

.0 Adrenals
.1 Androgens and anabolic congeners
.2 Oestrogens
.3 Insulins and antidiabetic agents
.4 Anterior pituitary extracts
.5 Posterior pituitary extracts
.6 Progestogens
.7 Thyroid and thyroid derivatives
.8 Antithyroid agents
.9 Other hormones and synthetic substitutes

E852 Accidental poisoning by primarily systemic and haematologic agents AM CM

.0 Antihistamine and anti-emetic drugs
.1 Antineoplastic agents
.2 Other electrolytic, caloric and water balance agents AM
.3 Vitamins
.4 Other primarily systemic agents
.5 Iron and its compounds AM
.6 Anticoagulants AM
.7 Vitamin K products AM
.8 Other coagulants AM
.9 Other primarily haematologic agents AM

E853 Accidental poisoning by analgesics and antipyretics AM CM

.0 Opiates and synthetic analogues
.1 Salicylates and congeners AM
.2 Cinchophen and congeners
.3 Colchicine
.4 Aniline derivatives
.8 Other coal tar derivatives AM
.9 Other analgesics and antipyretics AM

E854 Accidental poisoning by other sedatives and hypnotics AM, NS CM

.0 Barbiturates AM NS
.1 Chloral hydrate NS
.2 Paraldehyde NS
.3 Bromides NS
.9 Other sedatives and hypnotics AM NS

E855 Accidental poisoning by autonomic nervous system and psychotherapeutic drugs AM, NS CM

.0 Antidepressants AM NS
.1 Tranquilizers AM NS
.2 Other psychotherapeutic agents AM NS
.3 Parasympathomimetics (cholinergics) NS
.4 Parasympatholytics (anticholinergics) NS
.5 Sympathomimetics (adrenergics) NS
.6 Autonomic nervous system relaxants NS
.9 Other AM NS

E856 Accidental poisoning by other central nervous system depressants and stimulants NS CM

.0 Anticonvulsants NS
.1 Skeletal muscle relaxants NS
.2 Anaesthetic gases NS
.3 Other CNS depressants NS
.4 Amphetamine NS
.8 Other CNS stimulants NS
.9 Other and unspecified NS

E857 Accidental poisoning by cardiovascular drugs AM, HD CM

.0 Cardiac depressants
.1 Cardiac tonics
.2 Cholesterol lowering agents
.3 Ganglionic blocking agents NS
.4 Vasodilators AM
.5 Other hypotensive agents AM
.6 Sclerosing agents
.9 Other

E858 Accidental poisoning by gastro-intestinal drugs AM CM

.0 Antacids and antidiarrhoeal agents
.1 Intestinal irritant cathartics
.2 Emollient cathartics
.3 Saline cathartics
.4 Faecal softeners
.5 Other cathartics
.6 Emetics
.9 Other

E859 Accidental poisoning by other and unspecified drugs and medicaments AM CM

.0 Local anaesthetics NS
.1 Mercurial diuretics AM
.2 Xanthine derivatives AM
.3 Other diuretics AM
.4 Agents acting directly on musculo-skeletal system AM
.5 Liniments AM
.6 Ointments AM
.7 Other medicinals for external use
.8 Other specified drugs
.9 Drug NOS

Accidental poisoning by other solid and liquid substances (E860-E869)

Excludes (contact) dermatitis due to detergents (692.0), oils and greases (692.1), solvents (692.2), and other chemicals (692.4)

E860 Accidental poisoning by alcohol AM, NS
As ICD E860

E861 Accidental poisoning by cleansing and polishing agents AM ES

E862 Accidental poisoning by disinfectants AM ES

E863 Accidental poisoning by paints and varnishes AM ES

E864 Accidental poisoning by petroleum products and other solvents AM ES
As ICD E851 and E852

E865 Accidental poisoning by pesticides, fertilizers, plant foods AM ES

E866 Accidental poisoning by heavy metals and their fumes AM ES

E867 Accidental poisoning by corrosives and caustics, not elsewhere classified ES

E868 Accidental poisoning by noxious foodstuffs and poisonous plants CM

E869 Accidental poisoning by other and unspecified solid and liquid substances ES CM

Accidental poisoning by gases and vapors (E870-E877)

E870 Accidental poisoning by gas distributed by pipeline

E871 Accidental poisoning by liquified petroleum gas distributed in mobile containers

E872 Accidental poisoning by other utility gas

E873 Accidental poisoning by motor vehicle exhaust gas
As ICD E891

E874 Accidental poisoning by carbon monoxide from incomplete combustion of domestic fuels NS

E875 Accidental poisoning by other carbon monoxide NS

E876 Accidental poisoning by other gases and vapors
As ICD E893 and E894

E877 Accidental poisoning by unspecified gases and vapors
As ICD E895

Accidental falls (E880-E887)

E880 Fall on or from stairs or steps

E881 Fall on or from ladders or scaffolding

E882 Fall from or out of building or other structure

E883 Fall into hole or other opening in surface

E884 Other fall from one level to another

E885 Fall on same level from slipping, tripping or stumbling

E886 Fall on same level from collision, pushing or shoving by or with other person

E887 Other and unspecified fall

Accidents caused by fires (E890-E899)

E890 Accident caused by conflagration in private dwelling

E891 Accident caused by conflagration in other building or structure

E892 Accident caused by conflagration not in building or structure

E893 Accident caused by ignition of clothing

E894 Accident caused by ignition of highly inflammable material

E895 Accident caused by controlled fire in private dwelling

E896 Accident caused by controlled fire in other building or structure

E897 Accident caused by controlled fire not in building or structure

E898 Accident caused by other specified fires

E899 Accident caused by unspecified fire

Accidents due to natural and environmental factors (E900-E909)

E900 Excessive heat AM, NS
As ICD E931 except sunburn (692.8)

E901 Excessive cold
As ICD E932

E902 High and low air pressure
As ICD E930

E903 Effects of travel and motion

E904 Hunger, thirst, exposure and neglect AM
As ICD E926 and E933

E905 Bites and stings of venomous animals and insects
As ICD E927 AI

E906 Other accidents caused by animals
As ICD E928

E907 Lightning
As ICD E935 NS

E908 Cataclysm
As ICD E934

E909 Accident due to other natural and environmental factors

Other accidents (E910-E929)

E910 Accidental drowning and submersion
Excludes drowning and submersion in transport accidents

.0 In recreational activities
.9 Other and unspecified

E911 Inhalation and ingestion of food causing obstruction or suffocation
As ICD E921 NS

E912 Inhalation and ingestion of other object causing obstruction or suffocation
As ICD E922 NS.

E913 Accidental mechanical suffocation HD

.0 In bed or cradle
As ICD E924
.9 Other and unspecified
As ICD E925

E914 Foreign body entering accidentally eye and adnexa
As ICD E920
EY

E915 Foreign body entering accidentally other orifice
As ICD E923

E916 Struck accidentally by falling object

E917 Striking against or struck accidentally by objects

E918 Caught accidentally in or between objects AM

E919 Over-exertion and strenuous movements

E920 Accident caused by cutting or piercing instruments
As ICD E913 with sub-divisions:

.0 Powered hand tools
.1 Other hand tools
.2 Other machinery
.8 Other
.9 Unspecified

E921 Accident caused by explosion of pressure vessel
As ICD E915 with sub-divisions:

.0 Boilers
.1 Gas cylinders
.8 Other
.9 Unspecified

E922 Accident caused by firearms weapons
As ICD E919 with sub-divisions:

.0 Accidentally self-inflicted
.9 Other and unspecified

E923 Accident caused by explosive material

.0 Fireworks
.1 Blasting materials
.2 Explosive gases
.8 Other
.9 Unspecified

E924 Accident caused by hot substance, corrosive liquid, and steam
As ICD E917 except burns NOS (E899)

E925 Accident caused by electric current AM
As ICD E914 with sub-divisions:

.0 Home wiring or appliances
.1 Industrial wiring or appliances
.8 Other
.9 Unspecified

E926 Accident caused by radiation
As ICD E918 with sub-divisions:

.0 Non-ionizing
.1 Ionizing

E927 Vehicle accidents not elsewhere classifiable

E928 Machinery accidents not elsewhere classifiable

E929 Other and unspecified accidents

Surgical and medical complications and misadventures (E930-E949)

Excludes (contact) dermatitis due to drugs and medicaments (692.3) and accidental overdose of drugs and wrong drug given in error (E850-E858)

E930 Complications and misadventures in operative therapeutic procedures FM CM

Not to be used for primary death classification if the condition for which the treatment was given is known

.0 In surgical treatment, excluding effects of anaesthetic management
.1 In anaesthesia during operative treatment
.2 In infusion or transfusion during operative treatment FM
.9 In other procedures during operative treatment

E931 Complications and misadventures in other and unspecified therapeutic procedures

Not to be used for primary death classification if the condition for which treatment was given is known FM CM

.0 In use of X-rays and radioactive substances FM
.1 In administration of drugs and biologicals
.2 In infusion and transfusion FM
.3 In local applications
.8 In other therapeutic procedures
.9 In unspecified therapeutic procedures

E932 Complications and misadventures in diagnostic procedures CM

Not to be used for primary death classification if a diagnosis was made

.0 In surgical procedures, excluding effects of anaesthetic management
.1 In anaesthesia
.2 In use of X-rays or radioactive substances
.3 In administration of drugs and biologicals
.8 In other diagnostic procedures
.9 In unspecified diagnostic procedures

E933 Complications and misadventures in prophylaxis with bacterial vaccines AI

.0 BCG vaccine
.1 Typhoid and paratyphoid vaccine
.2 Cholera vaccine
.3 Plague vaccine
.4 Tetanus vaccine
.5 Diphtheria vaccine
.6 Pertussis vaccine, including combinations with a pertussis component
.8 Other and unspecified bacterial vaccines
.9 Mixed bacterial vaccine, except combinations with a pertussis component

E934 Complications and misadventures in prophylaxis with other vaccines

.0 Smallpox vaccine NS
.1 Rabies vaccine NS
.2 Typhus vaccine
.3 Yellow fever vaccine
.4 Measles vaccine NS
.5 Poliomyelitis vaccine
.6 Other and unspecified viral or rickettsial vaccines
.7 Mixed viral/rickettsial and bacterial vaccines, except combinations with a pertussis component
.9 Other and unspecified vaccines

E935 Complications and misadventures in other prophylactic procedures CM

.0 In surgical procedures, excluding effects of anaesthetic management
.1 In anaesthesia during prophylactic procedures
.2 In use of X-rays and radioactive substances
.3 In administration of drugs and biologicals
.9 In other and unspecified prophylactic procedures

E936 Complications and misadventures in other non-therapeutic procedures CM

.0 In surgical procedures, excluding effects of anaesthetic management
.1 In anaesthesia
.9 In other and unspecified procedures

Late effects of accidental injury (E940-E949) CM

E940 Late effect of motor vehicle accident

E941 Late effect of other transport accident

E942 Late effect of accidental poisoning ES

E943 Late effect of accidental fall

E944 Late effect of accident caused by fire

E945 Late effect of accident due to natural and environmental factors ES

E946 Late effect of other accident

E947 Late effect of surgical operation

E948 Late effect of irradiation ES r

E949 Late effect of other surgical and medical procedures ES

Suicide and self-inflicted injury (E950-E959)

Categories E950-E959 include injuries in suicide and attempted suicide and other self-inflicted injuries when specified as intentional. Suicide said to be "due to" any disease is to be classified as suicide

E950 Suicide and self-inflicted poisoning by solid or liquid substances fm

As ICD E970, E971

E951 Suicide and self-inflicted poisoning by gases in domestic use

As ICD E972

E952 Suicide and self-inflicted poisoning by other gases

As ICD E973

E953 Suicide and self-inflicted injury by hanging and strangulation

As ICD E974

E954 Suicide and self-inflicted injury by submersion (drowning)

As ICD E975

E955 Suicide and self-inflicted injury by firearms and explosives

As ICD E976

E956 Suicide and self-inflicted injury by cutting and piercing instruments

As ICD E977

E957 Suicide and self-inflicted injury by jumping from high place

As ICD 978

E958 Suicide and self-inflicted injury by other and unspecified means

As ICD E979

E959 Late effect of suicide and self-inflicted injury

As ICD E963

Homicide and injury purposely inflicted by other persons (E960-E969)

Categories E960-E969 exclude injuries due to legal intervention (E970-E979) and to war operations (E990-E999)

E960 Fight, brawl, rape

Excludes strangulation (E963), submersion (E964), and injuries caused by weapons (E965, E966)

E961 Assault by corrosive or caustic substance, except poisoning

E962 Assault by poisoning

As ICD E950

E963 Assault by hanging and strangulation

E964 Assault by submersion (drowning)

E965 Assault by firearms and explosives

As ICD E981

E966 Assault by cutting and piercing instruments

As ICD E982

E967 Assault by pushing from high place

E968 Assault by other and unspecified means

E969 Late effect of injury purposely inflicted by other person

As ICD E964

Legal intervention (E970-E978)

Categories E970-E979 include injuries during legal action by police or other law-enforcing agents, including military on duty

E970 Injury due to legal intervention by firearms

E971 Injury due to legal intervention by explosives

E972 Injury due to legal intervention by gas

E973 Injury due to legal intervention by blunt object

E974 Injury due to legal intervention by cutting and piercing instruments

E975 Injury due to legal intervention by other specified means

E976 Injury due to legal intervention by unspecified means

E977 Late effect of injuries due to legal intervention

E978 Legal execution

Injury undetermined whether accidentally or purposely inflicted (E980-E989)

Categories E980–E989 are for use when it is not determined whether the injuries were accidental, suicidal or homicidal. They include self-inflicted injuries not specified either as accidental or as intentional

E980 Poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted

E981 Poisoning by gases in domestic use, undetermined whether accidentally or purposely inflicted

E982 Poisoning by other gases, undetermined whether accidentally or purposely inflicted

E983 Hanging and strangulation, undetermined whether accidentally or purposely inflicted

E984 Submersion (drowning), undetermined whether accidentally or purposely inflicted

E985 Injury by firearms and explosives, undetermined whether accidentally or purposely inflicted

E986 Injury by cutting and piercing instruments, undetermined whether accidentally or purposely inflicted

E987 Falling from high place, undetermined whether accidentally or purposely inflicted

E988 Injury by other and unspecified means, undetermined whether accidentally or purposely inflicted

E989 Late effect of injury, undetermined whether accidentally or purposely inflicted

Injury resulting from operations of war (E990-E999)

Categories E990–E999 include injuries caused by war and civil insurrections, but exclude accidents during training of military personnel, manufacture of war material and transport, unless attributable to enemy action. Injuries by explosion of bombs and mines placed during the war, if the explosion occurred after cessation of hostilities, are included in category E998

E990 Injury due to war operations by fires and conflagrations

E991 Injury due to war operations by bullets and fragments

E992 Injury due to war operations by explosion of marine weapons

E993 Injury due to war operations by other explosion

E994 Injury due to war operations by destruction of aircraft
As ICD E997

E995 Injury due to war operations by other and unspecified forms of conventional warfare
As ICD E998

E996 Injury due to war operations by nuclear weapons

E997 Injury due to war operations by other forms of unconventional warfare

E998 Injuries due to war operations but occurring after cessation of hostilities
As ICD E999

E999 Late effect of injury due to war operations
As ICD E965

N XVII. ACCIDENTS, POISONINGS AND VIOLENCE (NATURE OF INJURY, N800-N999)

FRACTURES (N800-N829) A,I

The following fourth digits are applicable for categories N800–N829 unless otherwise indicated:

.0 Closed fracture
.1 Open fracture
.9 Late effect

Fracture of skull, spine, and trunk (N800-N809)

N800 Fracture of vault of skull NS

N801 Fracture of base of skull NS

N802 Fracture of face bones NS
- .0 Nasal bones, closed NS
- .1 Nasal bones, open NS
- .2 Mandible, closed DE NS
- .3 Mandible, open DE NS
- .4 Other, closed DE NS
- .5 Other, open DE NS
- .9 Late effect, any facial bones DE NS

N803 Other and unqualified skull fractures NS

N804 Multiple fractures involving skull or face with other bones DE, NS

N805 Fracture and fracture dislocation of vertebral column without mention of spinal cord lesion
- .0 Cervical, closed NS
- .1 Cervical, open NS

.2 Dorsal or thoracic, closed NS
.3 Dorsal or thoracic, open NS
.4 Lumbar, closed NS
.5 Lumbar, open NS
.6 Sacrum and coccyx, closed NS
.7 Sacrum and coccyx, open NS
.8 Late effect, any vertebra NS

N806 Fracture and fracture dislocation of vertebral column with spinal cord lesion
Excludes: spinal cord lesion without fracture (N958) NS

.0 Cervical, closed NS
.1 Cervical, open NS
.2 Dorsal or thoracic, closed NS
.3 Dorsal or thoracic, open NS
.4 Lumbar, closed NS
.5 Lumbar, open NS
.6 Sacrum and coccyx, closed NS
.7 Sacrum and coccyx, open NS
.9 Late effect, any vertebra NS

N807 Fracture of rib(s), sternum and larynx

.0 Rib, closed
.1 Rib, open
.2 Sternum, closed
.3 Sternum, open
.4 Larynx, closed NS
.5 Larynx, open NS
.9 Late effect, rib(s), sternum or larynx

N808 Fracture of pelvis AM

N809 Multiple and ill-defined fractures of trunk AM

Fracture of upper limb (N810-N819)

N810 Fracture of clavicle AM

N811 Fracture of scapula AM

N812 Fracture of humerus AM

.0 Upper extremity, closed
.1 Upper extremity, open
.2 Shaft, or unspecified part, closed
.3 Shaft, or unspecified part, open
.4 Lower extremity, closed
.5 Lower extremity, open
.9 Late effect, any part

N813 Fracture of radius and ulna (either or both) AM

.0 Upper extremity or unspecified part, closed
.1 Upper extremity or unspecified part, open
.2 Shaft, closed
.3 Shaft, open
.4 Lower extremity, closed
.5 Lower extremity, open
.9 Late effect, any part

N814 Fracture of carpal bone(s) AM

N815 Fracture of metacarpal bone(s) AM

N816 Fracture of one or more phalanges of hand AM

N817 Multiple fractures of hand bones AM

N818 Other, multiple, and ill-defined fractures of upper limb AM

N819 Multiple fractures both upper limbs, and upper limb with rib(s) and sternum AM

Fracture of lower limb (N820-N829)

N820 Fracture of neck of femur AM

N821 Fracture of other and unspecified parts of femur AM

.0 Shaft or unspecified part, closed
.1 Shaft or unspecified part, open
.2 Lower extremity, closed
.3 Lower extremity, open
.9 Late effect, either part

N822 Fracture of patella AM

N823 Fracture of tibia and fibula (either or both)

.0 Upper extremity or unspecified part, closed
.1 Upper extremity or unspecified part, open
.2 Shaft, closed
.3 Shaft, open
.9 Late effect, either part

N824 Fracture of ankle AM

N825 Fracture of one or more tarsal and metatarsal bones AM

N826 Fracture of one or more phalanges of foot AM

N827 Other, multiple, and ill-defined fractures of lower limb AM

N828 Multiple fractures involving both lower limbs, lower with upper limb, and lower limb(s) with rib(s) and sternum AM

N829 Fracture of unspecified bones AM

DISLOCATION WITHOUT FRACTURE (N830-N839) AM

Excludes: congenital dislocation (755, 756)
fracture dislocation (N800-N829)

N862 Injury to other and unspecified intrathoracic organs CM HL
- .0 Without mention of open wound into thorax
- .1 With open wound into thorax
- .9 Late effect

N863 Injury to gastro-intestinal tract AM CM
- .0 Without mention of open wound into abdominal cavity AM
- .1 With open wound into abdominal cavity AM
- .9 Late effect AM

N864 Injury to liver AM CM
- .0 Without mention of open wound into abdominal cavity AM
- .1 With open wound into abdominal cavity AM
- .9 Late effect AM

N865 Injury to spleen AM CM
- .0 Without mention of open wound into abdominal cavity AM
- .1 With open wound into abdominal cavity AM
- .9 Late effect AM

N866 Injury to kidney AM CM
- .0 Without mention of open wound into abdominal cavity AM
- .1 With open wound into abdominal cavity AM
- .9 Late effect AM

N867 Injury to pelvic organs AM CM
- .0 Without mention of open wound into abdominal cavity
- .1 With open wound into abdominal cavity
- .9 Late effect

N868 Injury to other and unspecified intra-abdominal organs AM CM
- .0 Without mention of open wound into abdominal cavity
- .1 With open wound into abdominal cavity
- .9 Late effect

N869 Internal injury, unspecified or involving intrathoracic and intra-abdominal organs AM CM
- .0 Without mention of open wound into thoracic or abdominal cavity
- .1 With open wound into thoracic or abdominal cavity
- .9 Late effect

LACERATION AND OPEN WOUND (N870-N908)

Excludes: burn (N940-N949)
crushing without open wound (N920-N929)
foreign body entering through orifice (N930-N939)
late amputation stump complication (following surgical amputation) (N998.1)
superficial injury (N910-N918)
that incidental to:
cerebral injury (N850-N854)
dislocation (N830-N839)
fracture (N800-N829)
internal injury (N860-N869)
nerve injury (N950-N959)

Laceration and open wound of head, neck and trunk (N870-N878)

N870 Open wound of eye and orbit EY
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N871 Enucleation of eye EY

N872 Open wound of ear NS CM
- .0 Without mention of complication NS
- .1 Complicated NS
- .9 Late effect NS

N873 Other and unspecified laceration of head NS CM
- .0 Scalp without mention of complication NS
- .1 Scalp complicated NS
- .2 Nose without mention of complication NS
- .3 Nose complicated NS
- .7 Other face without mention of complication NS
- .8 Other face complicated NS
- .9 Late effect, nose, other face and scalp NS

N874 Open wound of neck NS CM
- .0 Without mention of complication NS
- .1 Complicated NS
- .9 Late effect NS

N875 Open wound of chest (wall) CM, HL
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N876 Open wound of back CM, HL
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N877 Open wound of buttock AM, CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N878 Open wound of genital organs (external) including traumatic amputation HD
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N879 Other, multiple and unspecified open wounds of head, neck and trunk AM CM
- .0 Other specified sites of trunk without mention of complication
- .1 Other specified sites of trunk complicated
- .7 Multiple and unspecified sites without mention of complication
- .8 Multiple and unspecified sites complicated
- .9 Late effect, other specified, multiple and unspecified sites

Laceration and open wound of upper limb (N880-N887)

N880 Open wound of shoulder and upper arm AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N881 Open wound of elbow, forearm and wrist AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N882 Open wound of hand(s) except finger(s) alone AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N883 Open wound of finger(s) AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N884 Multiple and unspecified open wound of upper limb AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N885 Traumatic amputation of thumb (complete) (partial)
- .0 Without mention of complication AM CM
- .1 Complicated
- .9 Late effect

N886 Traumatic amputation of other finger(s) (complete) (partial) AM CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N887 Traumatic amputation of arm and hand (complete) (partial) AM CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

Laceration and open wound of lower limbs (N890-N897)

N890 Open wound of hip and thigh AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N891 Open wound of knee, leg (except thigh) and ankle AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N892 Open wound of foot except toe(s) alone AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N893 Open wound of toe(s) AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N894 Multiple and unspecified open wound of lower limb AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N895 Traumatic amputation of toe(s) (complete) (partial)
- .0 Without mention of complication AM CM
- .1 Complicated
- .9 Late effect

N896 Traumatic amputation of foot (complete) (partial) AM CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

N897 Traumatic amputation of leg(s) (complete) (partial) AM CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

Laceration and open wounds of multiple location (N900-N909)

N900 Multiple open wounds of both upper limbs AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N901 Multiple open wounds of both lower limbs AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N902 Multiple open wounds of both upper and lower limb(s) AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N903 Multiple open wounds of both hands AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N904 Multiple open wounds of both head and limb(s) NS AM CM
- .0 Without mention of complication NS
- .1 Complicated NS
- .2 With tendon involvement NS
- .9 Late effect NS

N905 Multiple open wounds of both head and trunk AM CM NS
- .0 Without mention of complication NS
- .1 Complicated NS
- .2 With tendon involvement NS
- .9 Late effect NS

N906 Multiple open wounds of both trunk and limb(s) AM CM
- .0 Without mention of complication
- .1 Complicated
- .2 With tendon involvement
- .9 Late effect

N907 Multiple open wounds of face and other sites AM CM
- .0 Without mention of complication
- 1 Complicated
- .2 With tendon involvement
- .9 Late effect

N908 Multiple open wounds of other and unspecified location AM CM
- .0 Without mention of complication
- .1 Complicated
- .9 Late effect

SUPERFICIAL INJURY (N910-N918)

Excludes: burn (N940-N949)
contusion (N920-N929)
insect bite, venomous (N989.4)

The following fourth digits are applicable to categories N910-N918 unless otherwise indicated:
- .0 Without mention of infection
- .1 Infected

N910 Superficial injury of face, neck, scalp CM NS

N911 Superficial injury of trunk AM CM

N912 Superficial injury of shoulder and upper arm AM CM

N913 Superficial injury of elbow, forearm and wrist AM CM

N914 Superficial injury of hand(s) except finger(s) alone AM CM

N915 Superficial injury of finger(s) AM CM

N916 Superficial injury of hip, thigh, leg and ankle AM CM

N917 Superficial injury of foot and toe(s) AM CM

N918 Superficial injury of other, multiple and unspecified sites AM CM

CONTUSION AND CRUSHING WITH INTACT SKIN SURFACE (N920-N929)

Excludes: concussion (N850, N860-N869)
that incidental to:
cerebral injury (N850-N854)
dislocation (N830-N839)
fracture (N800-N829)
internal injury (N860-N869)
nerve injury (N950-N959)

AM CM

N920 Contusion of face, scalp, and neck except eye(s) NS

N921 Contusion of eye and orbit CM EY

N922 Contusion of trunk AM CM

N923 Contusion of shoulder and upper arm AM, CM

N924 Contusion of elbow, forearm and wrist AM, CM

N925 Contusion of hand(s) except finger(s) alone AM, CM

N926 Contusion of finger(s) AM, CM

N927 Contusion of hip, thigh, leg and ankle AM, CM

N928 Contusion of foot and toe(s) AM, CM

N929 Contusion of other, multiple and unspecified sites

FOREIGN BODY ENTERING THROUGH ORIFICE (N930-N939)

Excludes: foreign body in open wound (N800-N839, N851-N908)
foreign body inadvertently left in operation wound (N998.6)

N930 Foreign body in eye and adnexa EY CM

N931 Foreign body in ear CM NS

N932 Foreign body in nose CM NS

N933 Foreign body in pharynx and larynx CM NS

N934 Foreign body in bronchus and lung CM HL

N935 Foreign body in mouth, oesophagus, stomach AM CM

N936 Intestine and colon AM CM

N937 Anus and rectum AM CM

N938 Digestive system, unspecified AM CM

N939 Foreign body in genito-urinary tract AM CM

BURN (N940-N949)

Excludes: blister (N910-N918)
burn due to swallowing corrosive substance (N983)
effect of:
electricity (N995.6)
lightning (N994.0)
radiation other than burn (N990)

The following fourth digits are applicable to categories N940-N949 unless otherwise indicated:

.0 Burn, unspecified degree, without mention of complication
.1 Burn, first degree, without mention of complication
.2 Burn, second degree, without mention of complication
.3 Burn, third degree, without mention of complication
.8 Complicated burn
.9 Late effect

N940 Burn confined to eye EY, CM

N941 Burn confined to face, head and neck CM, AM

N942 Burn confined to trunk AM, CM

N943 Burn confined to upper limb except wrist and hand AM, CM

N944 Burn confined to wrist(s) and hand(s) AM, CM

N945 Burn confined to lower limb(s) AM, CM

N946 Burn involving face, head and neck with limb(s) AM, CM

N947 Burn involving trunk with limb(s) AM, CM

N948 Burn involving face, head and neck with trunk and limb(s) AM, CM

N949 Burn involving other and unspecified parts AM CM

INJURY TO NERVES AND SPINAL CORD (N950-N959)

The following fourth digits are applicable for categories N950-N959 unless otherwise indicated:

.0 Injury to nerve, without mention of open wound
.1 Injury to nerve, with open wound
.9 Late effect

N950 Injury to optic nerve(s) CM, EY

N951 Injury to other cranial nerve(s) CM NS

N952 Injury to nerve(s) in upper arm CM NS

N953 Injury to nerve(s) in forearm CM NS

N954 Injury to nerve(s) in wrist and hand CM NS

N955 Injury to nerve(s) in thigh CM NS

N956 Injury to nerve(s) in lower leg AM, CM, NS

N957 Injury to nerve(s) in ankle and foot AM, CM NS

N958 Spinal cord lesion without evidence of spinal bone injury CM NS

- .0 Cervical without mention of open wound NS
- .1 Cervical with open wound NS
- .2 Dorsal or thoracic without mention of open wound NS
- .3 Dorsal or thoracic with open wound NS
- .4 Lumbar without mention of open wound NS
- .5 Lumbar with open wound NS
- .7 Sacral without mention of open wound NS
- .8 Sacral with open wound NS
- .9 Late effect, any part NS

N959 Other nerve injury including nerve injury in several parts CM NS

- .0 Cervical sympathetic without mention of open wound NS
- .1 Cervical sympathetic with open wound NS
- .6 Other and in several parts without mention of open wound NS
- .7 Other and in several parts with open wound NS
- .9 Late effect, either NS

ADVERSE EFFECTS OF CHEMICAL SUBSTANCES (N960-N989)

Excludes: dermatitis due to contact (692)
external chemical burns (N940-N949)

Adverse effect of medicinal agents (N960-N979)

N960 Adverse effect of antibiotics AM, NS GM, AI

- .0 Penicillin, any AM
- .1 Antifungal antibiotics
- .2 Chloramphenicol AM
- .3 Erythromycins
- .4 Streptomycins AM
- .5 Tetracyclines
- .9 Other antibiotics

N961 Adverse effect of other anti-infectives AM, GM, AI

- .0 Sulfonamides AM, ES
- .1 Arsenic anti-infectives ES
- .2 Silver and its compounds AM, ES
- .3 Quinoline and hydroxyquinoline derivatives
- .9 Other anti-infectives ES

N962 Adverse effect of hormones and synthetic substitutes AM CM HD

- .0 Adrenals AM
- .1 Androgens and anabolic congeners AM
- .2 Oestrogens AM, ES, NS
- .3 Insulins and antidiabetic agents AM
- .4 Anterior pituitary extracts AM, NS
- .5 Posterior pituitary extracts AM, NS
- .6 Progestogens AM, ES
- .7 Thyroid and thyroid derivatives AM
- .8 Antithyroid agents AM
- .9 Other hormones and synthetic substitutes AM, ES

N963 Adverse effect of primarily systemic agents AM GM

- .0 Antihistaminic and anti-emetic drugs AM
- .1 Antineoplastic agents
- .2 Acidifying agents AM
- .3 Alkalinizing agents AM
- .4 Other electrolytic, caloric and water balance agents AM
- .5 Enzymes
- .6 Vitamins
- .9 Systemic agents, not elsewhere classified AM

N964 Adverse effect of agents primarily affecting blood constituents AM GM HI

- .0 Iron and its compounds AM
- .1 Liver and liver extracts AM
- .2 Anticoagulants AM, NS
- .3 Vitamin K products AM
- .4 Other coagulants AM
- .9 Other agents primarily affecting blood constituents AM

N965 Adverse effect of analgesics and antipyretics AM, ES GM

- .0 Opiates and synthetic analogs
- .1 Salicylates and congeners AM, ES
- .2 Cinchophen and congeners
- .3 Colchicine ES
- .4 Aniline derivatives AM ES
- .5 Other coal-tar derivatives ES
- .9 Other analgesics and antipyretics AM ES

N966 Adverse effect of anticonvulsants ES, NS GM

- .0 Dione derivatives NS
- .1 Hydantoin derivatives ES NS
- .9 Other anticonvulsants NS

N967 Adverse effect of other sedatives and hypnotics AM, ES, NS GM

- .0 Barbiturates AM, ES, NS
- .1 Chloral hydrate NS
- .2 Paraldehyde NS
- .3 Bromides ES NS
- .9 Other sedatives and hypnotics NS

N968 Adverse effect of other central nervous system depressants ES, NS GM

- .0 Central nervous system muscle relaxants NS
- .1 Anaesthetic gases ES NS
- .9 Other NS

N969 Adverse effect of local anaesthetics GM NS

N970 Adverse effect of psychotherapeutics ES, NS
- .0 Antidepressants ES, NS
- .1 Tranquilizers ES, NS
- .9 Other psychotherapeutic agents

N971 Adverse effect of other central nervous system stimulants GM NS

N972 Adverse effect of agents primarily affecting the autonomic nervous system GM ES, NS
- .0 Parasympathomimetics (cholinergics) ES, NS
- .1 Parasympatholytics (anticholinergics) NS
- .2 Sympathomimetics (adrenergics) NS
- .3 Autonomic nervous system relaxants NS
- .9 Other NS

N973 Adverse effect of agents primarily affecting cardiovascular system GM ES HL
- .0 Cardiac depressants
- .3 Cardiac tonics
- .4 Cholesterol lowering agents ES
- .5 Ganglionic blocking agents NS
- .6 Vasodilators
- .7 Other hypotensive agents
- .8 Sclerosing agents
- .9 Other

N974 Adverse effect of drugs primarily affecting gastro-intestinal system AM GM
- .0 Antacids and antidiarrheal agents AM
- .1 Intestinal irritant cathartics AM
- .2 Emollient cathartics AM
- .3 Saline cathartics AM
- .4 Faecal softeners AM
- .5 Other cathartics AM
- .6 Emetics AM
- .9 Other AM

N975 Adverse effect of diuretics AM, ES GM
- .0 Mercurial diuretics ES
- .1 Xanthine derivatives
- .2 Carbonic acid anhydrase inhibitors
- .3 Saluretics
- .9 Other diuretic agents

N976 Adverse effect of agents acting directly upon musculoskeletal system GM AM, NS
- .0 Oxytocics NS
- .1 Spasmolytics NS
- .2 Gold and its compounds NS
- .9 Other NS

N977 Adverse effect of other and unspecified drugs GM
- .0 External medicinals, not elsewhere classified
- .1 Pharmaceutical dyes, not elsewhere classified
- .2 Diagnostic agents
- .8 Other specified drugs, not elsewhere classified
- .9 Drugs, unspecified

N978 Adverse effect of two or more medicinal agents in specified combinations GM, ES, NS (exc. 1.1)
- .0 Opium derivatives with barbiturates or tranquilizers NS
- .1 Salicylates with decongestants, antihistamines, etc.
- .2 Barbiturates with salicylates or other non-addicting analgesics NS
- .3 Non-barbiturate sedatives with salicylates or other non-addicting analgesics NS
- .4 Psychopharmacologic agents with barbiturates

N979 Alcohol in combination with specified medicinal agents AM,
- .0 Opium derivatives
- .1 Barbiturates
- .2 Non-barbiturate sedatives
- .3 Antihistamines
- .4 Psychopharmacologic agents

Toxic effect of substances chiefly non-medicinal as to source (N980-N989)

N980 Toxic effect of alcohol AM, NS
- .0 Ethyl alcohol NS
- .1 Methyl alcohol NS
- .2 Isopropyl alcohol NS
- .9 Other NS

N981 Toxic effect of petroleum products ES
- .0 Kerosene ES
- .1 Gasoline ES
- .2 Petroleum naphtha ES
- .9 Other ES

N982 Toxic effect of industrial solvents AM, ES
Excludes petroleum products N981
- .0 Benzine and homologues ES
- .1 Carbon tetrachloride ES
- .2 Carbon disulfide ES
- .9 Other ES

N983 Toxic effect of corrosive aromatics, acids and caustic alkalis ES
- .0 Corrosive aromatics
- .1 Acids
- .2 Caustic alkalis
- .9 Caustic NOS

N984 Toxic effect of lead and its compounds (including fumes) AM, ES

N985 Toxic effect of other metals chiefly non-medicinal as to source AM, ES
- .0 Mercury and its compounds ES
- .1 Arsenic and its compounds ES
- .2 Manganese and its compounds ES
- .3 Beryllium and its compounds ES
- .9 Other ES

N986 Toxic effect of carbon monoxide ES, NS

N987 Toxic effect of other gases, fumes or vapours ES
- .0 Liquefied petroleum gases (butane, propane) ES
- .1 Other hydrocarbon gas (methane, water-gas, acetylene) ES
- .2 Nitrogen dioxide ES
- .3 Sulfur dioxide ES
- .4 Freon ES
- .9 Other ES

N988 Toxic effect of noxious food-stuffs CM, AI, ES
- .0 Shellfish
- .1 Mushrooms ES
- .2 Other plants used as food
- .9 Other

N989 Toxic effect of other substances chiefly non-medicinal as to source ES
- .0 Cyanide (including gas)
- .1 Strychnine
- .2 Chlorinated pesticides ES
- .3 Other pesticides ES
- .4 Venom
- .5 Soaps and detergents ES
- .9 Other ES

OTHER ADVERSE EFFECTS (N990-N999)

N990 Effect of radiation AM, ES, CA, GM
Excludes: dermatitis due to radiation (692.7)
sunburn (692.8)
burns (N940-N949)
- .0 Effect of radioactivity, neither diagnostic nor therapeutic ES
- .1 Adverse effect of diagnostic X-ray
- .2 Adverse effect of radioactive isotope or tracer substance
- .3 Other radiation ES
- .4 Adverse effect of radiotherapy, external
- .5 Adverse effect of radiotherapy, internal AM
- .6 Adverse effect of other radiotherapy
- .9 Unspecified radiation

N991 Effects of reduced temperature GM
- .0 Frostbite of face
- .1 Frostbite of hand
- .2 Frostbite of foot
- .3 Frostbite of other and unspecified sites
- .4 Immersion foot
- .9 Other

N992 Effects of heat AM GM
Excludes sunburn (692.8)
- .0 Heat stroke (heat pyrexia) NS
- .1 Heat syncope NS
- .2 Heat cramps
- .3 Heat exhaustion, anhydrous
- .4 Heat exhaustion, salt and/or water depletion AM
- .5 Heat exhaustion, NOS
- .6 Heat fatigue, transient
- .7 Heat oedema
- .9 Other heat effects

N993 Effects of air pressure GM, HL
- .0 Barotrauma, otitic
- .1 Barotrauma, sinus
- .2 Other and unspecified effects of high altitude
- .3 Caisson disease

N994 Effects of exposure and deprivation CM
- .0 Effects of lightning NS
- .1 Drowning and non-fatal submersion
- .2 Effects of hunger EE
- .3 Effects of thirst
- .9 Other effects of exposure, not elsewhere classified

N995 Other general effects of external causes GM
- .0 Effects of excessive exertion
- .1 Motion (sea) sickness
- .2 Car and train sickness
- .3 Air sickness
- .4 Other motion (travel) sickness
- .5 Asphyxiation and strangulation
- .6 Electrocution and non-fatal effects of electric current
- .9 Other general effects of external causes not elsewhere classified

N996 Certain early complications of trauma AM, GM, HL
- .0 Air embolism
- .1 Fat embolism NS
- .2 Secondary and recurrent haemorrhage

.3 Traumatic aneurysm and arterial injury
.4 Nerve injury complicating bone injury (fracture) NS
.5 Local infection of wound
.6 "Shock" AM
.7 Traumatic anuria (crush syndrome) AM
.8 Volkmann's ischemic contracture
.9 Other early complications of trauma

N997 Injury other and unspecified GM, AM
.0 Face and neck, except eyes NS
.1 Trunk
.2 Shoulder and upper arm
.3 Elbow, forearm and wrist
.4 Hand except finger(s)
.5 Finger(s)
.6 Hip and thigh
.7 Knee, leg, ankle and foot
.8 Other specified site, including multiple
.9 Unspecified site

N998 Complications of surgical procedures AM GM
.0 Reaction to lumbar or spinal puncture NS
.1 Late amputation stump complication
.2 Post-operative shock AM
.3 Post-operative haemorrhage or haematoma AM
.4 Accidental puncture or laceration
.5 Disruption of operation wound
.6 Foreign body inadvertently left in operation wound
.7 Post-operative wound infection
.8 Persistent post-operative fistula
.9 Other complications of surgical procedures

N999 Other complications of medical care AM
.0 Generalized vaccinia AI
.1 Post-immunization encephalitis NS
.2 Serum hepatitis AI HL
.3 Other infection AI
.4 Anaphylactic shock AM AI
.5 Other serum reaction AI
.6 ABO incompatibility reaction AI, HL
.7 Rh incompatibility reaction AI, HL
.8 Other transfusion reaction HL
.9 Other

Excludes: contact dermatitis due to drugs (692.3)
adverse effects due to drugs (N960-N979)

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February 3, 1977

NATIONAL INSTITUTES OF HEALTH

1978 Program Areas of Special Concern
(In thousands of dollars)

Appropriation/Program	1976 Actual	1977 Appropriation	1978 Congressional Justification
National Cancer Institute			
Nutrition	$5,385	$7,389	$7,640
Cancer Task Forces	29,589	30,835	30,692
Smoking and Health	9,500	10,000	10,000
Cancer Research Centers	128,411	138,553	139,569
Cancer Control	56,471	60,101	60,835
Cancer Construction	25,496	22,873	12,895
Combined Treatment Modalities	57,087	60,775	61,775
Environmental Carcinogenesis	134,666	146,450	148,950
Virus Cancer Research	102,026	98,836	97,756
Immunology Research	71,336	77,216	78,326
Other Cancer Research 1/	110,270	128,399	138,851
Research Manpower Development	30,311	33,510	31,647
Subtotal	760,548	814,937	818,936
Training Programs	(18,160)	(20,000)	(18,163)
Pap Testing	(9,695)	(11,500)	(11,000)
Breast Cancer Detection and Treatment	(29,000)	(34,700)	(33,200)
Diabetes	(235)	(250)	(250)
National Heart, Lung, and Blood Institute			
Hypertension	52,250	56,059	57,045
Arteriosclerosis	69,508	74,546	75,861
Coronary Heart Disease	45,215	48,827	49,681
Pulmonary Disease	58,984	63,466	64,585
Blood Resources and Thrombosis	32,296	34,903	35,387
Hemophilia	7,500	8,046	8,188
Cooley's Anemia	3,000	3,500	3,700
Sickle Cell Disease	18,031	19,000	19,335
Cerebrovascular and Pheripheral Vascular Diseases	10,419	11,252	11,449
Arrhythmias and Heart Failure and Shock	39,317	42,458	43,201
Congenital and Rheumatic Heart Disease, Cardiomyopathy and Infections	13,368	14,436	14,689
Circulatory Assistance	18,676	20,168	20,521
Subtotal	368,564	396,661	403,642
Training Programs	(20,559)	(21,988)	(19,954)
Diabetes	(7,000)	(11,900)	(12,400)

1/ Includes research in the areas of Epidemiology, Tumor Biology, Diagnostic Research, and Preclinical Treatment Research and Rehabilitation.

Appropriation/Program	1976 Actual	1977 Appropriation	1978 Congressional Justification
National Institute of Dental Research			
Caries	$12,193	$13,827	$14,495
Periodontal Diseases	11,321	12,786	13,376
Restorative Materials	3,048	3,387	3,478
Craniofacial Anomalies	9,144	9,702	9,956
Pain Control and Behavioral Studies	2,613	2,509	2,899
Soft Tissue, Stomatology and Nutrition	5,225	6,162	6,577
Dental Research Institutes	7,146	7,200	7,200
Subtotal	50,690	55,573	57,981
Training Programs	(5,059)	(4,131)	(2,974)
Diabetes	(400)	(600)	(600)
National Institute of Arthritis, Metabolism, and Digestive Diseases			
Cystic Fibrosis	2,050	2,100	2,100
Arthritis	17,709	22,389	25,761
Cooley's Anemia	1,311	1,188	1,251
Diabetes	14,538	35,727	34,012
Digestive Diseases/Gastroenterology	24,725	27,588	28,061
Kidney Disease	18,848	23,064	24,340
(Artificial Kidney)	(2,734)	(5,420)	(5,450)
Nutrition	9,763	9,538	10,304
Psoriasis	1,542	1,893	1,986
Endocrinology	23,423	23,564	23,760
Metabolism (except Cystic Fibrosis)	31,126	31,478	32,178
Hematology (except Cooley's Anemia)	10,438	10,476	11,254
Dermatology (except Psoriasis)	3,036	3,717	4,298
Orthopedics	8,028	7,771	8,976
Direct Operations and Program Management	8,396	8,507	8,680
Subtotal	174,933	209,000	216,961
Training Programs	(1,879)	(9,646)	(11,777)
National Institute of Neurological and Communicative Disorders and Stroke			
Stroke	9,965	10,869	11,285
Epilepsy	12,960	14,135	14,676
Trauma, Spinal Cord & Head Injury	10,304	11,320	11,754
(Regeneration)	(1,970)	(2,164)	(2,247)
Multiple Sclerosis	7,085	10,000	10,383
Fundamental Neurosciences Research	16,278	17,762	18,442
Communicative Disorders Research	20,360	22,208	23,059
Neurological Disorders Research	63,442	69,206	71,862
Diabetes (Diabetic Neuropathy)	(1,606)	(1,860)	(1,931)
Subtotal	140,394	155,500	161,461
Training Programs	(7,709)	(7,100)	(6,572)
Total Multiple Sclerosis Related Res.	(9,590)	(11,060)	(11,484)

Appropriation/Program	1976 Actual	1977 Appropriation	1978 Congressional Justification
National Institute of Allergy and Infectious Diseases			
Asthma and Allergic Disease Centers Program	$3,456	$3,832	$4,181
Hepatitis	2,677	3,023	3,133
Influenza and Other Respiratory Infections	6,203	7,503	8,203
Sexually Transmitted Diseases	4,324	5,198	6,098
Hospital Associated Infections	3,114	3,434	3,584
Nucleic Acid Recombinants	2,257	4,056	4,913
Tropical Diseases	5,413	5,913	6,613
Meningitis	443	513	663
The Immune System and its Disorders	37,442	40,765	44,628
(Clinical Immunology & Transplanation)	(12,334)	(13,346)	(14,551)
Fundamental Research Related to Immunologic, Infectious & Allergic Diseases	60,233	66,763	71,426
Subtotal	125,562	141,000	153,442
Training Programs	(7,809)	(8,081)	(6,481)
National Institute of General Medical Sciences			
Pharmacology-Toxicology	25,940	27,904	27,913
Biomedical Engineering	18,688	17,465	17,612
Trauma Research Centers	2,079	2,900	2,900
Burn Research Centers	607	1,750	1,950
Genetics	57,786	63,583	71,561
(Cooley's Anemia/Sickle Cell Disease)	(400)	(450)	(450)
Cellular and Molecular Basis of Disease	65,231	71,820	78,867
Minority Access to Research Careers (MARC)	268	1,783	2,211
Clinical and Physiological Sciences	16,346	17,795	16,882
(Diabetes)	(775)	(1,000)	(1,000)
Subtotal	186,945	205,000	219,896
Training Programs	(40,845)	(43,851)	(39,630)
National Institute of Child Health and Human Development			
Population	56,211	59,481	66,444
Pregnancy and Infancy	28,298	34,686	36,429
(Sudden Infant Death Syndrome)	(7,445)	(7,700)	(7,700)
Growth and Development	27,417	26,989	28,021
Mental Retardation	23,946	24,387	24,867
Subtotal	135,872	145,543	155,761
Training Programs	(9,508)	(9,745)	(9,202)
Diabetes	(2,230)	(4,619)	(4,750)
Nutrition	(12,838)	(13,528)	(13,950)

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Appropriation/Program	1976 Actual	1977 Appropriation	1978 Congressional Justification
National Institute on Aging			
Clinical and Comparative Physiology of Aging	$6,122	$9,825	$11,240
Molecular and Cellular Basis of Aging.	8,913	12,606	14,440
Behavioral and Societal Aspects of Aging	3,909	6,822	7,860
Development of Animal Models for Aging Research	277	747	960
Subtotal	19,221	30,000	34,500
Training Programs	(1,750)	(2,200)	(1,990)
Diabetes	(450)	(563)	(575)
Nutrition	(540)	(1,318)	(1,400)
Senility	(857)	(1,500)	(1,700)
National Eye Institute			
Retinal and Choroidal Diseases	13,432	19,933	19,951
Corneal Diseases	8,359	9,156	8,631
Diabetic Retinopathy	5,008	6,627	6,563
Cataract	5,087	6,702	6,924
Glaucoma	7,856	9,262	10,507
Sensory-Motor Disorders and Rehabilitation	10,357	12,320	12,405
Subtotal	50,099	64,000	64,981
Training Programs	(4,642)	(4,640)	(4,143)
Diabetes	(5,246)	(9,065)	(9,065)
National Institute of Environmental Health Sciences			
Environmental Health Sciences Centers.	5,287	7,210	8,331
Marine Biomedical Research Centers	---	---	600
Environmental Mutagenesis and Reproductive Toxicology (Environmentally caused genetic and birth defects)	7,750	10,407	12,858
(Mutagenicity Screening)	(--)	(600)	(1,000)
Etiology of Environmental Diseases and Disorders (Causes of environmental diseases and disorders)	9,838	12,324	13,680
Environmental Pharmacology and Toxicology (Mechanisms of action of environmental agents)	11,593	16,225	18,477
(Toxicity Bioassay)	(--)	(600)	(1,000)
Environmental Pathogenesis (Development of environmental diseases and disorders)	2,319	2,975	4,154
Subtotal	36,787	49,141	58,100
Training Programs	(1,745)	(2,243)	(1,485)
Asbestos	(1,700)	(1,860)	(2,200)

Appropriation/Program	1976 Actual	1977 Appropriation	1978 Congressional Justification
Research Resources			
Clinical Research	$43,660	$48,444	$57,463
Biotechnology Research	12,547	13,185	13,383
Laboratory Animal Sciences and Primate Research	21,315	22,696	20,866
Minority Biomedical Support	7,782	9,993	9,147
Biomedical Research Support	43,929	42,060	41,000
Chemical/Biological Information-Handling Research	1,023	1,122	1,215
Subtotal	130,256	137,500	143,074
Training Programs	(334)	(515)	(515)
Cooley's Amenia	(300)	(330)	(345)
Nutrition	(5,553)	(6,158)	(7,078)
Diabetes	(6,075)	(6,355)	(7,378)
TOTAL	2,179,871	2,403,855	2,488,735

NATIONAL INSTITUTES OF HEALTH

Cystic Fibrosis
(In thousands)

	1977	1978
NHLBI	$1,600	$1,600
NIAMDD	2,100	2,100
NIAID	1,150	1,250
NICHD	70	70
DRR	113	132
Total	5,033	5,152

Diabetes

NHLBI	11,900	12,400
NIAMDD	39,826	37,907
NICHD	4,618	4,746
NEI	9,0 5	9,065
NINCDS	1,860	2,088
DRR	6,355	7,378
Other	2,413	2,425
Total	76,038	76,009

Recombinant DNA Activities

NCI	8,078	8,041
NHLBI	333	394
NIDR	90	90
NIAMDD	1,452	1,723
NIAID	4,850	5,800
NIGMS	2,677	3,711
NICHD	451	468
DRR	92	--
FIC	240	281
DRG	30	30
DRS	26	33
Total	18,319	20,571

NATIONAL INSTITUTES OF HEALTH

Nutrition

NCI	7,389	7,640
NHLBI	24,300	24,500
NIDR	1,500	1,600
NIAMDD	9,538	10,304
NINCDS	1,142	1,108
NIAID	--	150
NIGMS	1,500	1,900
NICHD	13,500	13,950
NIA	1,318	1,400
NEI	1,533	1,631
NIEHS	2,090	2,270
DRR	8,389	9,820
Total	72,199	76,273

Arthritis
(In thousands)

	1977	1978
NCI	$523	$523
NHLBI	815	815
NIDR	647	647
NIAMDD	24,677	28,743
NINCDS	352	352
NIAID	1,108	1,108
NIGMS	1,402	1,402
NICHD	472	472
NIA	457	457
Total	30,453	34,519

EARMARKS

Mr. MICHEL. Does it concern you when Congress earmarks certain amounts for certain diseases as say was done for diabetes? Do you think it is wise for Congress to get into this business of earmarking?

Answer. Unquestionably, Congress has a legitimate and important role in establishing policy and priorities, but detailed earmarking may have unintended effects on other programs. For example, in order to meet the congressional mandates in the area of diabetes, the National Institute of Arthritis, Metabolism and Digestive Diseases has had to divert needed resources from its other important programs. Restricting the utilization of funds through the process of earmarking can also limit our flexibility to take advantage of research breakthroughs. The other side of that coin is that should earmarking occur in an area which is not yet ready for exploitation, the result may be an ineffective use of the limited resources available.

Mr. MICHEL. Much of the allocation for research in various disease areas seems more often than not to be based on the amount of pressure brought to bear by various interest groups. Do you think that is a proper way to determine spending priorities in this area?

Answer. The earmarkings for certain diseases do appear to coincide with the strength of the pressure group. It is important and even necessary that the public participate in the legislative process, although spending priorities should be determined more broadly by need and opportunity rather than by pressure.

Mr. MICHEL. Are you personally satisfied with the current spending priorities at NIH, as they have generally been set by Congress?

Anwer. I have no strong dissatisfaction with the priorities Congress has set. I do believe, however, the Director of NIH needs authority to make limited adjustments between appropriations during the operating year in order to adjust to changing requirements and opportunities.

RESEARCH BALANCE

Mr. MICHEL. The Cancer and the Heart and Lung Institutes are currently receiving half of the NIH research funds. We are continually receiving complaints from various proponents of research in other disease areas that the amounts being given Cancer and Heart and Lung are shortchanging the other areas, and that we need to strike a better balance. Do you think they have a valid complaint?

Answer. It is difficult for me to ascertain whether the Heart and/or Cancer Institutes are receiving their increases at the expense of other appropriations. I certainly hope this is not true. It is important for us to maintain some balance in the future, because biomedical research is highly interrelated and it is impossible to predict where new breakthroughs might occur.

FUNDING PRIORITIES

Mr. MICHEL. Are we funding lower priority research in the Cancer and Heart and Lung areas, because they are receiving substantial funding, than in the other disease areas?

Answer. I suppose the immediate inclination is to think that the more money—the higher would be the priority score funded and a resulting funding of lower priority projects. In actual operation, the total number and the number of quality applications increases as the funds increase. The caliber of the grants funded by the National Cancer Institute and the National Heart, Lung, and Blood Institute is as high as other institutes with substantially less money.

DISABILITY PAYMENTS

Mr. MICHEL. I read in one of your publications that the Government is spending $1 billion in disability payments to individuals crippled by arthritis during this decade. Do you have any comparable figures for NIH as a whole for the other disease areas?

Answer. I have checked with the Social Security Agency as well as the institutes of NIH and they are unable to identify comparable figures for other disease areas.

Indirect Costs

Mr. Michel. How much of the total NIH funding during the current fiscal year is being spent for indirect costs?

Answer. Of the total amount for regular research grants of nearly $1 billion we estimate that approximately $270 million will be spent on indirect costs.

Mr. Michel. What is the present indirect cost rate for NIH, both as a percentage of overall costs and of direct costs?

Answer. The indirect cost rate varies from one institution to another, and from mechanism to mechanism. In 1976, the overall indirect cost rate for NIH was 27 percent when computed as a percent of total costs, and about 37 percent when computed as a percent of direct costs.

Mr. Michel. I understand that research grants given out by private groups and foundations normally have a substantially lower indirect cost rate than the Federal Government. Why is that?

Answer. Indirect cost rates for grantee institutions are negotiated by DHEW for all its agencies, including NIH. We do not have direct access to information about the indirect cost payment policies of private groups or foundations which award grants. We have discussed this question with officials of two major universities, and must base our response upon the information they provided.

There is no single, standard method for determining which costs of research shall be direct costs and which indirect. For example, an institution may receive indirect costs for Federal programs at a rate of 36 percent of salaries and wages. For non-Federal grants, it may recover indirect costs at a rate of 25 percent of total direct costs. In both cases, the proportion of the total grant which is paid to cover indirect or overhead costs to the university is approximately the same. Most institutions cannot afford to accept grants unless total indirect costs are paid.

Some institutions, however, may be able to accept grants which do not pay full indirect costs, since they may be able through endowments to absorb the difference. In these cases, which are few, the indirect cost rate for the non-Federal grants may actually be lower.

Salaries of Investigators

Mr. Michel. Last year you told us that a study was being conducted on the question of whether universities are making raises, promotions, et cetera, for professors dependent on their obtaining research grants. Has that study been completed, and, if so, what does it show?

Answer. The Rand Corp. has been studying the effect of Federal biomedical research programs on academic medical centers. A report was issued in March 1976, on the relationships between NIH funding and faculty salary levels. This study compared salaries in the aggregate for a given academic level, rather than examining factors which might affect the salaries of particular individuals.

The study shows that, in departments with higher levels of NIH funding, faculty salaries tend to be lower, particularly for the junior faculty. The salaries of chairmen of these departments, however, show a positive relationship to the amount of NIH funding, implying that they may be paid according to their success in managing their departments and competing for grants.

The results of the study suggest that raises or promotions for professor are not solely dependent upon their obtaining research grants. This may vary from one institution to another, of course.

Mr. Michel. Last year you told us that 62.3 percent of NIH research grants was being used to pay salaries, but you could not tell us what the average salary paid to principal investigators was. Isn't this formation normally included as part of the grant application, and isn't it fed into your computers? Can your provide us with the information this year?

Answer. The salaries of individuals are considered to be confidential, and no data on salaries paid to principal investigators are captured in the NIH information system for grants. The only data captured in the system are the totals awarded for personnel for each grant, including fringe benefits as well as direct salary costs.

Top 20 Grantee Institutions

Mr. Michel. Last year you provided us with a list of the top 20 institutions in terms of total NIH research funds received, and the totals they received. Would you update that for this year and include the indirect cost rate for each school as well. This rate should be consistent for all and should be as a percentage of direct costs. If this requires an estimate or projection for some schools, that is all right because I want a consistent figure for all of them. Additionally, I would like in another column the total indirect cost monies going to each school.

Answer. I would be happy to provide this information for the record. It should be noted that the indirect cost rate expressed on this table is not the same as the negotiated indirect cost rate used to determine the amount of indirect costs to be paid to a given institution.

[The information follows:]

FY 1976 (TWELVE MONTH) NIH RESEARCH GRANTS* BY INSTITUTION

FOR TOP TWENTY RESEARCH GRANT RECIPIENTS

INSTITUTION	DIRECT COST	INDIRECT COST	TOTAL COST	RATE**	RATE***
HARVARD UNIVERSITY	19,823,401	8,923,749	28,747,150	45.0	31.0
JOHNS HOPKINS UNIVERSITY	20,180,122	8,121,261	28,301,383	40.2	28.7
UNIVERSITY OF CALIFORNIA, LOS ANGELES	20,463,449	5,968,900	26,432,349	29.2	21.6
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO	19,841,674	5,659,235	25,500,909	28.5	22.2
YALE UNIVERSITY	17,787,457	7,274,529	25,061,986	40.9	29.0
UNIVERSITY OF WISCONSIN, MADISON	18,640,283	6,080,176	24,720,459	32.6	24.6
UNIVERSITY OF WASHINGTON	19,645,577	4,815,114	24,460,691	24.5	19.7
STANFORD UNIVERSITY	16,769,892	7,590,325	24,360,217	45.3	31.2
UNIVERSITY OF PENNSYLVANIA	17,505,896	6,701,582	24,207,478	38.3	27.7
WASHINGTON UNIVERSITY	16,563,708	6,691,870	23,255,578	40.4	28.8
COLUMBIA UNIVERSITY	17,488,275	4,481,827	21,970,102	25.6	20.4
UNIVERSITY OF CHICAGO	14,630,119	5,575,832	20,205,951	38.1	27.6
UNIVERSITY OF MINNESOTA	15,037,376	4,270,443	19,307,819	28.4	22.1
YESHIVA UNIVERSITY	12,377,888	6,492,127	18,870,015	52.4	34.4
SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH	12,598,251	5,863,462	18,461,713	46.5	31.8
DUKE UNIVERSITY	12,597,721	5,672,691	18,270,412	45.0	31.0
NEW YORK UNIVERSITY	12,449,493	4,379,766	16,829,259	35.2	26.0
UNIVERSITY OF CALIFORNIA, SAN DIEGO	12,673,934	3,819,738	16,493,672	30.1	23.2
UNIVERSITY OF MICHIGAN	11,141,642	5,169,323	16,310,965	46.4	31.7
CORNELL UNIVERSITY	10,829,825	4,720,547	15,550,372	43.6	30.4
TOTAL FOR TOP TWENTY INSTITUTIONS	319,045,983	118,272,497	437,318,480	37.1	27.0

* EXCLUDES GENERAL RESEARCH SUPPORT GRANTS AND RESEARCH CAREER AWARDS.
** INDIRECT COSTS AWARDED AS A PERCENT OF DIRECT COSTS AWARDED.
*** INDIRECT COSTS AWARDED AS A PERCENT OF TOTAL COSTS AWARDED.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

MECHANISM TABLE

	1977	1978	Change
Regular Grants	$999,618,000	$1,057,691,000	+$58,073,000
Noncompeting	(733,984,000)	(768,795,000)	(+34,811,000)
Competing	(265,634,000)	(288,896,000)	(+23,262,000)
Special Programs	413,171,000	386,148,000	-27,023,000
Multidisciplinary Centers	(200,030,000)	(202,905,000)	(+2,875,000)
Other	(213,141,000)	(183,243,000)	(-29,898,000)
Training Programs	134,140,000	122,886,000	-11,254,000
Individual Awards	(29,446,000)	(31,247,000)	(+1,801,000)
Institutional Awards	(104,694,000)	(91,639,000)	(-13,055,000)
Research and Development Contracts	388,488,000	391,838,000	+3,350,000
Intramural Research	249,071,000	268,474,000	+19,403,000
Direct Operations	160,467,000	172,972,000	+12,505,000
Program Management	36,434,000	37,479,000	+1,045,000
Disease Control	60,625,000	61,233,000	+608,000
Construction Grants	22,001,000	12,000,000	-10,001,000
Subtotal	2,464,015,000	2,510,721,000	+42,406,000
Buildings & Facilities	118,548,000	70,053,000	-48,495,000
Total obligations	2,582,563,000	2,580,774,000	-1,789,000

DHEW - National Institutes of Health

OBLIGATIONS BY ACTIVITY

	1977		1978		Change	
	Positions	Amount	Positions	Amount	Positions	Amount
National Cancer Institute	2,031	$814,937,000	2,022	$818,936,000	-9	$3,999,000
National Heart, Lung, and Blood Institute	747	396,661,000	744	403,642,000	-3	6,981,000
National Institute of Dental Research	282	55,573,000	281	57,981,000	-1	2,408,000
National Institute of Arthritis, Metabolism, & Digestive Diseases	588	209,000,000	586	216,961,000	-2	7,961,000
National Institute of Neurological and Communicative Disorders and Stroke	543	155,500,000	541	161,461,000	-2	5,961,000
National Institute of Allergy & Infectious Diseases	621	141,000,000	618	153,442,000	-3	12,442,000
National Institute of General Medical Sciences	164	205,000,000	163	219,896,000	-1	14,896,000
National Institute of Child Health and Human Development	377	145,543,000	375	155,761,000	-2	10,218,000
National Institute on Aging	200	30,000,000	200	34,500,000	--	4,500,000
National Eye Institute	152	64,000,000	151	64,981,000	-1	981,000
National Institute of Environmental Health Sciences	331	49,141,000	331	58,100,000	--	8,959,000
Research Resources	77	137,500,000	76	102,074,000	-1	-35,426,000
Fogarty International Center	51	7,992,000	51	8,369,000	--	377,000
National Library of Medicine	472	35,234,000	470	36,746,000	-2	1,512,000
Office of the Director	547	16,934,000	545	17,871,000	-2	937,000
Central Services	4,097	---	4,097	---	--	---
Subtotal, Biomedical Research	11,280	2,464,015,000	11,251	2,510,721,000	-29	46,706,000
Buildings & Facilities	--	118,548,000	--	70,053,000	--	-48,495,000
(Budget Authority)	--	(67,400,000)	--	(65,650,000)	--	(-1,750,000)
Total NIH	11,280	2,582,563,000	11,251	2,580,774,000	-29	-1,789,000
(Budget Authority)		(2,531,414,000)		(2,576,371,000)		(44,957,000)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

OBLIGATIONS BY OBJECT

	1977 Approp.	1978 Estimate	Change
Total number of permanent positions	11,280	11,251	-29
Full-time equivalent of all other positions	2,084	2,714	+630
Average number of all employees	12,827	13,428	+601
Personnel compensation:			
Permanent positions	$142,706,000	$145,380,000	+$2,674,000
Positions other than permanent	15,519,000	16,858,000	+1,339,000
Other personnel compensation	4,570,000	4,802,000	+232,000
Special personal service payments	27,000	27,000	0
Total personnel compensation	162,822,000	167,067,000	+4,245,000
Personnel benefits:			
Civilian	22,565,000	23,233,000	+668,000
Benefits for former personnel	---	---	---
Travel & transportation of persons	7,296,000	8,568,000	+1,272,000
Transportation of things	1,055,000	1,131,000	+76,000
Rent, communications, & utilities	13,016,000	14,130,000	+1,114,000
Printing and reproduction	5,076,000	5,410,000	+334,000
Other services	741,196,000	718,932,000	-22,264,000
Project contracts	(520,405,000)	(535,762,000)	(+15,357,000)
Payment to NIH management fund	(101,833,000)	(113,119,000)	(+11,286,000)
Other	(118,958,000)	(70,051,000)	(-48,907,000)
Supplies and materials	35,765,000	38,638,000	+2,873,000
Equipment	15,338,000	16,465,000	+1,127,000
Lands and structures	---	---	---
Investments and loans	---	---	---
Grants, subsidies, & contributions	1,578,459,000	1,587,225,000	+8,766,000
Insurance claims and indemnities	2,000	2,000	0
Interest and dividends	---	---	---
Refunds	---	---	---
Quarters and subsistance	-27,000	-27,000	0
Total, Direct Obligations	2,582,563,000	2,580,774,000	-1,789,000

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action
1977 House Report	
1. The Committee directed that funds provided be used to restore positions to 1976 authorized level in each organizational element. (p.23)	Positions in 1977 for each organization were maintained at 1976 level. NCI, NIA, and NIEHS were provided additional new positions.
2. The Committee expects another report on NIH dissemination activities of research results. (p.24)	The report is drafted and will be ready prior to Hearings. NIH Committee on Communications has continuing program on dissemination activities.
1977 Senate Report	
1. The Committee requested a report on the potential usefulness of unused buildings and equipment at Fort Detrick before 1978 hearings. (p.40)	Report is in draft form and will be ready prior to Hearings.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

COMPARABLE

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$1,136,235,000	$1,130,409,000	$1,191,224,000	$1,131,560,000
1969	1,174,429,000	1,115,372,000	1,179,730,000	1,135,660,500
1970	1,116,653,000	1,111,924,000	1,224,911,000	1,095,462,194 1/
1971	1,137,491,000	1,220,565,000	1,281,129,000	1,247,842,000
1972	1,380,599,000	1,472,271,000	1,636,484,000	1,534,407,500
1973	1,549,977,000	1,776,729,000	1,972,921,000	1,778,329,000 2/
1974	1,578,258,000	1,789,140,000	1,929,045,000	1,784,331,000 3/
1975	1,832,716,000	1,790,440,000 4/	2,191,250,000	2,088,579,000
1976	1,804,885,000	2,150,322,000 5/	2,266,648,000 5/	2,304,962,000 6/
1977	2,165,047,000	2,440,778,000	2,656,096,000	2,530,778,000
Suppl.	700,000			
1978	2,576,371,000			

1/ Appropriation after reduction.

2/ Represents continuing resolution. No enacted appropriation.

3/ Appropriation after reduction.

4/ Excludes contracts ($246,293,000) and Medical Library Assistance ($6,282,000) not considered by House due to lack of authorization.

5/ Excludes fellowships and training grants--not considered due to lack of authorization. ($123,646,000).

6/ Appropriation Authority based on 1976 appropriation plus continuing resolution for training programs ($123,646,000) and OD pay raise supplemental ($474,000).

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

ACTUAL

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$1,079,787,000	$1,076,461,000	$1,129,262,000	$1,076,461,000
1969	1,130,644,000	1,089,463,000	1,140,766,000	1,109,753,500
1970	1,084,420,000	1,085,626,000	1,197,115,000	1,067,629,000 1/
1971	1,118,584,000	1,192,386,000	1,252,950,000	1,212,847,000
1972	1,319,873,000	1,408,554,000	1,570,984,000	1,506,156,000
1973	1,619,780,000	1,762,565,000	1,965,795,000	1,762,565,000 2/
1974	1,576,770,000	1,787,142,000	1,927,902,000	1,790,425,000 3/
1975	1,839,784,000	1,787,328,000 4/	2,198,350,000	2,092,897,000
1976	1,805,000,000	2,150,755,000 5/	2,267,081,000 5/	2,302,126,000 6/
1977	2,165,047,000	2,440,778,000	2,656,096,000	2,530,778,000
Suppl.	700,000			
1978	2,576,371,000			

1/ Appropriation after reduction.

2/ Represents continuing resolution. No enacted appropriation.

3/ Appropriation after reduction.

4/ Excludes contracts ($246,293,000) and Medical Library Assistance ($6,282,000) not considered by House due to lack of authorization.

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

Biomedical Research

I. Basic Assumptions

The basic goals of the National Institutes of Health (NIH) are (1) to develop knowledge of the biological bases of health and disease and (2) to develop safe and effective interventions for prevention, detection, diagnosis and treatment of disease and for rehabilitation.

In order to achieve this goal, NIH has responsibility for five interdependent types of activity:

- expanding understanding of diseases through biomedical research in laboratories and clinics,

- developing applications of research findings to solutions of health care problems and measures for the diagnosis and prevention of disease,

- testing and evaluating applications through mechanisms such as controlled clinical trials,

- facilitating the transfer of the results of NIH findings to the practicing community and to organizations responsible for health care and prevention through a range of measures, including control and demonstration programs such as those in the National Cancer Institute and National Heart, Lung, and Blood Institute,

- developing the manpower, biotechnology, communications, data base, and other support resources needed to maintain the above-listed activities.

The interdependence of these activities is significant in the organization of resources to accomplish the basic NIH goal:

- Fundamental research is the source of knowledge about basic life processes upon which successful applied research must build.

- Applied research and development, clinical testing, and demonstration are necessary to translate new research knowledge into interventions useful in medical practice,

- Manpower and other resource development are needed to take advantage of research opportunities and to meet ongoing research requirements,

- Discoveries in one program area contribute to discoveries in other program areas,

- In addition, many discoveries are the consequence of developing a critical mass of research manpower drawn from diverse program areas.

The balance/imbalance among these activities is affected by the allocation of resources and reflects the interaction of three basic factors:

- research opportunities to be exploited at a given time, including perceptions of the relative state-of-the-art in various problem areas, personnel available, technical developments, and new ideas or information,

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- professional and public perceptions of the significance and priorities of different health problems requiring action,

- public values, reflected in legislation, executive action, or judicial decisions and in changing national priorities and organizational arrangements.

II. Background Issues

To the extent that NIH achieves its basic goal, significant assistance can be provided to other agencies in meeting other priority health goals, such as:

- improving the efficacy of medical practice through the validation of knowledge supporting new medical interventions,

- developing effective systems to identify and monitor environmental hazards to human health,

- increasing public awareness of effective disease prevention measures and potential health hazards in personal habits and life-styles.

An effective balance in the organization of programs and activities is essential to the accomplishment of the basic NIH goal. In order to strike such an effective balance, the following issues must be considered and dealt with to the extent possible:

- The interface between research and service - involving clinical trial, control, demonstration, and knowledge dissemination activities - involves a determination of the role of NIH in relation to other agencies and organizations for translating knowledge into practice. A corollary balance issue is competition for funds and personnel among research components.

- In order to maintain an effective research effort, resources to provide management options are needed with respect to the development of required research skills, the updating of facilities to meet research requirements, and the maintenance of stability in the support of research programs.

- Decision and allocation processes require reassessment, especially in view of the decreasing buying power of the research dollar, the impact of NIH decisions on the nation's biomedical research effort, and new funding demands as a consequence of legislation creating new commissions and institutes.

III. Fiscal Year 1978 Budget Policy

The 1978 budget request reflects funds needed to continue support of ongoing productive research efforts. In addition, there are four general areas of basic science in biology and medicine which at this time appear to be moving forward most rapidly, are generally considered to be most promising, and are attracting the attention of the finest minds in research. These four disciplines are basic to our understanding of virtually all disease processes and are represented in the research programs of each of the institutes which comprise the NIH.

Genetics - This research includes the further understanding of the molecular mechanisms which determine the transmittal of biological characteristics as well as the processes which may interfere with the normal transmission of information from parent to offspring. Also included are the increasing number of techniques which permit the investigator to regulate

and control the genetic process by which genes determine what characteristics. Many diseases, e.g. diabetes, cancer, cystic fibrosis, etc., are recognized today to have genetic correlations and the understanding of such diseases and their treatment are critically dependent upon an increasing knowledge of genetics.

Immunology - Higher organisms have developed elaborate mechanisms by which they respond to foreign substances, particularly to foreign proteins and complex sugars. Enormous strides have been made in the past few years in our understanding of these immune processes. We have learned much about the structures of antibodies which the organism manufactures when a foreign substance is presented to it. We also have learned a great deal about the cells which generate these antibodies, the nature of the provocation which initiates the process and the forces which regulate it. We have learned that there are immunologic aspects to many diseases other than those which have been considered to be infectious. These include many varieties of arthritis as well as cancer. Immunology has grown from a subdivision of microbiology into a basic science in its own right. There is every prospect for continued success in the basic pursuit of this process, the understanding of which will, in turn, determine not only increased understanding of disease but also, in many instances, the treatment and prevention of disease.

Virology - This is the study of the smallest and, in some regards, the simplest forms of life. Viruses characteristically are incapable of independent survival and live as parasites in the cells of higher animals or in bacteria. Because of the rapid developments in chemistry, cytology, immunology, and genetics we are today in a far stronger position to understand and to explore the nature of virus particles. We can see them, we can culture them, we can purify them, and we can study their performances utilizing a wide variety of techniques. Viruses have been linked to the cancer process and also to a variety of presently untreatable degenerative diseases of the central nervous system. They also cause major respiratory diseases which account for an enormous share of disability and call upon medical services. These facts alone would appear to demand a high level of endeavor in this important field. In addition, however, because of their relative simplicity of structure and because of the fact that they contain relatively few constituents, they provide an extraordinarily useful model for the study of biological processes which might defy analysis at this time in more complex cells.

Cell Biology - We have identified many of the minute structures which are characteristic of cells - the units of which all living organisms are composed. We are now beginning to understand how the several parts of the cell operate and how they relate to each other. The nature of the cell membrane and of the process whereby materials pass in and out of the cell across this membrane is the subject of intensive and very fruitful study. The functions of the several identified structures of the cell, the mitochondrion, the microsome, the lysosome, the endoplasmic reticulum, the microtubule, etc., is an area of most intense and exciting study. It is becoming possible today to identify abnormalities of these very small structures within the cell and to associate such abnormalities with disease processes in the animal as a whole. A more complete understanding of the cell, its constituents, and its functions is of paramount importance to the continuing development of biomedical science.

Other decisions incorporated in the funds requested include:

- Five million dollars has been provided to the National Institute of Child Health and Human Development to be used for studies of the reproductive process, antenatal and infant nutrition, birth defects and adolescent pregnancy.

- Emphasis on post-doctoral individual fellowships as recommended by the National Academy of Sciences. We are proposing funds for approximately 1,000 new post-doctoral individual fellowships but no new funds are requested for pre-doctoral individual fellowships or institutional National Research Service Awards, with the exception of the Minority Access to Research Careers (MARC) program in the National Institute of General Medical Sciences.

- As called for in the Toxic Substances Control Act, funds have been provided for a cooperative effort between the National Cancer Institute and the Environmental Protection Agency in the area of environmental carcinogenesis.

- Funds have been provided to the National Institute for Allergy and Infectious Diseases for the expansion of research on immunogenetics and transplantation, the expansion of research on the immune system, and for the expansion of efforts toward the development of safer technology for use in DNA recombinant and other genetic recombinant research.

- Continued support for the growth of the National Institute on Aging is provided through a funding increase to expand efforts in clinical, biological, and societal aspects of aging.

- Additional support has been provided to the National Institute of Environmental Health Science, the principal federal agency for biomedical research on the effects of chemical, physical, and biological environmental agents on man's health and well being.

- Funds are not requested in 1978 for the continuation of the Biomedical Research Support Grants Program.

- Twenty-nine administrative positions have been removed in 1978 with the goal of minimizing potential layering and duplication in the Public Health Service.

- Funds have been included for the second stage of construction of the Ambulatory Care Research Facility. This decision is based on (1) the need for an intramural research facility to permit emphasis on ambulatory care as a means of expediting the translation of basic research into clinical application; (2) the need for renovations essential for the Clinical Center to keep pace with modern clinical techniques as required for a research program; and (3) the need to extend the professional base and scientific guidance in support of extramural clinical trials.

MONDAY, MARCH 7, 1977.

NATIONAL CANCER INSTITUTE

WITNESSES

DR. GUY R. NEWELL, ACTING DIRECTOR, NATIONAL CANCER INSTITUTE
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. VINCENT T. DeVITA, JR., DIRECTOR, DIVISION OF CANCER TREATMENT, NATIONAL CANCER INSTITUTE
DR. DIANE J. FINK, DIRECTOR, DIVISION OF CANCER CONTROL AND REHABILITATION, NATIONAL CANCER INSTITUTE
DR. JAMES A. PETERS, DIRECTOR, DIVISION OF CANCER CAUSE AND PREVENTION, NATIONAL CANCER INSTITUTE
EARLE L. BROWNING, FINANCIAL MANAGER, NATIONAL CANCER INSTITUTE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. The committee will come to order.

We now have the National Cancer Institute. The presentation will be made by Dr. Guy R. Newell, Acting Director of the National Cancer Institute.

I see we have your biographical sketch here, Doctor, which we will insert in the record at this point.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH OF DR. GUY R. NEWELL

Name: Guy Rene Newell, Jr., M.D.
Position: Acting Director, National Cancer Institute.
Birthplace and date: Bogalusa, Louisiana; September 21, 1937.
Education: Tulane University, 1959, B.S., Tulane University, 1962, M.D., Harvard School of Public Health, 1968, M.S. in Hygiene (Epidemiology).

Experience

Present: Acting Director, National Cancer Institute.
1973–76: Deputy Director, National Cancer Institute.
1972–73: Associate Professor and Head, Section of Chronic Diseases, Dept. of Epidemiology and Biostatistics, Tulane University.
1970–72: Assistant Professor, Department of Epidemiology and Biostatistics, Tulane University.
1968–70: Executive Secretary, Biometry and Epidemiology Contract Review Committee, National Cancer Institute.
1968–70: Assistant for Program, Viral Oncology Area, National Cancer Institute.
1967–68: Assistant in Medicine (Oncology), Peter Bent Brigham Hospital.
1965—67: Assistant Resident in Medicine, The Johns Hopkins Hospital Baltimore, Maryland.
1963–65: Research Planning Associate, Office of the Director, National Cancer Institute, NIH.
1962–63: Intern in Medicine, The Johns Hopkins Hospital, Baltimore, Maryland.

Association memberships: American Academy of Political and Social Science; American Association for the Advancement of Science; American Association for Cancer Research; American Society of Clinical Oncologists; American Federation for Clinical Research; American Medical Association; American Public Health Association; and Society for Epidemiological Research.

Publications: Author or co-author on over 40 scientific publications.

Mr. FLOOD. Do you have some people with you here you would like us to know?

Dr. NEWELL. Yes, thank you, sir.

On my far left, Mr. Chairman, and on your right, Dr. James Peters, the Director of our Division of Cancer Cause and Prevention. Next to him, Dr. Vincent DeVita, Director of our Division of Cancer Treatment. On my left is Dr. Diane Fink, Director of our Division of Cancer Control and Rehabilitation. On my right is Mr. Browning, our Financial Manager at NCI, Dr. Fredrickson, you know, and Miss Ellen Wormser from the Comptroller's Office.

Mr. FLOOD. We have your statement which we will place in the record at this point, Doctor.

[The statement follows:]

STATEMENT BY THE ACTING DIRECTOR, NATIONAL CANCER PROGRAM, NATIONAL CANCER INSTITUTE, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, ON "NATIONAL CANCER INSTITUTE"

Mr. Chairman, and members of the committee, the purpose of the national cancer program since its establishment in late 1971 has been to reduce the burden of cancer either by preventing it or by curing it. Mr. Chairman, we are able to show results in terms of decreasing mortality and cost savings for cancer patients. I can show results in these terms.

BENEFIT TO PEOPLE

There are definite improvements in some cancer mortality rates. Different types of cancer afflict specific age groups, and for the types in age groups under 35, cancer death rates have decreased for the Nation as a whole.

In the under-15 age group, the decrease is due largely to better treatment for acute leukemia, and brain, kidney, and bone cancers. I have evidence that today a large majority of children with acute lymphocytic leukemia (ALL) has access to the very best in medical care, and this is a major advance. We collect data on a continuing basis on all new cancer cases in 10 percent of the country (covering 20,000,000 Americans). This coverage includes all hospitals in the areas. In one year, 101 new cases of ALL in children under 15 developed. Among these children, the median time from first symptom to seeing a doctor was 1 month; it took 1 additional week to first diagnosis, and just 1 more day to first treatment. The survival of these children was comparable with the survival of children treated by one of the best clinical cooperative groups. Mr. Chairman, I think these exciting findings reflect our ability to transfer complicated technology to the benefit of people.

In the 15 to 34 age group, the decreased mortality rates are due largely to successful treatment of Hodgkin's disease and other lymphomas. A key point here is that research leads first conceived in the mid-1960's are reflected in decreasing mortality for the Nation as a whole only 10 years later. This may seem like a long time-lag. I assure you it is not. Consider that the initial clinical trial usually takes 5 years. If results are favorable, they must be confirmed. Treatment regimens are usually complicated, with toxic side effects, so that application in local and community hospitals may be technically unfeasible at first, and require either modification of the regimen or extensive professional retraining.

In the 35–55 ages, the death rate has remained constant. However, as you will hear during my discussion of treatment, technology learned from our successes in younger people is being transferred to the common tumors of adults, including colon-rectum, lung, breast, uterus, prostate, and urinary organs. Above age 55, death rates are increasing slightly, probably due to a combination of new cases caused by cigarette smoking, industrialization factors, and inadequate treatment.

Technology transfer programs supported by NCI have considerable cost savings for patients. The Comprehensive Cancer Center at the University of Alabama, for example, estimated that its programs saved patients $1.1 million last year. These included savings in hospitalization costs not required because recurrent breast cancer was avoided or delayed by postoperative drugs. Hospitalization and transportation costs were saved because community practitioners, including nurse practitioners, were trained to examine women for early uterine cervical cancer. Necessary biopsies were performed in local clinics by gynecologists trained by the Center.

CAUSE AND PREVENTION

This committee has shown strong interest in expanding the Federal efforts to protect the public from cancers associated with exposures to environmental hazards, and has asked us to take certain actions. I would like to bring you up-to-date on our progress.

Of the 77 new staff positions, 17 were designated for the newly established Environmental Epidemiology Branch to expand its studies of the geographic and other variations in cancer in the United States. The remaining 60 positions were designated for the carcinogenesis program for laboratory studies to identify cancer-causing chemicals. We are actively recruiting personnel for these positions.

Although we have encountered problems with the carcinogenesis testing program, I am pleased to report considerable progress. First, consistent with the perception of national need, I have expanded the carcinogenesis program by establishing two Associate Director positions for carcinogenesis—one devoted full time to the testing program and the other to the research program. These activities will complement each other in our efforts to identify cancer-producing substances with existing methods, and improve on those methods so that substances can be identified more rapidly, efficiently, and at lower cost.

Second, priorities have been reordered to place more emphasis on reporting results of those chemicals already on test. Many logistical problems have been overcome or will be solved during the coming year. Appearing before this committee the last time, Dr. Rauscher reported that 203 chemicals were off test, and that about 20 of those had gone through the complete pathology and biometric analysis. Since that time, pathology and biometric analysis were completed on about another 35 chemicals. A total of 25 draft reports is expected to be completed shortly. Our activities in this area are being greatly accelerated to catch up on this backlog. At present, we have completed animal testing of more than 250 chemicals.

Third, we have established the Clearinghouse on Environmental Carcinogens whose functions include chemical selection, experimental design, data evaluations and risk assessment.

Fourth, we have expanded our collaborative efforts: with the National Institute for Occupational Safety and Health, by an interagency agreement of $3 million in fiscal year 1977 to suppor 21 projects; with the Department of Labor, to incorporate scientific information on occupationally related cancers into educational materials for more than 100,000 workers; and with the National Institute of Environmental Health Sciences, to evaluate existing methods of in vitro (in the test tube) testing and conduct research on new methods.

Fifth, we are surveying carcinogenic agents to identify key carcinogens that warrant particular control activity, and to provide recommended, practical control and prevention methods for them. This project has completed its first year. Experts knowledgeable in specific areas have selected candidate chemicals, identified priorities for control, and begun to develop extensive information on 96 chemicals. Epidemiological data, toxicological data, and control prospectus for 20 chemicals have been produced. Monographs are under development for asbestos, vinyl chloride, and diethylstilbestrol (DES). The monographs will be available to the public, health practitioners, employers, and those who regulate occupational safety.

Problems still exist. One, specifically, is a national shortage of individuals with the requisite training to pursue these most important activities. These include chronic-disease epidemiologists, animal pathologists, toxicologists, and biometricians.

A continuing problem in cancer prevention is smoking. To counteract the increasing consumption of tobacco, a less hazardous cigarette was developed under

the auspices of the national cancer program. These cigarettes are in wide use, and it is hoped they will reduce the risk of developing lung and other cancers.

In response to a congressional mandate, the National Cancer Institute has developed a diet, nutrition, and cancer program to generate and disseminate information on diet and the causation and therapy of cancer. The nutrition program is funding research to increase appetite and food utilization in the cancer patient to maximize nutritional support during therapy and rehabilitation. The projects reflect the great opportunities to define in a short-time, perhaps 1 to 3 years, patient management methods of immediate benefit. Research for the definition of desirable dietary intake for health maintenance and disease prevention will require 5 to 10 years. The nutrition program also has prepared, in collaboration with the American Cancer Society and the Candlelighters, practical Dietary Handbooks for the management of adult and pediatric cancer patients.

DETECTION

In detection, our efforts are directed toward methods of detecting the common cancers as early as possible, when the tumor mass is smallest and treatment is most effective. Four sites—lung, colon-rectum, breast, and uterus—together account for about half of new cancer cases and cancer deaths.

Lung cancer (93,000 new cases, 83,800 deaths per year)

A detection project for early lung cancer, now in its fourth year, is showing promising results. A combination of sputum cytology, chest X-ray, and bronchoscopy is used to detect the exact location of early lung cancers at a time when they are amenable to surgical removal prior to metastatic spread. Cells suspected of being cancerous have been found in nearly 1 percent of the individuals tested per year. Many tumors were not visible on chest X-ray but were localized by bronchoscopy. Many tumors are multifocal early in their development. Information obtained in this project is adding greatly to our understanding of the biology of the disease and will eventually revolutionize current textbook descrptions of lung cancer.

Colon-rectal cancer (99,000 new cases, 49,200 deaths per year)

We have launched a screening project to learn if the occult blood test is effective in detecting early colon cancer, which strikes Americans more frequently than any other cancer except skin cancer. Of 45,000 individuals expected in the project, 15,000 will be in a control group and an additional 30,000 people between 50 and 80 years of age will be screened. Persons with a positive test for blood will receive a complete diagnostic workup to determine the cause of the bleeding. To date, 29,000 individuals have been entered into the project, and 24 cancers detected, representing 13 percent of all people with a positive Hemoccult test.

Breast cancer (88,700 new cases, 33,100 deaths per year)

In partnership with the American Cancer Society, the cancer control program is supporting the breast cancer detection demonstration program—(BCDDP)—a nationwide effort involving 27 BCDDP projects (29 screening centers) in 25 States. Some 270,000 women have received an initial, first annual screening and 130,000 have received a second annual screening. There will be smaller numbers for subsequent annual screenings. Some 1,544 women have been found to have cancer through project screenings as of the latest reports.

Of profound long-term importance is the fact that we have developed the technology to reduce radiation dosage to less than 1 rad delivered dose per exposure, while maintaining the quality of the X-ray. We have taken steps to transfer this technology to the general medical community by funding the Bureau of Radiologic Health of the Food and Drug Administration to develop monitoring and technical assistance programs through State health departments. To date, such monitoring has been implemented in four States and is being initiated in five others.

Uterine cancer (47,000 new cases, 11,000 deaths per year)

The cancer control program for uterine cervical cancer screening is being conducted in collaboration with more than 30 State and Territorial health departments. The objective was to mobilize statewide health care systems to motivate high-risk, hard-to-reach women to seek cervical screening services and be provided with quality followup diagnosis when needed. In the areas that have developed a comprehensive plan and reached the implementation stage, more

than 1,300 hospitals and clinics have screened approximately 544,000 women with at least one Pap smear. Altogether more than 750,000 screenings have been performed. At the time of the latest report, 290 women in a screening population of 231,723 were found to have cancer of the uterus, as confirmed by histology conducted by the medical community. This number will undoubtedly increase as reporting is received on current screenings.

TREATMENT

A major working hypothesis is that up to 60 percent of cancer patients have disseminated disease at the time of diagnosis; also that many patients experience recurrence because they probably had microscopic tumor cells that had spread from the original location but were not detectable at the first treatment. The rationale for cancer treatment, then, provides for the use of anticancer drugs earlier in the course of the disease to reach cancer cells wherever they are in the body, in combination with local treatment with surgery and/or radiation therapy. This approach offers the best opportunity to attack the cancer when the disease is initially diagnosed and the body's tumor burden is the smallest.

Much effort has been expended in the past year to integrate the activities of the clinical cooperative groups into the total clinical treatment program of the National Cancer Institute. In various clinical trials, we have influenced the treatment of 280,000 cancer patients, and about 28,000 of these were entered in clinical trial protocols. This is important because these 280,000 patients were seen and evaluated by expert oncologists and were provided the best medical advice available, even though only 1 out of 10 actually entered a clinical trial.

The emphasis in the clinical program is on combinations of drugs, testing new combinations against standard therapy. The cancers being treated are cancers of the breast, colon, and other parts of the gastrointestinal system including pancreas, as well as lung, and ovary. We are beginning combination treatment of prostate, bladder, and head and neck cancer.

The most recent results of the studies of breast cancer treatment have continued to show that early introduction of drug therapy for women found at surgery to have positive axillary nodes effectively delays and may prevent recurrence, particularly in premenopausal women. New studies have begun with additional drugs and the use of drugs with other methods of treatment, such as hormone therapy and immunotherapy, to increase survival while reducing the extent of surgery required.

In other studies, dramatic early results have been observed in combined chemotherapy and radiotherapy of small cell carcinoma of the lung, which accounts for about 20 percent of lung cancer cases. The addition of a new drug, cisplatinum (II) diamminedichloride, to a drug combination already in use has improved still further the significant response rate of a very malignant tumor of young adults, testicular cancer.

Although we now have nearly 40 drugs commercially available for treatment of cancer, we still do not have the best drugs. We are trying to establish a more rational system of selecting new compounds, and are establishing laboratory systems that will yield new types of agents for development into more effective anticancer drugs. The approach is to pass selected compounds through a prescreen, which will indicate the ones that are sufficiently active to be studied more extensively in a second stage for anticancer activity.

One new drug of considerable interest is maytansine, a plant product related to known antiviral drugs. It has high activity against leukemia and other tumors in laboratory animals. Chlorozotocin, a new drug identified within the past 2 years, has considerably less toxicity for the bone marrow than other related anticancer drugs, such as CCNU. Both new drugs have been started into clinical trials.

PROFESSIONAL AND PUBLIC INFORMATION

The National Cancer Act of 1971 established the cancer control program to promote and speed the delivery of knowledge about cancer to all who can benefit—physicians, patients and the public. In doing this, the Division of Cancer Control and Rehabilitation has established working arrangements with many community and health-related groups, such as the American Cancer Society, and together with our Office of Cancer Communications impacts directly on both professionals and public.

The role of the community physician is essential, since more than 80 percent of cancer patients are first seen and treated by their local physicians in community hospitals. The average general practitioner sees few cases of cancer in a year, and cannot be expected to keep fully informed on progress in the more than 100 diseases known as cancer. But developing a "cancer awareness" is not an impossible goal. We are attempting to assist practitioners to develop this "cancer awareness" by developing a centers outreach program for transferring the latest technology into practice.

To date, 14 Comprehensive Cancer Centers have received funds for this, and more than 800 community hospitals have received outreach assistance from centers. We have set up demonstration networks for leukemia, lymphoma, Hodgkin's disease, breast cancer, and head and neck cancer. Approximately 100 community hospitals are involved in each of the site-oriented networks. A new clinical oncology program will serve to expand treatment protocols at the community level. Each of nine primary hospitals will make formal agreements to work with 3 to 5 community hospitals and their associated practitioners who manage cancer patients. These hospitals will provide training, consultation, and assistance to practitioners in administering the latest in diagnosis and combined modality treatment. We have enlisted the participation of the Clinical Cooperative Groups, which conduct clinical therapeutic trials. Group members will enlist new affiliate members—practitioners with cancer patients—and give them direct assistance, thus also providing a broad based, high quality transfer of the latest knowledge.

With NCI funds, the Association of Community Cancer Centers (ACCC) is developing working arrangements with community physicians, showing them how their participation in the national cancer program can benefit their patients. If all projects in the planning stage reach implementation, hundreds of community hospitals will be direct participants; 68 already are.

Taken together, the centers-outreach, demonstration networks, clinical oncology programs, cooperative group expansion, and ACCC efforts are attempting to influence the cancer care of approximately 60 million people, or one-third of the population of the United States. Until the advent of the cancer control program, most teams capable of providing this level of care were located in only a few institutions throughout the country.

Other professional information included a conference to report to physicians on the latest information on breast cancer causes, detection and diagnosis, and treatment. Two brochures were published to provide information for physicians concerning irradiation-related thyroid cancer and effects of DES among daughters of mothers who received the drug during pregnancy.

A cancer Information Clearinghouse was established as a central point for information about cancer educational materials and services available from and for the cancer centers and other components of the national cancer program. Another activity, the International Cancer Research Data Bank program, operates a computer-based cancer information system called "Cancerline." It links the computer system at the National Library of Medicine in Bethesda with terminals in some 500 locations in the United States and several other countries. The data bank contains some 65,000 abstracts of the world's published literature on cancer and descriptions of 16,000 ongoing cancer research projects and clinical cancer therapy protocols.

Toll-free telephone services and resources for cancer information were established at many of the Centers to facilitate the response to inquiries. Fifteen telephone systems are in operation around the country. Although most of them started operation during the latter part of the year, they have handled about 20,000 calls from the general public and health professionals. Most of the calls were for specific information on the major types of cancer from patients, individuals with symptoms, and their families.

BASIC RESEARCH

Because in its fundamental nature cancer is a disease of the cell, basic research encompasses studies of the structure and behavior of cells, life processes within cells, and the immune defense system. The NCI continues to invest heavily in this type of investigator-initiated research.

Investigators have obtained evidence suggesting that virtually all human cells have coded information probably provided by viruses of the RNA type. This information is usually well suppressed by most people, but can be activated by

exposure to irradiation, chemical carcinogens, or other infecting viruses. The significance of this work is that there may be a common denominator mechanism for cancer within cells. Theoretically, then, it would be possible to find ways of preventing activation of cancer information and allowing people to live cancer-free in an environment that will continue to be contaminated.

Mr. Chairman, in conclusion, the National Canger Program is a national program of research, demonstration and communication—not health care delivery. The well-informed primary physician, practicing the team concept of cancer management in a community hospital and dealing with a cancer-conscious, well-informed public, provides the most immediate hope for saving victims of this disease.

APPROPRIATION REQUEST

Mr. Chairman, the request for the National Cancer Institute for fiscal year 1978 totals $818,936,000. The new request includes $223,641,000 for cause and prevention research; $49,446,000 for detection and diagnosis research; $263,006,000 for treatment research; $117,709,000 for cancer biology; $59,757,000 for cancer centers support; $31,647,000 for research manpower development; $12,895,000 for construction; and $60,835,000 for cancer control.

I shall be pleased to try to answer any questions and supply additional information desired for the record.

Mr. Chairman, this concludes my statement.

NONCOMPETING GRANTS

Mr. FLOOD. Now the 1978 budget of the Institute, the Cancer Institute, that is just about the same as the 1977 level. However, I notice in all that material that you submitted to the committee, there is a $2.3 million reduction for noncompeting research grants.

Does that mean you are cutting off research in midstream or how do you explain the reduction?

Dr. NEWELL. No; we are not cutting off the research, Mr. Chairman. We are, however, in a situation where we will only be able to fund about 38 percent of approved regular research grant applications.

Mr. FLOOD. Thirty-eight percent?

Dr. NEWELL. Yes, sir.

Mr. FLOOD. How do you explain the reduction? What do you mean you only can fund thirty-eight percent?

Dr. NEWELL. It means that we have chosen to put those dollars in other areas.

Mr. FLOOD. Oh, you have?

Dr. NEWELL. Yes, sir.

Mr. FLOOD. Then you have chosen to reduce the noncompeting research grants?

Mr. BROWNING. I don't believe there is a reduction in noncompeting grants. In the regular grant program, I am sorry, it is.

Mr. FLOOD. $2.3 million, isn't it?

Mr. BROWNING. Yes, sir.

Mr. FLOOD. In what we have here it is a $2.3 million cut in the noncompeting research grants, right? It is your material.

Dr. NEWELL. We are paying all noncompeting grant requirements in fiscal year 1978. The 1978 requirement is $2.3 million less than in 1977. We will put those dollars in other funded areas, Mr. Chairman, for competing renewal and new grants rather than this particular category.

Mr. FLOOD. How many new research grants will be awarded in 1978 and at what dollar level and how does that compare with 1977?

Dr. NEWELL. Three hundred and forty-eight new grants at $22.9 million in 1978.

Mr. FLOOD. Compared to what in 1977?

Dr. NEWELL. In 1977 there were 320 new grants, at $19.8 million.

POSITIONS

Mr. FLOOD. The budget also proposes to cut positions. Your language by the way is on page 33 of your justifications. I will quote your language: "Nine administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service."

What does that mean in English?

Dr. NEWELL. I understand, sir, that we are not unique in this regard.

Mr. FLOOD. There is no question about that. Do you mean the question or this?

Dr. NEWELL. The reduction, sir. Maybe Dr. Fredrickson would like to comment.

Dr. FREDRICKSON. The administration has directed a reduction of a total of 29 positions at NIH in areas not related to program. The Cancer Institute has a decrement of 9 from that total of 29.

CHEMICAL TESTING

Mr. FLOOD. In your statement which we have in the record, Doctor, you say that more emphasis is going to be placed on reporting results of the chemicals already tested and that you have overcome a lot of logistical problems that you have in that area. Since we don't understand what you mean, will you explain a little more what that means to the committee?

Dr. NEWELL. Yes, sir.

Dr. Rauscher testified last year to you, sir, that there were some 203 compounds off test. Shortly after that we recognized that we were not getting final reports as we had planned and as we had promised you. We began to take yet another look at the testing program and we did find some fairly severe problems with it.

We have made, I think, some remarkable accomplishments since then. We have three final reports out and available. We have nine reports that are in draft form and should be out by the end of this month. We have 213 compounds for which the bioassay has actually been completed.

Mr. FLOOD. Of course, Doctor, we know very well from our many years with you that before a final test can be written on a chemical test in animals, it is necessary to complete the pathology and all the biometric analysis. We know all about that.

Dr. NEWELL. Yes, sir.

Mr. FLOOD. Is that what you are talking about now, the number?

Dr. NEWELL. Yes, sir, I am talking about the number of compounds in each category. I can submit it for the record in more detail.

Mr. FLOOD. You were backlogged. What is the present backlog of chemicals tested and how quickly do you plan to get rid of that backlog?

Dr. NEWELL. We except to have at least nine reports out by the end of this month and we expect to have two to five reports thereafter per week. We have addressed the pathology backlog problem and that is no longer a problem. All the pathology is done and complete.

Part of the problem is a vertification procedure that we have to go through because some of the reports, as you know, will end up in court at some time in the future. So, we do have a fairly extensive vertification procedure.

Mr. FLOOD. What you can do for the record is, identify the chemicals on which you have completed your animal testing and give us some indication of the time when you expect to issue a final report on each one of the chemicals.

Dr. NEWELL. Yes, sir.

[The information follows:]

National Cancer Institute

Chemical Testing

The attached tables reflect those chemicals on which animal testing has been completed. Table I reflects compounds for which final reports are available. Table II reflects compounds for which reports have been drafted. Table III reflects compounds for which bioassay has been completed and reports are being drafted. Included in each table is the usage for each chemical as well as the anticipated date that a final report on the chemical will be issued.

The use code on the following tables is identified as follows:

CODE		USAGE
Food	.....	Food or Food Additives
Pest	.....	Pesticide
Phar	.....	Pharmaceuticals/Biologicals
Solv	.....	Solvents
Dye	.....	Dye or Dye Manufacture
Inter	.....	Chemical Intermediate or Catalyst
Reag	.....	Chemical Reagent
Other	.....	Other, Unclassified
Misc	.....	Miscellaneous Categories

Table I. Compounds for which final reports are available.

STANDARD PROTOCOLS

NCI #	CHEMICALS	USE	Report Date
C00191	CHLORDECONE (KEPONE)	pest	1/76
C02686	CHLOROFORM	solv	6/76
C04546	ETHYLENE, TRICHLORO-	solv	1/76

Table II. Compounds for which reports have been drafted.

STANDARD PROTOCOLS

NCI #	CHEMICALS	USE	Report Date
C02766	ACETIC ACID, NITRILOTRI-	other	4/77
C01445	ACETIC ACID, NITRILOTRI-, TRISODIUM SALT, MONOHY	inter	4/77
C00099	CHLORDANE	pest	4/77
C00113	DICHLOROVOS (VAPONA)	pest	5/77
C00135	DIMETHOATE	pest	3/77
C00157	ENDRIN	pest	3/77
C04626	ETHANE, 1,1,1-TRICHLORO- (METHYL CHLOROFORM)	pest	3/77
C00180	HEPTACHLOR	pest	4/77
C01741	PHENFORMIN	phar	3/77

Table III. Compounds for which bioassay has been completed and reports are being drafted.

STANDARD PROTOCOLS NCI #	CHEMICALS	USE	Report Date
C01967	ACENAPHTHENE, 5-NITRO-	inter	8/77
C02108	ACETAMIDE	phar	1/78
C01887	ACETANILIDE, 3-AMINO-4-ETHOXY-	phar	12/77
C03974	ACETIC ACID, (ETHYLENEDINITRILO)TETRA-, TRISODIU	phar	5/77
C01978	P-ACETOPHENETIDE, 3'-NITRO-	other	11/77
C04137	ACRIDINE, 3,6-DIAMINO-, MONOHYDROCHLORIDE	phar	3/77
C01536	ACRONYCINE	phar	9/77
C04682	ACTINOMYCIN D	phar	1/78
C02095	ADIPAMIDE	none	12/77
C01456	AFLATOXIN B1	phar	3/78
C00044	ALDRIN	pest	7/77
C02437	AMINOCHLORODIPHENYL ETHER	pest	12/77
C03736	ANILINE	dye	12/77
C02039	ANILINE, P-CHLORO-	phar	7/77
C02255	ANILINE, 2,4-DIMETHOXY-, HYDROCHLORIDE	dye	10/77
C01821	ANILINE, N,N-DIMETHYL-P-NITROSO-	dye	6/77
C01990	ANILINE, 4,4'-METHYLENE-BIS(N,N-DIMETHYL)-	reag	8/77
C01707	ANILINE, 4,4'-THIODI-	inter	9/77
C02460	ANILINE, 2,4,6-TRICHLORO-	dye	12/77
C03587	ANILINE, 2,4,5-TRIMETHYL-, HYDROCHLORIDE	dye	12/77
C02288	ANILINE, 2,4,6-TRIMETHYL, HYDROCHLORIDE	dye	12/77
C02993	P-ANISIDINE, 2-METHYL-	dye	9/77
C01934	O-ANISIDINE, 5-NITRO-	inter	8/77
C01989	ANISOLE, 2,4-DIAMINO-, SULPHATE	none	11/77
C01730	ANTHRANILIC ACID	phar	3/78
C01945	ANTHRANILIC ACID, 4-NITRO-	inter	6/77
C01876	ANTHRAQUINONE, 2-AMINO-	dye	8/77
C01901	ANTHRAQUINONE, 1-AMINO-2-METHYL-	dye	6/77
C01923	ANTHRAQUINONE, 2-METHYL-1-NITRO-	none	3/77
C02697	ASPIRIN, PHENACETIN, CAFFEINE (APC)	phar	7/77
C04728	ARABINOSYLCYTOSINE	phar	1/78
C02120	L-ARGININE GLUTAMATE	phar	12/77
C01569	5-AZACYTIDINE	phar	9/77
C03474	AZATHIOPRINE	phar	1/78
C00056	AZINPHOS-METHYL	pest	7/77
C06371	AZIRIDINE, 2-METHYL-	inter	7/77
C02926	AZOBENZENE	pest	3/78
C02426	BENZENE, 1-CHLORO-2,4-DINITRO-	dye	12/77
C02415	BENZENE, 1-CHLORO-2-NITRO-	dye	12/77
C02404	BENZENE, 1-CHLORO-4-NITRO-	dye	12/77
C00419	BENZENE, PENTACHLORONITRO- (PCNB)	pest	7/77
C01912	BENZIMIDAZOLE, 6-NITRO-	other	11/77
C02006	BENZOPHENONE, 4,4'-BIS(DIMETHYLAMINO)-	dye	6/77
C03550	P-BENZOQUINONE, DIOXIME	other	10/77
C02664	BIPHENYL, CHLORO-	other	3/78

Table III. Compounds for which bioassay has been completed and reports are being drafted.

STANDARD PROTOCOLS

NCI #	CHEMICALS	USE	Report Date
C06382	BIS(2-HYDROXYETHYL)DITHIOCARBAMIC ACID, POTASSIUM	none	7/77
C01592	1,4-BUTANEDIOL, DIMETHANESULFONATE	phar	9/77
C02131	N-BUTYLUREA	other	11/77
C00077	CAPTAN	pest	7/77
C00544	CARBAMATE, 4-DIMETHYLAMINO-3,5-XYLYL-N-METHYL-	pest	7/77
C04808-1	CARBANILIDE, 4,4'-DIACETYL-BIS(AMIDINOHYDRAZONE)	phar	1/78
C04808-2	SULFONATE		
C01898	CARBAZOLE, 3-AMINO-9-ETHYL-	other	9/77
C03043	CARBAZOLE, 3-AMINO-9-ETHYL-, HYDROCHLORIDE	dye	9/77
C04591	CARBON DISULFIDE	solv	12/77
C06417	CARBONIC ACID, CYCLIC ETHYLENE ESTER	inter	7/77
C00055	CHLORAMBEN	pest	7/77
C03485	CHLORAMBUCIL	phar	1/78
C00408	CHLOROBENZILATE	pest	5/77
C00533	CHLOROPICRIN	pest	6/77
C01558	CHOLESTEROL, (P-(BIS(2-CHLOROETHYL)AMINO)PHENYL)	phar	12/77
C01467	CYCASIN	none	3/78
C02277	CYCLAMATE, SODIUM SALT	food	12/77
C04900	CYCLOPHOSPHAMIDE (CYTOXAN)	phar	1/78
C00102	DACONIL	pest	6/77
C01718	DAPSONE	phar	8/77
C01683	DARAPRIM	phar	3/78
C04693	DAUNOMYCIN	phar	1/78
C00475	P,P'-DDD	pest	7/77
C00555	P,P'-DDE	other	7/77
C00464	P,P'-DDT	pest	7/77
C01581	BETA-DEOXYTHIOGUANOSINE	phar	10/77
C04933	O,P'-DDD (MITOTANE)	pest	3/78
C06393	DIALLATE	pest	7/77
C03269	DIARYLANILIDE YELLOW	dye	8/77
C03656	DIBENZO-P-DIOXIN	inter	1/78
C03667	DIBENZO-P-DIOXIN, 2,7-DICHLORO- (DCDD)	pest	1/78
C03678	DIBENZO-P-DIOXIN, 1,2,3,4,6,7,8,9-OCTACHLORO-	pest	1/78
C01661	DIBENZYLINE HYDROCHLORIDE	phar	10/77
C04795	DIBROMODULCITOL	phar	1/78
C04762	DIBROMOMANNITOL	phar	1/78
C03270	TRIS(2,3-DIBROMOPROPYL)PHOSPHATE	other	9/77
C02028	DIBUTYLTIN DIACETATE	inter	8/77
C00486	DICOFOL (KELTHANE)	pest	8/77
C02448	DICYCLOPENTADIENE DIOXIDE	other	12/77
C00124	DIELDRIN	pest	6/77
C00599	DIELDRIN, PHOTO-	pest	8/77
C01547	DIMETHANE SULFONATE	phar	5/77

Table III. Compounds for which bioassay has been completed and reports are being drafted.

NCI #	CHEMICALS	USE	Report Date
	STANDARD PROTOCOLS		
C00395	DIOXATHION (DELNAVE)	pest	8/77
C02700	DIPENTYLAMINE, N-NITROSO-	none	3/78
C02244	DIPHENYLAMINE, 4-NITROSO-	other	9/77
C03009	2,5-DITHIOBIUREA	inter	12/77
C03918	DMBA	inter	3/78
C01605	EMETINE	phar	9/77
C00566	ENDOSULFAN	pest	6/77
C01570	ESTRADIOL MUSTARD	phar	12/77
C00522	ETHANE, 1,2-DIBROMO-	pest	8/77
C04535	ETHANE, 1,1-DICHLORO-	solv	5/77
C00511	ETHANE, 1,2-DICHLORO-	solv	7/77
C04604	ETHANE, HEXACHLORO-	solv	11/77
C03554	ETHANE, 1,1,2,2-TETRACHLORO-	pest	6/77
C04579	ETHANE, 1,1,2-TRICHLORO-	solv	7/77
C06406	ETHER, BIS(2-CHLOROETHYL)-	pest	7/77
C01694	ETHIONAMIDE	phar	10/77
C04580	ETHYLENE, TETRACHLORO-	solv	7/77
C05710	GRISEOFULVIN	pest	3/78
C04819	GUANAZOLE	phar	1/78
C02653	HEXACHLOROPHENE	pest	3/78
C03054	HYDANTOIN, DICHLORODIMETHYL-	pest	8/77
C04739	HYDRAZINE, 1-ACETYL-2-PICOLINOYL-	phar	1/78
C01854	HYDRAZINE, 1,1-DIPHENYL-	reag	8/77
C03258	HYDROXYLAMINE, N-NITROSO-N-PHENYL-, AMMONIUM SAL	reag	9/77
C04831	HYDROXYUREA	phar	1/78
C04717	IMIDAZOLE-4-CARBOXAMIDE-5-(3,3-DIMETHYL-1-TRIAZE	phar	1/78
C01616	IMIDAZOLE MUSTARD (BIC)	phar	1/78
C02175	ISOCYANIC ACID, 3,3'-DIMETHOXY-4,4'-BIPHENYLENE	inter	9/77
C01638	ISOPHOSPHAMIDE	phar	6/77
C01478	LASIOCARPINE	phar	3/78
C01489	LEAD ACETATE	dye	3/78
C00204	LINDANE	pest	5/77
C00215	MALATHION	pest	6/77
C04853	MELPHALAN	phar	1/78
C04944	O-MELPHALAN	phar	3/78
C04886	6-MERCAPTOPURINE	phar	1/78
C04637	METHANE, TRICHLOROFLUORO-	solv	12/77
C04568	METHANE, TRIIODO-	phar	11/77
C03190-1	METHANSULFON-M-ANISIDE, 4'-(9-ACRIDINYLAMINO)-	phar	3/77
C03190-2	MONOHYDROCHLORIDE		
C03849	METHIODAL SODIUM	other	10/77
C04671	METHOTREXATE	phar	1/78
C04875	METHOTREXATE, DICHLORO-	phar	1/78
C00497	METHOXYCHLOR	pest	6/77
C02380	4,4'-METHYLENE-BIS-(2-CHLOROANILINE) HYDROCHLORI	other	12/77

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Table III. Compounds for which bioassay has been completed and reports are being drafted.

STANDARD PROTOCOLS

NCI #	CHEMICALS	USE	Report Date
C03010	METHYL ORANGE B	reag	12/77
C04784	METHYLTHIOINOSINE	phar	1/78
C06428	MIREX	pest	7/77
C04706	MITOMYCIN C	phar	1/78
C02164	MORPHOLINE, 4-NITROSO-	reag	3/78
C01956	NAPHTHALENE, 1-NITRO-	dye	9/77
C00431	NICLOSAMIDE	pest	11/77
C03792	NITHIAZIDE	phar	12/77
C00420	NITROFEN	pest	9/77
C04740	1-NITROSOUREA, 1-(2-CHLOROETHYL)-3-CYCLOHEXYL-	phar	1/78
C02084	NITROUS ACID, SODIUM SALT	food	11/77
C06439	OXAMIDE, DITHIO-	reag	7/77
C04126	2-OXETANONE, 3,3-DIMETHYL-	inter	10/77
C00226	PARATHION	pest	8/77
C03963	PHENOL, 4-AMINO-2-NITRO-	dye	10/77
C03305	M-PHENYLENEDIAMINE, 4-CHLORO-	other	12/77
C03292	O-PHENYLENEDIAMINE, 4-CHLORO-	inter	6/77
C02482	M-PHENYLENEDIAMINE, DIHYDROCHLORIDE	reag	12/77
C02493	O-PHENYLENEDIAMINE, DIHYDROCHLORIDE	dye	12/77
C03941	O-PHENYLENEDIAMINE, 4-NITRO-	reag	7/77
C02222	P-PHENYLENEDIAMINE, 2-NITRO-	reag	6/77
C02233	P-PHENYLENEDIAMINE, N-PHENYL-, HYDROCHLORIDE	dye	8/77
C00588	PHOSPHAMIDON	pest	6/77
C04922-1	PHOSPHORODIAMIDIC ACID, N,N-BIS(2-CHLOROETHYL)-N	phar	1/78
C04922-2	HYDROXYPROPYL CHCLOHEXYLAMINE SALT		
C00237	PICLORAM	pest	7/77
C01627	2,6-PIPERAZINEDIONE-4,4'-PROPYLENE DIOXOPIPERAZI	phar	1/78
C02813	PIPERONYL BUTOXIDE	pest	3/78
C02824	PIPERONYL SULFOXIDE	pest	3/78
C04897	PREDNISONE	phar	1/78
C01810	PROCARBAZINE HYDROCHLORIDE	phar	7/77
C00500	PROPANE, 1,2-DIBROMO-3-CHLORO- (DBCP)	pest	8/77
C06440	1,2-PROPANEDIOL, 3-CHLORO-	dye	7/77
C04615	PROPENE, 3-CHLORO-	inter	6/77
C03076	PROPIONIC ACID, 3-NITRO-	phar	8/77
C01785	PYRAZINECARBOXAMIDE	phar	11/77
C01672	PYRIDIUM	phar	12/77
C02506	SACCHARINE	food	7/77
C06097	SACCHARIN, SODIUM SALT	food	12/77
C05981	SEMICARBAZIDE, MONOHYDROCHLORIDE	reag	7/77
C06462	SODIUM AZIDE	phar	7/77
C06473	SODIUM BISULFIDE	dye	7/77
C02459	4'-STILBENAMINE, 2,5-DIMETHOXY-	inter	12/77
C03167	STREPTOZOTOCIN	phar	1/78
C02200	STYRENE	other	9/77

Table III. Compounds for which bioassay has been completed and reports are being drafted.

STANDARD PROTOCOLS NCI #	CHEMICALS	USE	Report Date
C02211	STYRENE, BETA-NITRO-	inter	8/77
C03827	SUCCINIC ACID, MONO(2,2-DIMETHYLHYDRAZIDE)-	pest	9/77
C00453	SULFALLATE (CDEC)	pest	9/77
C02379	3,3',4,4'-TETRAAMINODIPHENYL TETRAHYDROCHLORIDE	reag	12/77
C00168	TETRACHLORVINPHOS	pest	6/77
C02471	TETRAFLUORO-N-PHENYLENE DIAMINE DIHYDROCHLORIDE	inter	12/77
C03065	THIAZOLE, 2-AMINO-5-NITRO-	phar	8/77
C04557	THIOPHENE, 2,5-DIHYDRO-, 1,1-DIOXIDE-	solv	9/77
C06451	THIOSEMICARBAZONE	reag	7/77
C01649	THIO TEPA	phar	10/77
C01832	TOLUENE-2,5-DIAMINE, SULFATE	other	7/77
C05129	TOLUENE, 2,4-DIAMINO-, HYDROCHLORIDE	inter	12/77
C01865	TOLUENE, 2,4-DINITRO-	dye	6/77
C02346	M-TOLUIDINE HYDROCHLORIDE	dye	12/77
C02040	P-TOLUIDINE, 3-CHLORO-	inter	8/77
C02051	O-TOLUIDINE, 5-CHLORO-	inter	9/77
C02357	P-TOLUIDINE, HYDROCHLORIDE	dye	12/77
C01843	O-TOLUIDINE, 5-NITRO-	dye	7/77
C02153	P-TOLYLUREA	none	12/77
C00259	TOXAPHENE	pest	6/77
C02391	S-TRIAZINE, 2,4-DIAMINO-6-PHENYL-	inter	12/77
C00442	TRIFLURALIN	pest	7/77
C00260	TRIPHENYLTINHYDROXIDE	pest	10/77
C01729	TRYPTOPHAN, L-	food	11/77
C01490	URACIL, 2-THIO-	phar	3/78
C04773	UREA, 1,3-BIS(2-CHLOROETHYL)-1-NITROSO-	phar	1/78
C01763	UREA, 1-BUTYL-3-(P-TOLYLSULFONYL)-	phar	10/77
C01752	UREA, 1-((P-CHLOROPHENYL)SULFONYL)-3-PROPYL-	phar	11/77
C04524	UREA, N,N'-DICYCLOHEXYLTHIO-	inter	9/77
C02073	UREA, (P-ETHOXYPHENYL)-	food	12/77
C03372	UREA, ETHYLENETHIO-	other	7/77
C02017	UREA, 1-PHENYL-2-THIO-	reag	8/77
C02186	UREA, 1,1,3-TRIMETHYL-2-THIO-	inter	7/77
C04842	VINBLASTINE	phar	1/78
C04864	VINCRISTINE	phar	1/78
C06484	VINYLENE CARBONATE	solv	7/77
C02313	2,4-XYLIDINE HYDROCHLORIDE	dye	12/77
C02324	2,5-XYLIDINE HYDROCHLORIDE	dye	12/77
C03816	UREA, 1, 3-DIETHYL-2-THIO-	other	11/77

PARTICIPATION WITH NIOSH

Mr. FLOOD. Last year you will recall the committee directed the Cancer Institute to continue its participation with the National Institute of Occupational Safety and Health in the occupational carcinogenesis program. At that time we provide $3 million for just that purpose.

What have you done to date with that money? Do you intend to continue this activity in fiscal 1978?

Dr. NEWELL. Yes, sir, we made an interagency agreement with the National Institutes of Occupational Safety and Health for a little under $1 million during the transition quarter. Shortly after the first of the fiscal year $3 million was made available to NIOSH to support 21 separate studies.

Mr. FLOOD. When did you do that?

Dr. NEWELL. Shortly after the first of fiscal year 1977. I have a list of those 21 projects plus 3 in the transition quarter I can submit for the record.

Mr. FLOOD. Yes; that is what we want.

[The information follows:]

NCI–NIOSH projects

Transition quarter:

	Amount
1. Retrospective mortality study of miners exposed to amphibole mineral	$150,000
2. Mortality of pesticide formulators	470,000
3. Development of sampling and analytical methods for carcinogens	300,000
Total transition quarters	920,000

Fiscal year 1977:	
4. Occupational cancer surveillance	321,800
5. Kepone registry	91,800
6. Industrial hygiene and morbidity study of talc and other fibrous minerals	191,600
7. Mortality, medical and industrial hygiene study of vinylidene chloride workers	182,100
8. Mortality and industrial hygiene study of styrene-Butadiene rubber workers	205,100
9. Mortality and Industrial hygiene study of PCB	254,000
10. Industrial hygiene study of azo dye workers	26,100
11. Mortality and industrial hygiene study of trichloroethylene (TCE)	84,700
12. Mortality and industrial hygiene study of perchloroethylene (PCE)	210,800
13. Mortality, medical and industrial hygiene study of chlorinated hydrocarbons	109,900
14. Study of beryllium workers	223,800
15. Mortality and industrial hygiene study of nitrosamine/cutting oils	240,500
16. Mortality and reproductive effects of chloroprene	157,300
17. Mortality, medical and industrial hygiene study of the painting trades	209,900
18. Mortality and industrial hygiene study of printing trades	10,300
19. Mortality and industrial hygiene study of phosphate workers	138,900
20. Occupational carcinogenesis reduction by behavioral methods	187,100
21. Inhalation study of short asbestos fibers	47,900
22. Perform subtrachial testing of copper and lead smelter dust	20,200
23. Determine the effects of combined exposures to smelter dusts and SO_2	39,000
24. Evaluate personal protective equipment	105,000
Total 1977	3,057,800
Total transition quarter and 1977	3,977,800

EPIDEMIOLOGY

Mr. FLOOD. In the past we talked a good deal about the Cancer Institute epidemiology studies. You will recall that. As a result of all that, you have identified what you called cancer hot spots—that is quite a phrase, cancer hot spots—all over the country. What is the next step in the process now that you have all this information? Are you undertaking the studies to examine the life styles or are you looking at certain environmental agents which might explain these so-called cancer hot spots?

Dr. NEWELL. We are doing both. Let me give you an example.

In the area of lung cancer, we found that some of the highest areas of death were in the South, in the State of Louisiana and around that area. We are now funding through the University there, Tulane University, a followup project whereby the staff will survey death certificates in the State and begin to identify either occupational exposures or geographic areas where individuals lived within the State. We are doing the same thing for bladder cancer in the State of New Jersey, for example. We hope to send in either our own research teams or fund through grants local teams of investigators who can further pursue this.

Mr. FLOOD. You are talking about life styles and environmental exposure?

Dr. NEWELL. Yes; and new industries.

Mr. FLOOD. Do you have dollars in this budget, then, to initiate intensive studies on these cancer hot spots?

Dr. NEWELL. Yes, sir, we do. Our dollars for epidemiology have increased to a fair degree over the last several years as the area has become more important.

In the 1977 budget we spent $31 million in this area. I have allotted almost another $1 million bringing it up to $32 million this year, even though as you mentioned, in the budget there is only $4 million additional.

So I have taken away from some areas. Epidemiology is one of my higher priority areas.

Mr. FLOOD. Do you collect occupational data? I am talking about people who are disabled by cancer.

Dr. NEWELL. We did that in the survey, the so-called Third National Cancer Survey covering the years 1969, 1970 and 1971.

Mr. FLOOD. It is a continuing basis then?

Dr. NEWELL. We have continued these projects, yes, sir. We do a certain sampling of the population. It covers about 10 percent of the population of the total country.

NUTRITION

Mr. FLOOD. Doctor, we see a number of reports which explain how nutrition can improve the survival of cancer patients and also increase the cancer patient's quality of life. What is the Cancer Institute doing to foster research in this area?

Dr. NEWELL. During the last year, Mr. Chairman, we put $5.2 million new dollars in our nutrition program. We currently fund a little over $7.6 million which is in the 1978 estimate. The difference is we were already funding some ongoing grants, the difference between the $5.2 million and the $7.6 million.

Mr. FLOOD. Are you considering any new programs in 1978 in the area of nutrition and diet in the cancer patients? These are terms people understand. The minute you talk about nutrition and diet with reference to cancer patients you have an audience.

Dr. NEWELL. We would like to do more. We would like to spend up to $15 million. We could do so; however, with the limited budget I have given it a quarter of a million new dollars. But I don't think it is as high a priority as carcinogenesis testing.

Mr. FLOOD. Is that a lot?

Dr. NEWELL. It is not enough.

Mr. FLOOD. Why don't you get more? We spend a lot of money trying to attract attention. But the minute you start identifying nutrition and diet with cancer patients you have an audience. I repeat that for the purpose of emphasis.

Dr. NEWELL. Yes, sir.

Mr. FLOOD. Well, that is quite an answer, I can't argue with that.

Now we have had a lot of discussion in just the past couple of months. Thousands and thousands of women now are being unnecessarily exposed to excessive amounts of radiation while being screened for breast cancer. How carefully is your Institute examining that problem and what action have you taken to prevent that from continuing?

Dr. NEWELL. I think we have taken very responsible action in this regard.

Mr. FLOOD. We don't want to use tax dollars here to create doctor-induced illnesses, you know.

Dr. NEWELL. Absolutely not. We have supported the development of newer techniques to reduce the dose of radiation. In fact now we can get a very good radiographic film with the delivered dose of 1 rad or less for the total mammogram.

Mr. FLOOD. You had better translate "rad".

Dr. NEWELL. Absorbed radiation dose. In order to promote this throughout the country, we have initiated an agreement with the Bureau of Radiological Health. They are responsible for the implementation of radiation safety throughout the country. Through funds to them they are working now with State and local health departments to survey exactly what radiation exposures are in various parts of the country and to educate the radiologist and others to bring these doses down to 1 rad or less.

Mr. FLOOD. How long have you been doing this?

Dr. NEWELL. The interagency agreement is 1 year old.

Mr. FLOOD. By the way, Doctor Fink, there is no reason you can't tell us.

Dr. FINK. The Radiologic Physics Centers which developed the technology have been in operation 2 years. As Dr. Newell pointed out, the dose now attainable is one radiation absorbed dose. During the past year, we initiated the interagency agreement with the Bureau of Radiologic Health.

Mr. FLOOD. Are they listening to you on this, do you think?

Dr. FINK. Yes. I think the publicity on the issue of excess dose has certainly made women and physicians aware of the potential of radiation hazard in the mammographic examination. Using as an example our own breast detection units, it was very easy to bring the doses down to the acceptable 1 rad range.

Mr. FLOOD. I wonder why this should happen all of a sudden. All of a sudden because of publicity this happens. I wonder why that would not have been identified long before this?

Dr. NEWELL. I think, Mr. Chairman, it is a question of risk versus benefit. There is only one available clinical trial in the whole literature that addresses the benefit side of screening women for breast cancer. Several things happened all at once that sort of brought this together.

A reexamination of that one clinical study did not indicate as much benefit to women as was first thought, and I am talking about screening a symptomatic woman.

Secondly, a committee of experts in the field of radiation pointed out that low doses of radiation to exposed breast tissue could perhaps itself induce berast cancer over a 10- to 15-year period. So it was these two bits of information that brought the risk-benefit ratio closer together. It all happened at once and that is when all the publicity came about. You have heard this in the press yourself.

Mr. FLOOD. Yes.

Mr. Obey?

Mr. OBEY. Doctor, we are happy to have you with us.

Dr. NEWELL. Thank you, Mr. Obey.

CARCINOGENESIS POSITIONS

Mr. OBEY. Last year we had a considerable amount of discussion about manpower needs in the carcinogenesis program and the impact those needs had on the bioassay testing operations. Following that discussion this committee added 60 positions to the carcinogenesis program.

Could you provide for the committee a listing of job descriptions for each of the 60 positions created, an explanation of how each of those positions will assist bioassay operations and if the position does not relate to bioassay but another form of carcinogenesis work, can you tell us why it was felt it was a higher priority?

Could you also designate what branch and section each position will be assigned to?

Dr. NEWELL. We will have that for you.

[The information follows:]

[Clerks note: The 60 individual job descriptions has not been included in the following information.]

National Cancer Institute

Carcinogenesis Positions

The sixty positions provided for carcinogenesis efforts were largely in response to the needs of the total Carcinogenesis effort including research in in vitro studies, toxicology and metabolism, and pathology as well as the Bioassay (testing) Program. In order to better focus on improving the bioassay operations, reorganization of the operational structure is being brought about. Although the total research effort is essentially the same, the former Carcinogenesis Program is being organized into a Carcinogenesis Research Program and a Carcinogenesis Testing Program. In addition, a Clearinghouse for Environmental Carcinogens has been established to advise the Director, NCI, on matters concerning efforts to identify and evaluate chemical carcinogens as well as be responsive to requests for advice on environmental carcinogens. Another office, the Scientific Coordinator for Environmental Cancer, is a major source of expert advice in the fields of environmental cancer and toxicology, providing assessment of carcinogenic hazards to other government agencies and industry. A newly established Diet and Nutrition Program is investigating the role of nutritional elements and factors in the causation of cancer. The establishment of the two carcinogenesis programs as well as the administrative impact of the new positions requires additional administrative support in direct assistance to the new programs. Fifty-one of the new positions are contained in the Carcinogenesis Research and Carcinogenesis Testing Program. The remaining nine positions are distributed over the Clearinghouse, the Diet and Nutrition Program, the Scientific Coordinator's office and the Administrative Office concerned with environmental carcinogenesis activities.

The following table reflects a summary of the 60 positions for carcinogenesis efforts. Job descriptions for each position are also included.

60 Carcinogenesis Positions

Division of Cancer Cause and Prevention

Title	Grade	Number
Biological Scientist Administrator	GS-15	1
Health Scientist Administrator	GS-15	2
Veterinary Medical Officer	GS-15	1
Visiting Scientist	N/A	1
Chemist	GS-14	2
Education Officer	GS-14	1
Health Scientist Administrator	GS-14	1
Industrial Hygienist	GS-14	1
Pharmacologist (Toxicologist)	GS-14	5
Veterinary Medical Officer	GS-14	1
Veterinary Pathologist	GS-14	5
Visiting Associate	N/A	1
Cell Biologist	GS-13	1
Geneticist	GS-13	1
Health Scientist Administrator	GS-13	2
Medical Officer	CO-4	1
Microbiologist	GS-13	3
Statistician	GS-13	1

Title	Grade	Number
System Analyst	GS-13	1
Pathobiologist	GS-12	1
Staff Fellows	N/A	5
Administrative Assistant	GS-11	1
Computer Programmer	GS-11	1
Collaborative Program Assistant	GS-9	1
Microbiologist	GS-9	1
Biochemist	GS-7	1
Biologist	GS-7	3
Administrative Clerk	GS-6	1
Committee Assistant	GS-6	1
Biological Laboratory Technician	GS-5	1
Clerk (typing)	GS-5	2
Secretary	GS-5	6
Clerk-Typist	GS-4	3
Total		60

Summary by Organization

Division of Cancer Cause and Prevention

Organization	Number
Carcinogenesis Testing Program	31
Carcinogen Bioassay and Resources Branch	(13)
Office of Associate Director for Carcinogenesis Testing	(5)
Technical Information Resources Branch	(1)
Toxicology Branch	(3)
Tumor Pathology Branch	(9)
Carcinogenesis Research Program	20
Biology Branch	(3)
Carcinogen Metabolism and Toxicology Branch	(4)
Chemistry Branch	(4)
Experimental Pathology Branch	(4)
Lung Cancer Branch	(3)
Office of Associate Director for Carcinogenesis Research	(2)
Office of Division Director	9
Diet, Nutrition and Cancer Program	(1)
National Clearinghouse on Environmental Carcinogenesis	(4)
Scientific Coordinator for Environmental Cancer	(2)
Administrative Management Branch	(2)
Total	60

POSITIONS FOR ENVIRONMENTAL EPIDEMIOLOGY BRANCH

Mr. OBEY. Last year we talked about the personnel needs of the Environmental Epidemiology Branch. On page 129 of the last year's hearings, the Institute testified that they had not given the Branch the full 17 positions requested because of the lack of qualified people available in epidemiology. In other words, you did not think the slots could be filled.

I know it is early this year, but how are you coming in recruiting people for those slots?

Dr. NEWELL. Very well. We have given the 17 slots to the Environmental Epidemiology Branch which in fact doubles their size. Dr. Fraumeni has plans to hire five professionals with two to three backup persons each. He has 10 on board or name commitments. Three of those 10 are in fact senior-type professional epidemiologists. So we are well on mark in filling those positions.

Mr. OBEY. So you are telling me you do think you are going to be able to fill those 17 positions?

Dr. NEWELL. Yes, sir. It looks very hopeful.

Mr. OBEY. If recruitment is going that well, could we perhaps expand that area again in 1978? I wonder if you could ask Dr. Fraumeni and the branch chiefs of the carcinogenesis program to give you the number of people which they in their best professional judgment think they could use in fiscal year 1978, their best judgment as of today based on what they know about the positions they have received this year and the prospects for filling those positions?

Would you forward those remarks of Dr. Fraumeni and the branch chiefs in the carcinogenesis program along with your own evaluation of manpower needs in this area for inclusion in the record.

Dr. NEWELL. Yes, sir.

[The information follows:]

National Cancer Institute
Position Needs, FY 1978
Carcinogenesis Program and Environmental Epidemiology Branch

Environmental Epidemiology Branch

Remarks of Dr. Joseph Fraumeni - Based on our experience with recruitment this year, on the number of qualified investigators in the field of environmental epidemiology, and on the need for continued expansion of our program, we feel that the Environmental Epidemiology Branch could easily recruit and effectively utilize 12 new positions in FY 1978. These positions would include 5 epidemiologists, 3 research assistants, 2 secretaries, 1 computer programmer, and 1 statistical clerk. The enlarged staff will enable us to augment existing project areas, and initiate new lines of research.

Special emphasis will be placed on the following areas: (1) Research to identify the environmental causes of cancer in high-risk communities that we previously identified by mapping of cancer mortality on a county level. Many promising leads are being pursued, but more studies are needed to cover several cancers occurring excessively in various parts of the country. (2) To help clarify the environmental determinants of cancer, collaborative studies will be developed with component units of the Surveillance, Epidemiology and End Results (SEER) Program that has population-based cancer registries located around the country, and with several federal and state agencies having unique statistical or environmental data. (3) Studies to clarify the carcinogenic potential of several drugs, particularly hormones and cytotoxic agents. A major new program will utilize the several NCI-sponsored cancer therapy trials to monitor the occurrence of new cancers that might result from treatment. (4) Investigations to assess the carcinogenic influence of chemical pollutants in the workplace and in the general environment, including water and air. Occupational studies will emphasize hazards that may spread beyond plant confines or contribute to the "hot spots" on the cancer maps. (5) Epidemiologic and interdisciplinary studies to evaluate the nutritional constituents and mechanisms involved in cancer etiology. (6) Collaboration with laboratory investigators to evaluate the role of candidate viruses and genetic susceptibility in carcinogenesis.

Thus, the increased level of staffing will help ensure a comprehensive and well-balanced program in environmental epidemiology and will enlarge our capacity to develop leads and settle key questions in cancer etiology.

Carcinogenesis Program

The following summary of positions was requested by the branch chiefs in the Carcinogenesis Program as additional position needs for FY 1978.

Carcinogenesis Research Program

Office of the Associate Director - 2 positions

Lung Cancer Branch - 3 positions

Carcinogen Metabolism and Toxicology Branch - 1 position

Chemistry Branch - 4 positions

Experimental Pathology Branch - 10 positions

Biology Branch - 6 positions

Carcinogenesis Testing Program

Technical Information Resources Branch - 1 position

Pathology Branch - 2 positions

Carcinogen Bioassay Branch - 3 positions

Evaluation of Above Position Needs by Director, NCI

I fully endorse the position requirements of both Dr. Fraumeni and the Carcinogenesis branch chiefs. There are two problem areas: adequate space and the availability of qualified professionals. Without additional space, it would be difficult to accomodate many new positions in the above listed programs. We are presently trying to relieve overcrowded conditions in both the Epidemiology and Carcinogenesis Program areas.

The second consideration is that of qualified professionals to fill positions. A realistic evaluation of recruitment for the recently allocated 77 slots (17 for the Environmental Epidemiology Branch and 60 for the Carcinogenesis Program) serves to emphasis the scarcity of premium professionals (particularly toxicologists and epidemiologists). We are, due to this limited availability, instituting a special recruitment effort in filling the 77 positions. In addition, these areas are ones that are receiving emphasis throughout our training programs, specifically through National Research Service Awards.

In summary, I believe that the above constraints would make the immediate filling of sizeable additional positions in these areas difficult. However, I fully endorse the need for these positions as outlined by Dr. Fraumeni and the Carcinogenesis Program, Division of Cancer Cause and Prevention branch chiefs. I would like to also submit that there are position requirements in other organizational entities of NCI that could be effectively utilized in the area of environmental carcinogenesis as well as other areas including clinical trials. There is a need for approximately 25 positions throughout the Institute (excluding the Divison of Cancer Cause and Prevention) for efforts in carcinogenesis, including the support elements of grant and contract administration, cancer communications, personnel recruitment, and research safety. Additionally, the program of clinical treatment research, including the clinical trials area, would require an increase of 30 positions to effectively exploit this area of research.

Mr. OBEY. What effect, if any, will the President's hiring freeze have on these positions?

Dr. NEWELL. I quite honestly don't know, Mr. Obey. A 25-percent reduction was mentioned in the newspaper last week, and I heard something about a freeze this morning. We will certainly give these positions the highest priority in terms of any kind of hiring ability that we do maintain.

Mr. OBEY. As soon as you do have an evaluation, would you submit that also for the record?

[The information follows:]

EVALUATION OF PRESIDENT'S HIRING FREEZE

It now appears that the President's hiring freeze will have an effect on the recruitment and filling of the 60 positions for the carcinogenesis program and the 17 for the Environmental Epidemiology branch. The information we have received imposes a limitation on the hiring of Federal civilian employees pending the establishment of revised employment ceilings which are expected in April.

As we understand it, our current employment ceiling is, for the time being, to be maintained at the February 28 onboard strength in full-time permanent positions plus any hiring commitments made in writing before March 1. Any full-time permanent positions filled from outside of HEW on or after March 1 may not exceed 75 percent of the number of vacancies created by people leaving jobs in the Department after February 28.

Dr. NEWELL. I think, Mr. Obey, the 77 total positions in the environmental carcinogenesis area certainly puts us in much better shape than we were before.

However, throughout the Institute, considering other high priority areas, I do have a very pressing need for more positions, particularly in the area of clinical trials. The demands for us to monitor our clinical trials and demands by the FDA are really increasing quite a lot. That is a high priority area.

Also, we need positions in our contracts and grants areas because the applications in environmental carcinogenesis have increased because of the popularity and the timeliness of the area. Those applications are processed in another division, but it is all backup help for environmental carcinogenesis.

CHEMICAL TESTING

Mr. OBEY. Last year when you were asked to prepare a chart listing what chemicals you had initiated tests on and when those tests were completed and the status of the reporting on those tests, that chart showed that over 200 chemicals had been tested with no reports filed, 169 had been off test for more than 6 months and 129 had been off test for more than a year.

You indicated the progress you felt you were making in that area. Could you in the chart the chairman asked you to prepare, could you list all of the chemicals which have been ordered tested under the Institute's bioassay operations, the date the experiment was initiated, date terminated and whether the experiment showed sufficient numbers of tumors to indicate whether or not the chemical may be carcinogenic?

Dr. NEWELL. Yes, I can get that for you. We did encounter some severe problems with that part of the program. We were not aware of them at the time of the testimony. Once we became aware of them, we took a series of corrective measures.

For example, we created a new position of Associate Director for Bioassay Testing so a professional can spend full time on that area. We have renegotiated with our prime contractor that is responsible for doing this, based on a study which we initiated.

[The information follows:]

NATIONAL CANCER INSTITUTE

DATA ON CHEMICALS IN BIOASSAY TESTING PROGRAM

The following tables reflect a list of the chemicals which have been tested under the Institute's bioassay program, the date the experiment was initiated, the date the animals were sacrificed, anticipated date for report issuance, the usage of the chemical and the carcinogenicity results of the bioassay.

The use code on the following tables is identified as follows:

Code:	*Usage*
Food	Food or food additives.
Pest	Pesticide.
Phar	Pharmaceuticals/biologicals.
Solv	Solvents.
Dye	Dye or dye manufacture.
Intr	Chemical intermediate or catalyst.
Reag	Chemical reagent.
Other	Other, unclassified.
Misc	Miscellaneous categories.

TABLE I. COMPOUNDS FOR WHICH FINAL REPORTS ARE AVAILABLE:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(1)
C00191	CHLORDECONE (KEPONE)	08/71	05/74	01/76	PEST	+
C02686	CHLOROFORM	02/72	04/74	06/76	SOLV	+
C04546	ETHYLENE, TRICHLORO-	04/72	05/74	01/76	SOLV	+

(1) POSITIVE OR NEGATIVE WITHIN THE EXPERIMENTAL LIMITS OF THE BIOASSAY.

TABLE II. COMPOUNDS FOR WHICH DRAFT REPORTS ARE BEING WRITTEN:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(1)
C02766	ACETIC ACID, NITRILOTRI-	02/73	02/75	04/77	MISC	+
C01445	ACETIC ACID, NITRILOTRI-, TRISODIUM = SALT MONOHYDRATE	02/73	02/75	04/77	INTER	+
C00099	CHLORDANE	10/71	12/73	04/77	PEST	+
C00113	DICHLOROVOS (VAPONA)	08/72	10/74	05/77	PEST	NOT YET DETERMINED
C00157	ENDRIN	06/72	07/74	03/77	PEST	-
C00135	DIMETHOATE	11/71	12/73	03/77	PEST	-
C04626	ETHANE, 1,1,1-TRICHLORO-	10/72	11/74	03/77	PEST	NOT YET DETERMINED
C00180	HEPTACHLOR	10/71	01/74	04/77	PEST	+
C01741	PHENFORMIN	02/73	02/75	03/77	PHAR	-

(1) POSITIVE OR NEGATIVE WITHIN THE EXPERIMENTAL LIMITS OF THE BIOASSAY.

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TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C01967	ACENAPHTHENE, 5-NITRO-	01/73	12/75	08/77	INTER	
C02108	ACETAMIDE	10/71	08/73	01/78	PHAR	
C01887	ACETANILIDE, 3-AMINO-4-ETHOXY-	05/72	03/75	12/77	PHAR	
C01978	P-ACETOPHENETIDE, 3'-NITRO-	09/72	10/74	11/77	MISC	
C01536	ACRONYCINE	02/72	03/76	09/77	PHAR	
C04682	ACTINOMYCIN D	03/69	10/71	01/78	PHAR	
C02095	ADIPAMIDE	11/71	03/74	12/77	MISC	
C01456	AFLATOXIN B1	07/72	08/75	03/78	PHAR	
C00044	ALDRIN	06/72	07/74	07/77	PEST	
C02437	AMINOCHLORODIPHENYL ETHER	06/70	06/72	12/77	PEST	
C03736	ANILINE	07/73	07/75	12/77	DYE	
C02039	ANILINE, P-CHLORO-	04/72	08/74	07/77	PHAR	
C02255	ANILINE, 2,4-DIMETHOXY-, HCL	01/74	01/76	10/77	DYE	
C01821	ANILINE, N,N-DIMETHYL-P-NITROSO-	02/72	02/75	06/77	DYE	
C01990	ANILINE, 4,4'-METHYLENE-BIS(N,N-DIMETHY	10/72	07/74	08/77	REAG	
C01707	ANILINE, 4,4'-THIODI-	09/72	09/74	09/77	INTER	
C02460	ANILINE, 2,4,6-TRICHLORO-	01/70	01/72	12/77	DYE	
C03587	ANILINE, 2,4,5-TRIMETHYL-, HCL	06/70	06/72	12/77	DYE	
C02288	ANILINE, 2,4,6-TRIMETHYL-, HCL	06/70	06/72	12/77	DYE	
C02993	P-ANISIDINE, 2-METHYL-	01/73	02/75	09/77	DYE	
C01934	O-ANISIDE, 5-NITRO-	08/72	03/75	08/77	INTER	
C01989	ANISOLE, 2,4-DIAMINO-, SULPHATE	04/72	03/75	11/77	MISC	
C01730	ANTHRANILIC ACID	01/73	03/75	03/78	PHAR	
C01945	ANTHRANILIC ACID, 4-NITRO-	02/72	03/75	06/77	INTER	
C01876	ANTHRAQUINONE, 2-AMINO-	03/72	12/74	08/77	DYE	
C01901	ANTHRAQUINONE, 1-AMINO-2-METHYL-	09/72	10/74	06/77	DYE	
C01923	ANTHRAQUINONE, 2-METHYL-1-NITRO-	02/73	03/75	03/77	MISC	
C02697	ASPIRIN, PHENACETIN, CAFFEINE	06/72	08/74	07/77	PHAR	
C04728	ARABINOSYLCYTOSINE	06/69	07/71	01/78	PHAR	
C00408	CHLOROBENZILATE	05/71	06/73	05/77	PEST	
C04137	ACRIDINE, 3,6-DIAMINO-, HCL	06/73	07/75	03/77	PHAR	
C04535	ETHANE, 1,1-DICHLORO-	04/72	05/74	05/77	SOLV	
C03974	ACETIC ACID, (ETHYLENEDINITRILO)TETRA-=, TRISODIUM SALT	07/73	08/75	05/77	PHAR	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C02120	L-ARGININE GLUTAMATE	10/71	02/73	12/77	PHAR	
C01569	5-AZACYTIDINE	04/72	11/73	09/77	PHAR	
C03474	AZATHIOPRINE	06/69	05/71	01/78	PHAR	
C00066	AZINPHOS-METHYL	11/71	12/73	07/77	PEST	
C06371	AZIRIDINE, 2-METHYL-	01/68	03/70	07/77	INTER	
C02926	AZOBENZENE	06/73	07/75	03/78	PEST	
C02426	BENZENE, 1-CHLORO-2,4-DINITRO-	06/70	06/72	12/77	DYE	
C02415	BENZENE, 1-CHLORO-2-NITRO-	06/70	06/72	12/77	DYE	
C02404	BENZENE, 1-CHLORO-4-NITRO-	01/70	01/72	12/77	DYE	
C00419	BENZENE, PENTACHLORONITRO-	09/71	10/73	07/77	PEST	
C01912	BENZIMIDAZOLE, 6-NITRO-	03/72	03/75	11/77	MISC	
C02006	BENZOPHENONE, 4,4'-BIS(DIMETHYLAMINO)-	01/72	07/74	06/77	DYE	
C03850	P-BENZOQUINONE, DIOXIME	05/73	06/75	10/77	MISC	
C02664	BIPHENYL, CHLORO-	09/72	10/74	03/78	MISC	
C06382	BIS(2-HYDROXYETHYL)DITHIOCARBAMIC = ACID, POTASSIUM SALT	03/69	03/71	07/77	MISC	
C01592	1,4-BUTANEDIOL, DIMETHANESULFONATE	07/72	11/74	09/77	PHAR	
C02131	N-BUTYLUREA	05/72	03/74	11/77	MISC	
C00077	CAPTAN	11/71	05/74	07/77	PEST	
C00544	CARBAMATE, 4-DIMETHYLAMINO-3,5-XYLYL-N-	01/72	03/74	07/77	PEST	
C04608	CARBANILIDE, 4,4'-DIACETYL-BIS(AMIDI= NOHYDRAZONE), DIMETHANE SULFONATE	08/69	03/71	01/78	PHAR	
C01898	CARBAZOLE, 3-AMINO-9-ETHYL-	07/72	03/75	09/77	MISC	
C03043	CARBAZOLE, 3-AMINO-9-ETHYL-, HCL	07/72	03/75	09/77	DYE	
C04591	CARBON DISULFIDE	06/72	09/74	12/77	SOLV	
C06417	CARBONIC ACID, CYCLIC ETHYLENE ESTER	03/69	03/71	07/77	INTER	
C00055	CHLORAMBEN	12/71	04/74	07/77	PEST	
C03485	CHLORAMBUCIL	04/69	08/71	01/78	PHAR	
C00533	CHLOROPICRIN	03/72	04/74	06/77	PEST	
C01558	CHOLESTEROL, (P-(BIS(2-CHLOROETHYL)= IN AMINO)PHENYL) ACETATE	06/72	02/76	12/77	PHAR	
C01467	CYCASIN	08/73	08/75	03/78	MISC	
C02277	CYCLAMATE, SODIUM SALT	03/70	03/72	12/77	FOOD	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C04900	CYCLOPHOSPHAMIDE	05/69	05/71	01/78	PHAR	
C00102	DACONIL	02/72	06/74	06/77	PEST	
C01718	DAPSONE	05/72	05/74	08/77	PHAR	
C01683	DARAPRIM	01/73	01/75	03/78	PHAR	
C04693	DAUNOMYCIN	04/69	08/71	01/78	PHAR	
C04933	O,P'-DDD	09/69	08/71	03/78	PEST	
C00475	P,P'-DDD	08/71	09/73	07/77	PEST	
C00555	P,P'-DDE	07/71	11/73	07/77	MISC	
C00464	P,P'-DDT	02/72	11/73	07/77	PEST	
C01581	BETA-DEOXYTHIOGUANOSINE	07/73	04/75	10/77	PHAR	
C06393	DIALLATE	03/69	03/71	07/77	PEST	
C03269	DIARYLANILIDE YELLOW	03/73	03/75	08/77	DYE	
C03656	DIBENZO-P-DIOXIN	01/72	06/74	01/78	INTER	
C03667	DIBENZO-P-DIOXIN, 2,7-DICHLORO-	11/71	12/74	01/78	PEST	
C03678	DIBENZO-P-DIOXIN, 1,2,3,4,6,7,8,9-OCTAC	12/71	07/73	01/78	PEST	
C01661	DIBENZYLINE HYDROCHLORIDE	07/72	06/76	10/77	PHAR	
C04795	DIBROMODULCITOL	07/69	08/71	01/78	PHAR	
C04762	DIBROMOMANNITOL	08/69	06/71	01/78	PHAR	
C03270	TRIS(2,3-DIBROMOPROPYL)PHOSPHATE	03/74	07/76	09/77	MISC	
C02028	DIBUTYLTIN DIACETATE	09/72	09/74	08/77	INTER	
C00486	DICOFOL (KELTHANE)	09/71	10/73	08/77	PEST	
C02448	DICYCLOPENTADIENE DIOXIDE	01/70	01/72	12/77	MISC	
C00124	DIELDRIN	03/72	05/74	06/77	PEST	
C00599	DIELDRIN, PHOTO-	03/72	05/74	08/77	PEST	
C01547	DIMETHANE SULFONATE	05/72	12/74	05/77	PHAR	
C00395	DIOXATHION	06/71	07/73	08/77	PEST	
C02700	DIPENTYLAMINE, N-NITROSO-	07/72	08/75	03/78	MISC	
C02244	DIPHENYLAMINE, 4-NITROSO-	07/72	09/74	09/77	MISC	
C03009	2,5-DITHIOBIUREA	12/72	01/75	12/77	INTER	
C03918	DMBA	09/73	09/75	03/78	INTER	
C01605	EMETINE	06/72	10/74	09/77	PHAR	
C00566	ENDOSULFAN	01/72	02/74	06/77	PEST	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C01570	ESTRADIOL MUSTARD	07/72	04/74	12/77	PHAR	
C00522	ETHANE, 1,2-DIBROMO-	03/72	03/74	08/77	PEST	
C00511	ETHANE, 1,2-DICHLORO-	03/72	05/74	07/77	SOLV	
C04604	ETHANE, HEXACHLORO-	05/72	09/74	11/77	SOLV	
C03554	ETHANE, 1,1,2,2,-TETRACHLORO-	02/72	03/74	06/77	PEST	
C04579	ETHANE, 1,1,2-TRICHLORO-	05/72	08/74	07/77	SOLV	
C06406	ETHER, BIS(2-CHLOROETHYL)-	02/69	02/71	07/77	PEST	
C01694	ETHIONAMIDE	04/73	04/75	10/77	PHAR	
C04580	ETHYLENE, TETRACHLORO-	05/72	12/74	07/77	SOLV	
C05710	GRISEOFULVIN	10/71	10/73	03/78	PEST	
C04819	GUANAZOLE	05/69	08/71	01/78	PHAR	
C02653	HEXACHLOROPHENE	09/72	10/74	03/78	PEST	
C03054	HYDANTOIN, DICHLORODIMETHYL-	06/73	08/75	08/77	PEST	
C04739	HYDRAZINE, 1-ACETYL-2-PICOLINOYL-	06/69	08/71	01/78	PHAR	
C01854	HYDRAZINE, 1,1-DIPHENYL-	04/72	03/75	08/77	REAG	
C03258	HYDROXYLAMINE, N-NITROSO-N-PHENYL-, = AMMONIUM SALT	03/73	03/75	09/77	REAG	
C04831	HYDROXYUREA	04/69	05/71	01/78	PHAR	
C04717	IMIDAZOLE-4-CARBOXAMIDE-5-(3,3-DIMETHYL-1-TRIAZENO)-	07/69	10/71	01/78	PHAR	
C01616	IMIDAZOLE MUSTARD	09/69	08/71	01/78	PHAR	
C02175	ISOCYANIC ACID, 3,3'-DIMETHOXY-4,4'-BIPHENYLENE ESTER	05/73	05/75	09/77	INTER	
C01038	ISOPHOSPHAMIDE	02/72	10/73	06/77	PHAR	
C01478	LASIOCARPINE	07/73	07/75	03/78	PHAR	
C01489	LEAD ACETATE	08/72	09/74	03/78	DYE	
C00204	LINDANE	09/71	10/73	05/77	PEST	
C00215	MALATHION	12/71	04/74	06/77	PEST	
C04853	MELPHALAN	05/69	06/71	01/78	PHAR	
C04944	D-MELPHALAN	09/69	03/71	03/78	PHAR	
C04886	6-MERCAPTOPURINE	06/69	10/71	01/78	PHAR	
C04637	METHANE, TRICHLOROFLUORO-	01/72	12/74	12/77	SOLV	
C04568	METHANE, TRIIODO-	04/72	07/74	11/77	PHAR	
C03190	METHANSULFON-M-ANISIDE, 4'-(9-ACRIDINYLAMINO)-, MONOHYDROCHLORIDE	10/73	02/76	03/77	PHAR	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING OBTAINED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C03849	METHIODAL SODIUM	06/73	08/75	10/77	MISC	
C04671	METHOTREXATE	03/69	04/71	01/78	PHAR	
C04875	METHOTREXATE, DICHLORO-	06/69	09/71	01/78	PHAR	
C00497	METHOXYCHLOR	07/71	10/73	06/77	PEST	
C02380	4,4'-METHYLENE-BIS-(2-CHLOROANILINE) = HYDROCHLORIDE	06/70	06/72	12/77 12/77	MISC	
C03010	METHYL ORANGE B	12/72	03/75	12/77	REAG	
C04784	METHYLTHIOINOSINE	04/69	06/71	01/78	PHAR	
C00428	MIREX	02/70	02/72	07/77	PEST	
C04706	MITOMYCIN C	05/69	09/71	01/78	PHAR	
C02164	MORPHOLINE, 4-NITROSO-	01/74	01/76	03/78	REAG	
C01956	NAPHTHALENE, 1-NITRO-	03/72	02/75	09/77	DYE	
C00431	NICLOSAMID	11/71	12/73	11/77	PEST	
C03792	NITHIAZIDE	10/73	03/76	12/77	PHAR	
C00420	NITROFEN	12/71	01/74	09/77	PEST	
C04740	1-NITROSOUREA, 1-(2-CHLOROETHYL)-3-CYCL	02/70	09/71	01/78	PHAR	
C02084	NITROUS ACID, SODIUM SALT	11/71	03/73	11/77	FOOD	
C00439	OXAMIDE, DITHIO-	01/69	01/71	07/77	REAG	
C04126	2-OXETANONE, 3,3-DIMETHYL-	08/73	09/75	10/77	INTER	
C00226	PARATHION	12/71	01/74	08/77	PEST	
C03963	PHENOL, 4-AMINO-2-NITRO-	03/74	03/76	10/77	DYE	
C03305	M-PHENYLENEDIAMINE, 4-CHLORO-	04/73	04/75	12/77	MISC	
C03292	O-PHENYLENEDIAMINE, 4-CHLORO-	03/73	04/75	06/77	INTER	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C02482	M-PHENYLENEDIAMINE, DIHYDROCHLORIDE	01/70	01/72	12/77	REAG	
C02493	O-PHENYLENEDIAMINE, DIHYDROCHLORIDE	06/70	06/72	12/77	DYE	
C03941	O-PHENYLENEDIAMINE, 4-NITRO-	03/74	04/76	07/77	REAG	
C02222	P-PHENYLENEDIAMINE, 2-NITRO-	06/72	08/74	06/77	REAG	
C02233	P-PHENYLENEDIAMINE, N-PHENYL-, HCL	02/73	12/74	08/77	DYE	
C00588	PHOSPHAMIDON	03/72	04/74	06/77	PEST	
C04922	PHOSPHORODIAMIDIC ACID, N,N-BIS(2-= CHLOROETHYL)-N'-3-HYDROXYPROPYL = CYCLOHEXYLAMINE	09/69	08/71	01/78	PHAR	
C00237	PICLORAM	12/71	04/74	07/77	PEST	
C01627	2,6-PIPERAZINEDIONE-4,4'-PROPYLENE = DIOXOPIPERAZINE	05/72	01/74	01/78	PHAR	
C02813	PIPERONYL BUTOXIDE	07/73	08/75	03/78	PEST	
C02824	PIPERONYL SULFOXIDE	06/73	10/75	03/78	PEST	
C04897	PREDNISONE	05/69	10/71	01/78	PHAR	
C01810	PROCARBAZINE HYDROCHLORIDE	05/72	01/74	07/77	PHAR	
C00500	PROPANE, 1,2-DIBROMO-3-CHLORO-	03/72	08/73	08/77	PEST	
C06440	1,2-PROPANEDIOL, 3-CHLORO-	02/70	02/72	07/77	DYE	
C04615	PROPENE, 3-CHLORO-	05/72	08/74	06/77	INTER	
C03076	PROPIONIC ACID, 3-NITRO-	03/73	04/75	08/77	PHAR	
C01785	PYRAZINECARBOXAMIDE	01/73	02/75	11/77	PHAR	
C01672	PYRIDIUM	10/72	01/75	12/77	PHAR	
C02506	SACCHARINE	02/70	05/72	07/77	FOOD	
C06097	SACCHARINE, SODIUM SALT	03/70	03/72	12/77	FOOD	
C05981	SEMICARBAZIDE, MONOHYDROCHLORIDE	03/69	03/71	07/77	REAG	
C06462	SODIUM AZIDE	01/69	01/71	07/77	PHAR	
C06473	SODIUM BISULFIDE	02/69	02/71	07/77	DYE	
C02459	4'-STILBENAMINE, 2,5-DIMETHOXY-	03/70	03/72	12/77	INTER	
C03167	STREPTOZOTOCIN	12/69	06/71	01/78	PHAR	
C02200	STYRENE	09/73	09/75	09/77	MISC	
C02211	STYRENE, BETA-NITRO-	03/73	04/75	08/77	INTER	
C03827	SUCCINIC ACID, MONO(2,2-DIMETHYLHYDRAZI	06/73	07/75	09/77	PEST	

(2) ANALYSIS NOT COMPLETE.

TABLE III. COMPOUNDS FOR WHICH BIOASSAY HAS BEEN COMPLETED AND REPORTS ARE BEING DRAFTED (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(2)
C00453	SULFALLATE (CDEC)	06/71	07/73	09/77	PEST	
C02379	3,3',4,4'-TETRAAMINODIPHENYL TETRAHYDRO CHLORIDE	03/70	03/72	12/77	REAG	
C00168	TETRACHLORVINPHOS	03/72	04/74	06/77	PEST	
C02471	TETRAFLUORO-M-PHENYLENEDIAMINE DIHYDRO= CHLORIDE	03/70	03/72	12/77	INTER	
C03065	THIAZOLE, 2-AMINO-5-NITRO-	03/73	04/75	08/77	PHAR	
C04557	THIOPHENE, 2,5-DIHYDRO-, 1,1-DIOXIDE-	04/72	06/74	09/77	SOLV	
C06451	THIOSEMICARBAZONE	02/69	02/71	07/77	REAG	
C01649	THIO TEPA	05/72	03/75	10/77	PHAR	
C01832	TOLUENE-2,5-DIAMINE, SULFATE	03/72	02/75	07/77	MISC	
C05129	TOLUENE, 2,4-DIAMINO-, HYDROCHLORIDE	06/70	06/72	12/77	INTER	
C01865	TOLUENE, 2,4-DINITRO-	02/72	11/74	06/77	DYE	
C02346	M-TOLUIDINE HYDROCHLORIDE	06/70	06/72	12/77	DYE	
C02040	P-TOLUIDINE, 3-CHLORO	04/72	08/74	08/77	INTER	
C02051	O-TOLUIDINE, 5-CHLORO-	04/72	04/74	09/77	INTER	
C02357	P-TOLUIDINE, HYDROCHLORIDE	04/70	04/72	12/77	DYE	
C01843	O-TOLUIDINE, 5-NITRO-	04/72	07/74	07/77	DYE	
C02153	P-TOLYLUREA	12/71	03/74	12/77	MISC	
C00259	TOXAPHENE	08/71	09/73	06/77	PEST	
C02391	S-TRIAZINE, 2,4-DIAMINO-6-PHENYL-	10/69	10/71	12/77	INTER	
C00442	TRIFLURALIN	05/71	06/73	07/77	PEST	
C00260	TRIPHENYLTINHYDROXIDE	05/73	05/75	10/77	PEST	
C01729	TRYPTOPHAN, L-	02/73	02/75	11/77	FOOD	
C01490	URACIL, 2-THIO-	08/72	08/75	03/78	PHAR	
C04773	UREA, 1,3-BIS(2-CHLOROETHYL_-1-NITROSO-	04/69	01/71	01/78	PHAR	
C01763	UREA, 1-BUTYL-3-(P-TOLYLSULFONYL)-	03/73	05/75	10/77	PHAR	
C01752	UREA, 1-((P-CHLOROPHENYL)SULFONYL)-3-PR	07/73	07/75	11/77	PHAR	
C04524	UREA, N,N'-DICYCLOHEXYLTHIO-	06/73	07/75	09/77	INTER	
C02073	UREA, (P-ETHOXYPHENYL)-	10/71	10/73	12/77	FOOD	
C03372	UREA, ETHYLENETHIO-	02/69	02/71	07/77	MISC	
C02017	UREA, 1-PHENYL-2-THIO-	10/72	10/74	08/77	REAG	
C02186	UREA, 1,1,3-TRIMETHYL-2-THIO-	02/72	07/74	07/77	INTER	
C04842	VINBLASTINE	05/69	05/71	01/78	PHAR	
C04864	VINCRISTINE	06/69	08/71	01/78	PHAR	
C06484	VINYLENE CARBONATE	07/70	07/72	07/77	SOLV	
C02313	2,4-XYLIDINE HYDROCHLORIDE	06/70	06/72	12/77	DYE	
C02324	2,5-XYLIDINE HYDROCHLORIDE	01/70	01/72	12/77	DYE	
C03816	UREA, 1,3-DIETHYL-2-THIO-	07/73	09/77	11/77	OTHER	

(2) ANALYSIS NOT COMPLETE.

TABLE IV. COMPOUNDS FOR WHICH HISTOPATHOLOGY OF TEST ANIMAL HAS NOT BEEN COMPLETED:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(3)
C03770	ACETANILIDE, 4'-(CHLOROACETYL)-	11/73	02/76	11/77	DYE	
C02960	AMMONIUM, (2-CHLORCETHYL)TRIMETHYL-, CH	07/73	02/76	03/78	PEST	
C02299	ANILINE, 2,4,5-TRIMETHYL-	02/74	02/76	03/78	DYE	
C03747	O-ANISIDINE HYDROCHLORIDE	03/74	03/76	02/78	DYE	
C03758	P-ANISIDINE HYDROCHLORIDE	03/74	03/76	01/78	DYE	
C03032	ANISOLE, 2,3,5,6-TETRACHLORO-4-NITRO-	05/73	05/76	01/78	PEST	
C03521	1H-BENZOTRIAZOLE	05/73	07/75	01/78	INTER	
C01434	1-BUTANOL, 4-(BUTYLNITROSAMINO)-	06/70	09/74	07/78	MISC	
C02937	CALCIUM CARBIMIDE	03/74	06/76	03/78	PEST	
C03565	C.I. VAT YELLOW 4	09/73	09/75	03/78	DYE	
C03661	5BETA-CHOLAN-24-OIC ACID, 3ALPHA-HYDROX	06/73	09/75	11/77	REAG	
C02982	P-CRESIDINE	05/73	05/75	10/77	DYE	
C03598	P-CRESOL, 2,6-DI-TERT-BUTYL-	11/73	03/76	03/78	FOOD	
C03689	P-DIOXANE	12/71	06/74	01/78	SOLV	
C02680	DIPHENYLAMINE, N-NITROSO-	02/74	09/76	03/78	PEST	
C02868	ETHANE, 1,1-DICHLORO-2,2-BIS(P-ETHYLPHE	06/73	09/76	03/78	PEST	
C02857	ETHYL TELLURAC	07/73	11/75	03/78	PEST	
C02959	ETHYL TUADS	11/73	06/76	03/78	PEST	
C03261	ETHYLENEDIAMINE, N-1-NAPHTHYL-, DIHYDRO CHLORIDE	07/73	08/75	10/77	REAG	
C01423	GUANIDINE, 1-METHYL-3-NITRO-1-NITROSO-	06/72	08/74	07/78	INTER	
C02142	HEXANAMIDE	11/71	03/74	12/77	MISC	
C02891	LEAD DIMETHYLDITHIOCARBAMATE	11/73	11/75	03/78	PEST	
C03021	1,5-NAPHTHALENEDIAMINE	06/73	06/75	10/77	INTER	
C03952	NORPHENAZONE	10/73	12/75	12/77	DYE	
C02904	PHENOL, 2,4,6-TRICHLORO-	06/73	07/75	03/78	PEST	
C03930	P-PHENYLENEDIAMINE, DIHYDROCHLORIDE	02/73	05/76	12/77	REAG	
C03316	P-PHENYLENEDIAMINE SULFATE, 2-CHLORO-	08/73	08/75	12/77	INTER	
C02971	PHOSPHOROTHIOIC ACID, O,O-DIMETHYL O-=P-NITROPHENYL) ESTER	07/73	08/75	03/78	PEST	

(3) HISTOPATHOLOGY AND ANALYSIS NOT COMPLETE.

TABLE IV. COMPOUNDS FOR WHICH HISTOPATHOLOGY OF TEST ANIMAL HAS NOT BEEN COMPLETED:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(3)
C03612	PHTHALAMIDE	11/73	11/75	03/78	INTER	
C03601	PHTHALIC ANHYDRIDE	10/73	10/75	03/78	PEST	
C03907	PYRIDINE, 2-(CHLOROMETHYL)-, HCL	11/73	04/76	11/77	INTER	
C03838	PYRIDINE, 3-(CHLOROMETHYL)-, HCL	11/73	11/75	11/77	INTER	
C02835	SODIUM DIMETHYLDITHIOCARBAMATE	09/73	06/76	03/78	PEST	
C02302	TOLUENE-2,4-DIAMINE	10/73	02/76	03/78	DYE	
C02368	O-TOLUIDINE, 4-CHLORO-, HYDROCHLORIDE	01/70	01/72	12/77	DYE	
C02335	O-TOLUIDINE HYDROCHLORIDE	04/70	04/72	12/77	DYE	
C03781	TRIMETHYL PHOSPHATE	05/73	08/75	10/77	MISC	
C04820	URACIL MUSTARD	04/69	07/71	01/78	PHAR	
C02119	UREA	10/71	02/73	12/77	PHAR	
C03247	UREA, 1-((P-ACETYLPHENYL)SULFONYL)-3-=CYCLOHEXYL-	09/73	10/75	11/77	PHAR	
C03805	UREA, (2-BROMO-2-ETHYLBUTYRYL)-	05/73	08/75	10/77	PHAR	
C03327	UREA, 1-(HEXAHYDRO-1H-AZEPIN-1-YL)-3-=P-TOLYLSULFONYL)-	10/73	11/75	11/77	PHAR	

(3) HISTOPATHOLOGY AND ANALYSIS NOT COMPLETE.

TABLE V. COMPOUNDS FOR WHICH BIOASSAY TESTING HAS BEGUN BUT NO DATA ARE AVAILABLE:

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(4)
C50215	ACRYLONITRILE	SC			INTER	
C01514	ADRIAMYCIN	02/75	03/77	02/78	PHAR	
C50475	AGAR AGAR	SC			FOOD	
C08640	ALDICARB	02/75	02/77	02/78	MISC	
C50464	ALLYL ISOTHIOCYANATE	SC			PHAR	
C50613	AMINO UNDECANOIC ACID	SC			INTER	
C08684	ANILAZINE	02/75	02/77	02/78	PEST	
C50011	BENZOIN	02/75	05/77	05/78	PHAR	
C50282	2-BIPHENYLAMINE	10/76	10/78	10/79	INTER	
C50635	BISPHENOL A	SC			MISC	
C54375	BUTYL BENZYL PHTHALATE	SC			MISC	
C50646	CAPROLACTAM	SC			MISC	
C53781	C.I. DISPERSE YELLOW 3	SC			DYE	
C03510	CINNAMYL ANTHRANILATE	10/74	11/76	11/77	FOOD	
C08662	COUMAPHOS	12/74	01/77	01/78	PEST	
C50737	CYTEMBENA	11/76	11/78	12/78	MISC	
C53792	D & C RED #9	SC			DYE	
C50657	DIALLYLPHTHALATE	SC			MISC	
C50260	1,4-DIAMINO-3,6-DICHLOROBENZENE	SC			INTER	
C08673	DIAZINON	04/75	04/77	04/78	PEST	
C03703	DIBENZO-P-DIOXIN, 1,2,3,6,7,8-HEXACHLOR	01/75	11/77	11/78	PEST	
C03714	DIBENZO-P-DIOXIN, 2,3,7,8-TETRACHLORO-	01/75	11/77	11/78	PEST	
C03690	DIBENZO-P-DIOXIN, 2,3,7-TRICHLORO-	11/76	11/78	11/79	PEST	
C54262	1,1-DICHLOROETHYLENE	SC			OTHER	
C51581	CIS, 1,2-DICHLOROETHYLENE	SC			OTHER	
C54591	TRANS, 1,2-DICHLOROETHYLENE	SC			OTHER	
C52733	DI(2-ETHYLHEXYL)PHTHALATE	SC			MISC	
C50055	DIMETHYLTEREPHTHALATE	04/75	04/77	04/78	INTER	
C50668	4,4'-DIPHENYLMETHANE DIDSOCYANATE	SC			MISC	
C00522	ETHANE, 1,2-DIBROMO-	07/76	07/78	11/79	PEST	
C50384	ETHYL ACRYLATE	SC			MISC	
C50453	EUGENOL	SC			PHAR	
C08651	FENTHION	01/75	02/77	02/78	PEST	
C08695	FLUOMETURON	03/75	12/77	12/78	PEST	

SC -- CHEMICAL IN SUBCHRONIC TESTING. CHEMICALS HAVE BEEN SELECTED AND PRELIMINARY TESTING HAS BEGUN.

(4) BIOASSY IN PROGRESS.

TABLE V. COMPOUNDS FOR WHICH BIOASSAY TESTING HAS BEGUN BUT NO DATA ARE AVAILABLE (CONT'D):

NCI #	CHEMICAL NAMES	START DATE	SACR DATE	REPORT DATE	USE	CARCINOGENICITY(4)
C50748	GUM ARABIC	SC			FOOD	
C50395	GUM GUAR	SC			FOOD	
C54364	GUM TARA	SC			FOOD	
C50259	HEXAMETHYLMELAMINE	02/75	03/77	03/78	PHAR	
C50419	LOCUST BEAN GUM	SC			FOOD	
C00215	MALATHION	08/75	08/77	03/78	PEST	
C50362	MANNITOL	SC			INTER	
C50715	MELAMINE	SC			MISC	
C50000	MENTHOL	12/74	01/77	01/78	PHAR	
C50680	METHYL METHACRYLATE	SC			INTER	
C50102	METHYLENE CHLORIDE	SC			SOLV	
C54604	4,4'-METHYLENEDIANILINE	SC			OTHER	
C53838	ORANGE G (C.I. ACID ORANGE 10)	SC			DYE	
C50146	4,4'-OXYDIANILINE	09/76	09/78	09/79	INTER	
C04580	PERCHLOROETHYLENE	SC			SOLV	
C50124	PHENOL	10/75	02/79	02/80	PHAR	
C50588	PROPYL GALLATE	SC			FOOD	
C50599	PROPYLENE OXIDE	SC			INTER	
C50157	RESERPINE	10/75	10/77	08/78	PHAR	
C54546	SELSUN	02/76	02/78	02/79	PHAR	
C02722	STANNOUS CHLORIDE	SC			DYE	
C53929	SUDAN I (SOLVENT YELLOW 14)	SC			DYE	
C50022	SULFISONAZOLE	02/75	03/77	03/78	PHAR	
C52459	1,1,1,2-TETRACHLOROETHANE	SC			OTHER	
C04240	TITANIUM OXIDE(TI O2)	12/74	01/77	01/78	MISC	
C50317	TOLUENE-2,6-DIAMINE DIHYDROCHLORIDE	06/76	07/78	07/79	DYE	
C50533	2,4-TOLUENE DIISOCYANATE	SC			MISC	
C50226	ZEARALENONE	SC			INTER	
C50442	ZIRAM	SC			PEST	

SC -- CHEMICAL IN SUBCHRONIC TESTING. CHEMICALS HAVE BEEN SELECTED AND PRELIMINARY TESTING HAS BEGUN.

(4) BIOASSY IN PROGRESS.

Mr. OBEY. I will be getting into that in a couple of minutes.

IN-HOUSE RESEARCH

Of the amount appropriated for the Institute last year, what portion went for in-house research and internal operations?

Dr. NEWELL. It is 13 percent that goes for in-house research and the NIH management fund. Contracts are 37 percent and grants are 50 percent of the total budget.

CONTRACT REVIEW

Mr. OBEY. Since such a significant portion of your budget does go into contracts, do you have procedures for reviewing contract proposals in order to insure that those proposals meet minimum research standards?

Dr. NEWELL. Yes, sir. We abide by the Government regulations pertaining to contract procurement. All of our research contracts are reviewed by peer review groups which are chartered, made up of at least 75 percent of non-NCI and non-Government people, and chaired by an outside chairman.

Mr. OBEY. You have both in-house review and review by your advisory committees, don't you?

Dr. NEWELL. If it is a resource contract; if we are buying serum or cells we do consider that in-house, but we consider that a purchase contract. But all the research contracts are reviewed by outside committees which are chartered.

Mr. OBEY. As you know, I have been concerned about a number of NCI contracts.

Dr. NEWELL. Yes, sir.

Mr. OBEY. One is the prime contract arrangement with Tracor-Jitco. The way this has been explained is that you hire a contractor to manage your contracts because you did not feel you had the manpower to do so in-house. Is that a fair description?

Dr. NEWELL. Yes, sir.

Mr. OBEY. How much money have you spent each year through Tracor-Jitco?

Dr. PETERS. Currently $8.7 million.

Mr. OBEY. My office has been told that you intend to terminate that prime contractor arrangement. Is that correct?

Dr. PETERS. Not terminate it, but restructure it to bring more of the decision making process back into the NCI. We felt it would be better if NCI controlled it.

Our original justification for that contract was because we did not have the support in-house. Now through this committee's action we have received the additional positions and we feel the management should be back in NCI.

Mr. OBEY. What role will Tracor-Jitco play?

Dr. PETERS. More of a support role; in pathology, and report writing, in the routine logistics of getting the chemicals out to the subcontractors, to be sure they arrive with the animals on time, that sort of thing.

Mr. OBEY. Could you expand more for the record so we will understand what role they will be playing?

Dr. PETERS. Yes, sir.

[The information follows:]

ROLE OF TRACOR JITCO

The role of the prime contractor, Tracor Jitco, Inc., in the bioassay program of the National Cancer Institute (NCI) has changed appreciably since August 1976. NCI has taken additional responsibility for scientific management of the bioassay program including restructuring of the committees that deal with chemical selection, experimental design, and data evaluation to effect more efficient functioning of the program.

It is anticipated that the role of the prime contractor will change even more as the newly authorized staff positions for the National Cancer Institute are filled. As the new staff assumes the roles presently performed by Tracor Jitco, Inc., personnel, the Tracor Jitco orientation will shift gradually toward a strictly support function, for example, they will carry out NCI activities and decisions in the bioassay program. Specifically, Tracor Jitco will provide support to the NCI committees that deal with chemical selection, experimental design, and data evaluation; procure chemicals; prepare literature searches where necessary; maintain a list of qualified laboratories for animal testing; make contractual arrangements for placing chemicals on test; handle the routine administrative facets of bioassay; supplement NCI staff in monitoring the subcontractors throughout the country; and provide support personnel for specific tasks in pathology, statistics, and report writing.

Mr. OBEY. Mr. Chairman, my 10 minutes are up.

Mr. FLOOD. Mr. Early?

AUTHORIZING LEGISLATION

Mr. EARLY. Doctor, does the authorizing legislation for the cancer program expire this year?

Dr. NEWELL. My understanding, sir, is that we can continue to function under the Public Health Service Act. Because the amendments of 1974 are an amendment to that act, they will probably stay in effect so that we can continue to function pretty much as we are now.

Mr. EARLY. Is that all activities?

Mr. BROWNING. This is all activities. We can function under section 301 of the Public Health Service Act. The authorization levels were renewed in the National Cancer Act of 1971 as amended in 1974. That runs out at the end of 1977.

Mr. EARLY. So the authorization expires but you will not be curtailed?

Mr. BROWNING. Section 301 of the Public Health Service Act gives authority for funds as necessary. We can revert back to that.

Mr. EARLY. I would think that is pretty blanket funding.

Mr. BROWNING. We can revert to that if we have to.

Dr. FREDRICKSON. The 1-year extension has been discussed and is expected to take place.

Mr. EARLY. Do you see any major changes being made in the legislative authority which would affect priorities for 1978?

Dr. NEWELL. No, sir, not really because the authorization committee wished to renew the act for only 1 year. We submitted some changes but they were really changes more on a technical level and really no substantive changes at least for this year.

Mr. EARLY. So as far as our investigations they must be extremely general. We are not too restricted on any of them by legislation?

Dr. NEWELL. Yes, sir.

Mr. FLOOD. If the gentleman will yield, Mr. Mansfield, you seem to be mumbling there. Do you have any reaction there?

Mr. MANSFIELD. No; that is correct. We have no problem.

SURVIVAL RATE

Mr. EARLY. In your statement you say the survival rate for cancer patients in certain age groups is improving and in other age groups there has been no improvement at all. Why is this?

Dr. NEWELL. Yes, sir. If I could direct your attention to this chart which is part of your material, each line is a different age group. You will notice that in people under the age of 35, the death rates have been declining steadily starting in about 1967. The reason for that is that these are the kinds of cancers that we can now cure.

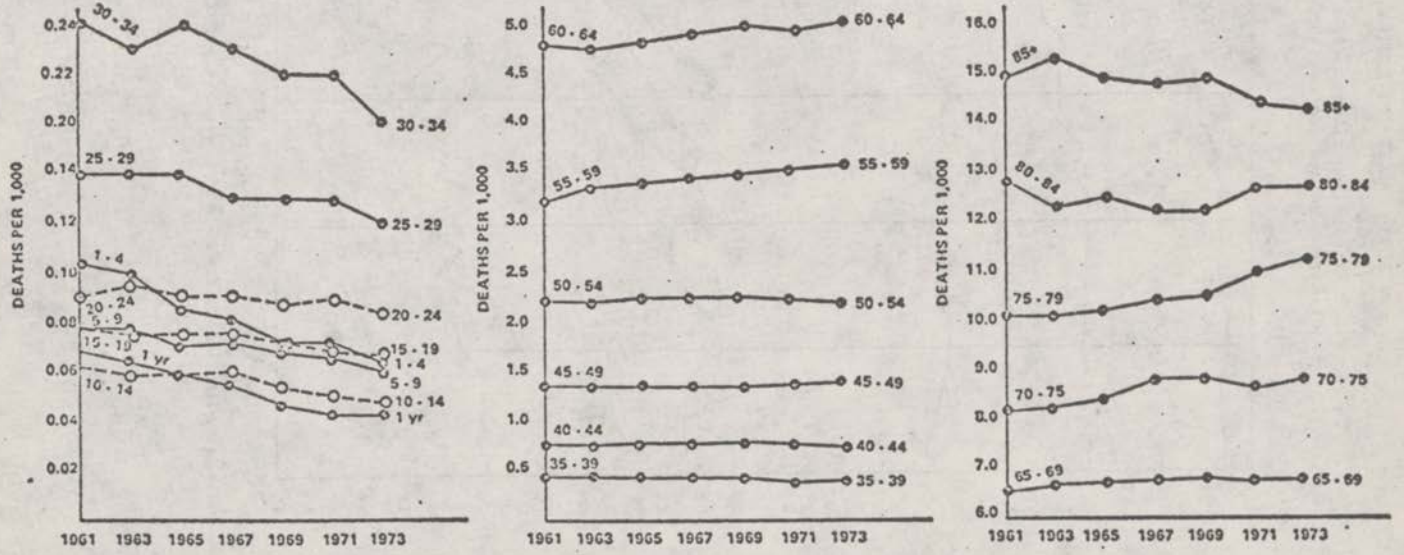
Mr. EARLY. Mr. Chairman, I would like to have the survival charts inserted in the record at this point.

Mr. FLOOD. It is so ordered.

[The information follows:]

NATIONAL CANCER INSTITUTE

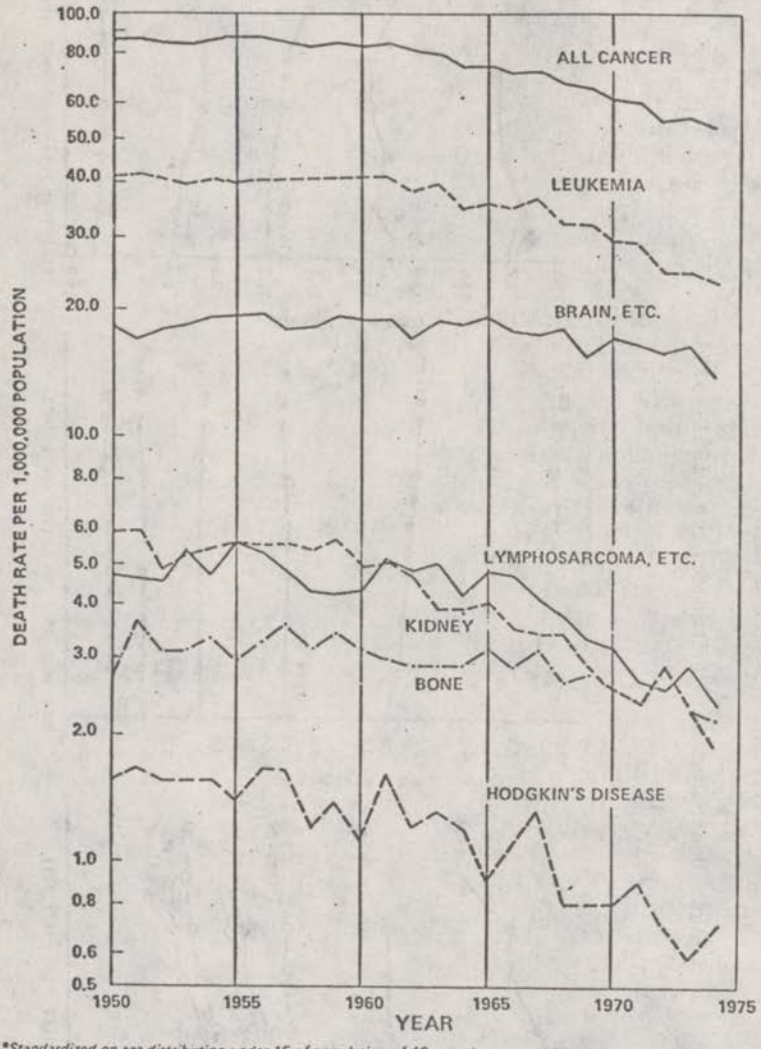
Cancer Death Rates - United States, 1961-1973



*Source of data: U.S. Public Health Service

NATIONAL CANCER INSTITUTE

Cancer Death Rates - In Children, Ages under 15,
Major Sites, United States, 1950-1974



*Standardized on age distribution under 15 of population of 46 counties around 1950. Source of data: U.S. Public Health Service.

Dr. NEWELL. I think it is important that just a few years ago we practically never spoke of curing cancer. Now we do. Dr. DeVita at the table here was very instrumental in developing the cure for Hodgkins disease.

Mr. FLOOD. Did you say cure?

Dr. NEWELL. That is correct, sir. I think this is reflected by the increase in survival rates.

The other thing important here is that the decrease in death rates is in fact reflected in national figures. It is not just decrease in a certain study population. It is reflected in the Nation as a whole which I think is very important.

The other thing that is important here is that the alleged 5.2 percent increase in cancer deaths in the year 1974–75 was a mistake. When we had the full year's experience, and required adjustments, we found that the overall rate increased by 0.7 percent. So that the so-called environmental time bomb as some people called it was a mistake.

Now the exciting thing, I think, Mr. Early, looking at this chart and I will ask Dr. DeVita to speak to it more if you care to hear more about it, is that the time is right to take some of the technology that we have learned from studying rarer cancers in children and young adults under the age of 35 and translating that into treatment of more common cancers of adults. I think it is within our grasp in the next few years if we are successful, and there is every reason to believe we will be, to effect a downturn in death rates in adults as well.

Mr. EARLY. So you are suggesting we are going to do more implementing from the studies rather than just studying the studies?

Dr. NEWELL. That is part of what I implied.

Mr. EARLY. I agree with you. It is decisionmaking time. We can keep studying forever and a day without obtaining what we are after.

CANCER CASES REPORTED

Tell me, is the number of reported cases of cancer in this group, is that also declining?

Dr. NEWELL. It depends on the type of cancer. Lung cancer is increasing very rapidly. Stomach cancer is decreasing. In black males, lung cancer and cancer of the prostrate is increasing. Pancreas cancer is increasing.

So it depends on the type of cancer. Overall incidence is increasing about 1 percent per year.

Mr. EARLY. Are we improving the problem or shifting the statistics?

Dr. NEWELL. It is more than just shifting the statistics.

MANPOWER

Mr. EARLY. Mr. Obey's question on those 60 positions for the carcinogenesis program, I think you suggested you have 17 positions.

Dr. NEWELL. Of the 77 positions, 17 were earmarked for the Environmental Epidemiology Branch. It is 10 of those 17 that we have name commitments for right now. Of the 60, we have a plan. We have 31 ongoing personnel actions out of the 60 and we have a plan to have the total 60 committed by the end of this fiscal year.

Mr. EARLY. What kind of people are you looking for?

Dr. PETERS. Experts in the field of epidemiology, toxicology, pharmacology, physiology, and other fields.

Mr. EARLY. Are these people in short supply?

Dr. PETERS. Yes, sir, particularly epidemiology and toxicology.

Mr. EARLY. Are you putting in money in developing this manpower?

Dr. PETERS. We are trying. It is difficult.

Mr. EARLY. Where is the difficulty in putting your money there?

Dr. PETERS. The difficulty is in attracting the right kind of people into these professional categories.

Mr. EARLY. My question is, are you spending your money to develop in that area?

Mr. BROWNING. In training under the National Research Services Awards Act, we are trying to emphasize that area.

Mr. EARLY. I would think the private sector would also need the same specialists.

Dr. PETERS. Indeed it does and there will be severe competition for them, particularly with the passage of the Toxic Substances Control Act.

Mr. EARLY. Wouldn't the private market want it?

Dr. PETERS. The requirements for premarketing under the Toxic Substances Control Act will make it an extremely severe problem.

Mr. EARLY. So you are working with the profession as far as developing along those lines?

Dr. PETERS. Wherever we can, but I predict we will be in competition with industry for these people.

LESS HAZARDOUS CIGARETTE

Mr. EARLY. You say in your statement you have developed a less hazardous cigarette. Can you tell us more about that?

Dr. NEWELL. Mr. Early, the decision was made some years ago that it didn't seem like we were doing very well in educating people not to begin smoking cigarettes and to educate people who were smokers to stop. There were some exceptions. By and large the physician community stopped cigarette consumption and people with higher education decreased their cigarette consumption, but there was still a large portion of the population that could not be instructed to do that.

The decision was made that another approach would be to develop so-called less hazardous cigarettes. I think we realize some inherent danger in that we did not want to encourage anybody to begin smoking or continue.

Mr. EARLY. What is it made from?

Dr. NEWELL. It has been made from regular tobacco but they have been able to leach out the tar and reduce the nicotine.

Mr. EARLY. How do you know how hazardous it is?

Dr. NEWELL. Early figures from epidemiologic studies indicate that people who began smoking the filtered cigarette have a lower risk of developing lung cancer than those who started smoking earlier and continued to smoke the high tar, high nicotine cigarette. The risks are lower. I would like to emphasize, it is not a safe cigarette.

Mr. EARLY. Who is the manufacturer?

Dr. NEWELL. Philip Morris. There are a couple on the market. Merit, Now, and Kent Lights. Merit is the most popular one.

Mr. EARLY. You mean people who smoke heavily are now shifting?

Dr. NEWELL. We have some data.

EQUIPMENT

Mr. EARLY. Last year we questioned Dr. Rauscher at length about the budget for equipment. Now if we look at your 1978 budget request and add that to what you spent in the last 3 years, the total expenditure will be over $20 million in a 4-year period. I am not a scientist, but I see in the table you provided for the record last year that such items as electron microscopes were purchased in 2 consecutive years. Can't we get longer use than that? Do we need new equipment all the time?

Dr. NEWELL. Better equipment becomes available from year to year.

Mr. EARLY. Is it improved equipment or purchasing the same microscopes?

Dr. NEWELL. No; this equipment has a turnover rate like all equipment does. New equipment comes out like the EMI Scanner, the brain and body scanner. We had one last year, it was being used all the time. So we purchased another one because the demand for that equipment was so great.

Mr. EARLY. We can't really afford the luxury of telling a scientist that this is a new piece of equipment, get rid of the other one and get a new one. You know the problems Mr. Flood has each year carrying this to the floor. It is getting more and more difficult.

As the people are hurting more fiscally, they are looking for cuts in every area. While cancer used to be a sacred cow, it is not as sacred as it was 10 years ago.

Dr. NEWELL. I understand that. I assure you we will not replace equipment in laboratories that doesn't need replacing. We will take a look at this.

Mr. EARLY. Is your intramural research program growing so rapidly that you need to buy new equipment to set up new laboratories?

Dr. NEWELL. No; we are limited in terms of intramural laboratories by the amount of space we have. The intramural program, the research part of it, has stayed at about 10 percent of our budget. This gets hit hard because of inflation, of course, pay raises and that kind of thing. That has been the reason why the intramural program has increased.

But in terms of research scope it is pretty much limited by the in-house space for it.

Mr. EARLY. Will you update the table on page 109 of last year's hearings and also provide a brief explanation as to why each category of equipment is needed in 1978?

Dr. NEWELL. Yes, sir.

[The information follows:]

Mr. EARLY. I would like the Office of the Secretary to provide for the record an assessment of the National Institutes of Health equipment management system.

Dr. NEWELL. All right.

[The information follows:]

National Cancer Institute

Equipment for 1977 & 1978
Object Class 31
(In thousands)

Type of Equipment	1977 Estimate	1978 Estimate
Environmental & Safety	$621,000	$584,000
Laminar flow modules (Clinical)	(110,000)	(100,000)
Tissue culture hood, laminar hoods, biocontainment equipment and biological safety cabinets	(511,000)	(484,000)
Microscopes	455,000	203,000
Electron miscroscopes	(360,000)	(100,000)
Other	(95,000)	(103,000)
Serum & Chemical Analysis	1,806,000	1,731,000
Spectrophotometers	(643,000)	(570,000)
Scintillation counters	(334,000)	(275,000)
Liquid & gas chromatographs	(221,000)	(249,000)
Photon counting fluorimetric system	(34,000)	(0)
Amino acid analyzer	(55,000)	(60,000)
Gamma counters & beta counters	(177,000)	(200,000)
Other (ultrasound units, nuclear diagnostic system, cytoflurograph, etc.)	(342,000)	(377,000)
Constant Temperature Storage Environmental Chambers (Walk-in freezers, liquid nitrogen freezers, incubators, etc.)	325,000	353,000
Animal Equipment & Cages	710,000	505,000
Laboratory Support	817,000	737,000
Centrifuges/rotors	(375,000)	(288,000)
Fraction collector	(61,000)	(70,000)
Ultracentrifuges/rotors	(206,000)	(185,000)
Other laboratory equipment	(175,000)	(194,000)
Mechanical Support (Pumps, power supply, water chiller, etc.)	180,000	65,000
Patient Care & Treatment	267,000	1,632,000
Endoscopic/thoracic surgery equipment	(100,000)	(150,000)
Bronchfiberscope/examining tables	(36,000)	(0)
Linear accelerators/accessories	(0)	(1,200,000)
Physiologic monitoring equipment	(50,000)	(100,000)
Other	(81,000)	(182,000)
ADP Equipment/Computer Support (Adjunct computer systems)	275,000	155,000
Office Furniture & Equipment (Typewriters, desks, office machines, tables, chairs, etc.)	324,000	272,000
Photography (Film monitors/enlargers, dryers)	250,000	65,000
Miscellaneous (Replacement equipment and other equipment essential to laboratory operations)	280,000	250,000
Total	$6,310,000	$6,552,000

Justification for Equipment - FY 1978

Category

Environmental & Safety - $584,000

The continued priority in the areas of Immunology, Biochemistry and Viral Oncology requires considerable support for research containment and employee safety equipment. It is necessary to provide safety equipment to protect laboratory workers against the possible hazards of working with tumor materials and certain virus preparations.

Microscopes - $203,000

To replace obsolete microscopes which would hamper the need to perform sensitive immunodiagnostic tests to better understand the role of virus in cancer causation.

Serum & Chemical Analysis - $1,731,000

Analysis of viral proteins is becoming increasingly important to a fuller understanding of viral involvement in the malignant process. Additional equipment is needed in this category to facilitate studies in this complex area of research. This kind of equipment will enable the programs to analyze large volumes of chemical and biological materials.

Constant Temperature Storage Environmental Chambers - $353,000

Tumor materials and virus preparations must be preserved in the frozen state for future studies or for transfer to other investigators. Incubators are required for the growth and study of large quantities of cells.

Animal Equipment & Cages - $505,000

These funds will be used for upgrading and/or replacing obsolete animal care equipment in support of laboratory research.

Laboratory Support - $737,000

This type of basic equipment is necessary to support the research programs and should remain constantly at this level due to program turnover, equipment replacement and the need to have the most advanced equipment in the field, such as centrifuges, ultracentrifuges, and oxidizers.

Mechanical Support - $65,000

With the volume of research presently being undertaken, we constantly have need to replace worn-out pumps, power supplies, etc.

Patient Care & Treatment - $1,632,000

NCI will need two linear accelerators that must be incorporated into the reconstruction of the Radiation Oncology Facility in conjunction with the Ambulatory Care Research Facility. It also includes funds for an intensive care monitoring unit for the Surgery Branch as well as replacement equipment and monitoring equipment for radiation studies such as a radiation beam detector system, upgrading of dosimetry equipment and composite phantom for the EMI whole body scanner.

ADP Equipment Computer Support - $155,000

Basically for the purchase of data storage and retrieval type systems to retain research information.

Justification for Equipment - FY 1978--continued

Category

Office Furniture & Equipment - $272,000

For normal replacement of obsolete equipment and office furniture.

Photography - $65,000

Needed to refurbish several old dark room facilities which process images from the electron microscope work.

Miscellaneous - $250,000

Equipment which does not fall into a specific category and is needed to replace equipment essential to laboratory operations.

EQUIPMENT MANAGEMENT SYSTEM ASSESSMENT

The Department is unable at this time to provide an assessment of the NIH equipment management system. A complete report will be submitted to the Subcommittee by September 15, 1977.

DETECTION AND DIAGNOSIS

Mr. FLOOD. All right, now, Doctor, you have been out there several years. We have recognized for a long time the importance of early detection and diagnosis of cancer. We have certainly discussed this subject at great length in the past.

Why, then, in this area do you have budgeted only $49 million, about 6 percent of your budget?

Dr. NEWELL. Yes, sir, this is an important area. However, it is an area that with a stable budget the balance is arrived at, Mr. Chairman, depending on where opportunities seem to be. The area is important for two reasons.

First of all, early detection gives you a better chance of cure—that is the overriding thing—because the burden of the tumor is less when it is detected early so therapy is more effective.

Mr. FLOOD. How do you use the term burden?

Dr. NEWELL. The amount of tumor, the mass. If a tumor is this big, it is more difficult to treat than if it is the size of my thumb. What we are doing in detection, though, is very positive. Early detection for lung cancer looks very promising. However, it is so complicated that I don't think that the stage it is in now is anywhere near ready for wide application. It is still research.

Mr. FLOOD. What areas of research in early detection and diagnosis are you going to emphasize in fiscal 1978?

Dr. NEWELL. In the area of cancer of the cervix where we do have a fairly inexpensive test that can be applied with virtually no risk to the individual, our efforts there have been directed toward providing early detection in women in high risk groups.

Mr. FLOOD. What is a high risk group?

Dr. NEWELL. A woman in a rural area, black or other nonwhite, low-income status group, usually multiple pregnancies early in life. We can go to those women. We have projects now with 34 States. We are working through the State health departments.

So in the early days of cervical cancer detection the women who got the tests were not the women who needed it the most. They were affluent women in which cervical cancer was low to begin with.

So our attention is on the high risk groups, and we are screening about half a million women now in the country.

Mr. FLOOD. Is that good?

Dr. NEWELL. Yes, sir.

COMMUNICATION

Mr. FLOOD. Here is another one that has become quite a subject in the last couple of years for a lot of reasons. In this budget material you submitted and I will say you certainly do submit material and that is good, but you submitted this to the committee and you state that the Cancer Institute conducted a variety of activities which included communicate research and cancer control, and all that information to physicians.

What kind of activities are you referring to that are so successful and how successful are these activities in this important area now?

Dr. NEWELL. We do conduct a variety of activities. We respond to about a half million requests a year for various publications describ-

ing different types of cancer. We respond to about 50 letters or telephone inquiries daily that come from all over the country.

Our clinicians deal with a lot of different physicians calling in for consultation. That is one way we do it. Through the cancer control program we are setting up communication offices in the comprehensive center so that it can deal with the community hospitals in its own area.

Our philosophy is that physicians should go locally for the best consultation and patients should get advice locally wherever good, local advice is available. There is a lot of good, local advice available in the country.

So we view our role as one of putting the people together in the right places.

Mr. FLOOD. Doesn't the physician know in his own backyard where the center is?

Dr. NEWELL. Many times not. This is something we are trying to improve. I think we are making good progress.

CANCER CONTROL

Mr. FLOOD. Talking about evaluation, do you have an evaluation of this very program to determine how many physicians are reached and what they think about what you are doing?

Dr. FINK. Through NCI cancer control and additions to the program Dr. Newell mentioned, we have a variety of activities that deal with the practicing physician. If I could characterize them, I would like to describe them in two major categories, the first being the short-term demonstration and the second being the long term demonstration.

Mr. FLOOD. About 85 percent of the cancer patients are treated in community hospitals.

Dr. FINK. That is right.

Dr. NEWELL. There are 4,000 community hospitals, Mr. Chairman, that have greater than 50 beds per hospital. We estimate that we deal either directly or indirectly with somewhere between 1,700 and 1,800 of such community hospitals.

Mr. FLOOD. People just don't believe that.

Go ahead.

Dr. FINK. Yes; I was going to describe some of the short-term projects which would be our field tests and demonstrations.

For example, we have developed networks of community hospitals linked with the major cancer hospital to deal with several of the major cancer sites such as childhood leukemia, Hodgkins disease, breast, head, and neck cancer.

In order that the information at the local cancer hospital diffuses to the local practitioner, we have the centers outreach.

Other types of field tests and demonstration, as I mention, include these networks, our centers outreach program and a program we called the community-based program which deals with not only the health professional but the public at large within the community.

Mr. FLOOD. What do you mean by health professionals?

Dr. FINK. Physicians, nurses, and other types of individuals that deal with cancer patients at the community level.

Mr. FLOOD. Paramedics?

Dr. FINK. It could be that. When you think of the kinds of networks we have, outreach from cancer centers, the community-based programs, we have involvement on the order of 1,800 hospitals that Dr. Newell mentioned.

In addition we have programs that I think will lead to the long-term, upgrading of cancer care at the community level. For example, there are organizations such as the American Academy of Family Practice or the Association of Community Cancer Centers which deal with the practicing oncologists at the community level. We have activities with these organizations to determine what their membership feels are the important means of getting information to the community.

Mr. FLOOD. For the record on this one, since you are doing all this, submit for the record at least a couple of studies that you have finished, in the last 18 months.

Dr. FINK. Yes, fine.

Mr. FLOOD. The ones that evaluated your information to program physicians.

Dr. FINK. There is one other study I was going to mention which was called the Pattern-of-Care study.

Mr. FLOOD. Give us for the record some examples of evaluations completed in the last 18 months.

[The information follows:]

Evaluation Studies - Information Dissemination

Examples of information disseminations to practicing physicians which have been evaluated in the last 18 months are:

1. The Patterns of Care Study has surveyed all institutions which provide radiation therapy in the United States. The American College of Radiology and Dr. Simon Kramer of Jefferson University School of Medicine developed the best current management consensus for certain common cancer sites through consultation with at least 50 senior oncologists. Through this study, the treatment of cancer patients has been surveyed nationwide. Early findings include the following--1,013 hospitals have cobalt 60 units or linear accelerators, 50 percent of all cancer patients are treated with X-ray therapy at some time in the course of their disease, 1,074 full-time radiotherapists see an average of 237 new cancer patients and only 20 percent of all patients are treated in university hospitals, while about 66 percent are treated in community hospitals and 14 percent are treated in free-standing, X-ray therapy facilities. Documentation of deviations from the management consensus will provide a rational basis for developing targeted physician education programs through the American College of Radiology and other avenues of professional education.

2. Leukemia/Lymphoma Networks - An important goal of the Cancer Control Program is to shorten the time between important advances in treatments and their application to the cancer patient. In 1973, the most advanced methods of chemotherapy were available in relatively few hospitals in the United States. Seven projects were initiated, and have now been evaluated, to extend the recent progress in chemotherapy and in combined-modality therapy from existing centers of cancer care and research to community hospitals and physicians. Through the prototype networks created under the Prototype Clinical Chemotherapy Program in Cancer Control, selected centers, or "primary" hospitals, have been able to link satellite or affiliate hospitals and physicians to their chemotherapy activities and thereby assist in providing a major part of the patient's treatment in the satellite setting. This has been accomplished through the provision of educational programs, treatment guidelines and data collection assistance and guidance through collaborative programs. Network development, protocol development, and network coordination were funded by NCI, with treatment costs provided through sources other than the NCI.

Initially, the projects included only chemotherapy for acute lymphocytic leukemia (ALL) among children, Hodgkin's disease, and the other lymphomas in adults. One project was expanded during the third year to include the treatment of the other hematologic malignancies, i.e., chronic lymphocytic leukemia, chronic granulocytic leukemia, and multiple myeloma.

All contractors in this project developed treatment protocols for childhood acute leukemia and six projects developed the necessary protocols for all stages of adult lymphomas. Over 1,800 patients have been registered in the program and have received therapy and followup under supervision of the physicians participating in the networks. Pediatric patients with ALL have received treatment, such as: a) remission induction therapy using vincristine and prednisone; b) prophylactic central nervous system therapy using cranial radiotherapy or methotrexate; and, c) maintenance therapy using the combined 6-mercaptopurine and methotrexate, with "pulse" treatments of vincristine and prednisone. All these protocols have shown good early results in remission induction rates, remission duration, survival rates and in retarding the development of CNS leukemia.

Adult patients with Hodgkin's disease and patients with non-Hodgkin's lymphoma have been treated with radiation therapy, chemotherapy, or combinations of both, following complete staging workup at either the primary institution or network hospitals. Many of those patients requiring resources available only at medical centers were later able to return to their local communities for maintenance chemotherapy and followup by their own physicians. These projects have evaluated protocols for treatment and the effectiveness of the network approach, and will provide comparison data on the results, in both remission duration and survival, for the group of patients treated in their community with similar patients treated in institutions engaged in primary clinical research.

Furthermore, some of the leukemia/lymphoma network programs are exploring the limitations and, in some cases, the impracticality of administering treatment in rural, community hospitals. Some of the networks established in rural areas proved impractical, where true treatment networks could not be achieved without significant changes in resources and capability at the local level. Other projects operated well in the rural environment. These contrasting situations are providing information on approaches needed for future programs that will address the particular problems of rural areas on a larger scope.

The projects continue to exhibit the ability to greatly improve treatment over a large geographic area through the use of seed money to establish and manage cooperative networks and develop the tools (e.g., protocols, data collection, tumor boards, patient consultation registries, etc.) that capitalize on the use of available resources and on the desire of physicians and institutions to provide the best known care. Even in areas where resources were severely limited, a higher level of quality care than was previously possible has been provided within the network through the development of communications links with the centers of cancer care and research.

The primary problems that have been encountered and, by and large, solved were: a) delays in overcoming the provider's dependence on previous patterns of referral and consultation; b) delays required to resolve problems in the development of protocols just recently evolved out of the research phase; c) delays in reaching physicians in outlying areas; and, d) delays caused by requirements to organize means to assist busy practitioners in data collection. These problems were overcome in all the projects which were highly successful in the second half of their time period.

A further attribute of the approach used was the continuous evaluation of outcomes and entry rates that resulted in both improved protocol modification, and, in some projects, the entry into the program of most of the cases in the geographic area covered by the network.

Mr. FLOOD. Prior to Dr. Rauscher's departure from the Cancer Institute, he was saying, "The cancer control program is where the emphasis has got to be."

How much emphasis does this budget we are talking about give to cancer control activity?

Dr. NEWELL. Seven and one-half percent emphasis.

Mr. FLOOD. Which areas, then, of the cancer control did you give high priority to?

Dr. NEWELL. I think I will let Dr. Fink answer that.

Dr. FINK. Cancer control in the Cancer Institute is relatively new, being only 3 years old. In the formative stages the major activities were the interventions of detection, treatment, and rehabilitation. In the coming year more emphasis will be placed on preventive medicine and environmental carcinogenesis.

CURABLE CANCERS

Mr. FLOOD. Here is one question I intended to ask last year; I made a note about it. This answer certainly should get a lot of attention.

Of the 100 separate cancers, how many of them can be categorized now as controlled?

Dr. NEWELL. I am referring this to Dr. DeVita.

Mr. FLOOD. I don't blame you.

Dr. DEVITA. I can't give a firm answer. I think many of them have been curable to some degree for many years, and I think when Dr. Newell is referring to the——

Mr. FLOOD. In fairness to you, I mean controllable in the sense that it can be contained and the patient's life prolonged.

Dr. DEVITA. In the majority some fraction of the patients with that type of cancer can have their life prolonged or can be cured. It is a matter of how many. In lung cancer, few; in bowel cancer it has been 40 percent of all patients with bowel cancer. Now we have hopes to apply some of the new techniques Dr. Newell was referring to, to be able to prolong the life or cure the remaining 60 percent. For every one of them some fraction can be cured, but it varies.

Dr. NEWELL. For example, in breast cancer we reported last year the early results of what we call the adjuvant trial, where we began giving women after initial surgery chemotheapy rather than waiting for the initial recurrence. I am pleased to be able to say the preliminary results of that trial are holding up, especially in pre-menopausal women, so we can prevent the recurrence in over 90 percent of women with ancillary lymph nodes of the breast cancer. Now this prevention of the recurrence——

Mr. FLOOD. Do you want to give an age bracket on premenopausal?

Dr. NEWELL. Under 50, essentially. But this is holding up, and the same technique of adding drugs right after the initial treatment, surgery or radiation, looks very promising for cancer of the colon and ovary and some head and neck cancers.

Mr. FLOOD. This question is undoubtedly going to get a lot of attention when the record appears. If you feel, and I am sure you will, under the circumstances that you want to develop the answer to that question at some length in the record, please do.

Dr. NEWELL. Fine.

[The information follows:]

National Cancer Institute

Controllable Cancers

Although we think of cancer as 100 or more diseases, it is important to emphasize that the fifteen most common cancers kill more than 90% of all patients. A fraction of each type of cancer is curable by surgery and/or radiotherapy, but the great majority of patients are not. We have learned how to cure patients with advanced metastatic tumors, usually the leukemias and lymphomas, with chemotherapy and are now applying these lessons to the cancers referred to above.

The following table entitled "Ranking of 16 Non-Hematologic Malignancies for Combined Modality Priority" reflects 16 non-hematologic, common types of cancers, in terms of their current priority for adjuvant studies, based on frequency and likelihood of control. It is appropriate to emphasize that for each type of cancer listed in the accompanying table, if the opportunity exists to test adjuvant treatment in the postoperative period, each large clinical trial usually costs about a million dollars per trial per disease. As shown in the table, tumors are listed in the order of the opportunity presented, based on the criteria mentioned above, from those with the highest likelihood of success (with breast cancer as number 1) to some visceral malignancies with little likelihood of any effective control with currently available tools, such as esophogeal and pancreatic cancer.

The first column entitled "cell kill potential as determined in patients with advanced disease" refers to current information about our ability or inability to treat patients with metastatic cancer (that is, widespread cancer) in these tumors with either single drugs or combinations of drugs. One should note that when the cell kill potential is high (i.e. we have an effective drug treatment) and the potential for cure with regional types of treatment, such as surgery or X-ray therapy (in the next column) is poor, (even though the ability to remove the tumor may be satisfactory) an ideal circumstance exists for the testing of both drugs and local treatment together at the time of the initial diagnosis. Take as an example breast cancer. In the first column we see that the cell kill potential is noted to be very high with 60% of patients with metastatic cancer responding to drug combinations, with a significant fraction achieving "complete remission" which means a tumor can be made to disappear entirely. In the next column it is noted that the cell cure potential by surgery is excellent; that is, it is possible to remove the tumor in most cases, although about 55% of all patients recur; the column on the extreme right headed "Incidence or impact of tumors" indicates that breast cancer is the most common cause of death from cancer in women. These ingredients give this tumor a high priority for clinical trials. It should also be noted that the Institute has given this tumor a very high priority and the results have been extraordinarily satisfactory with a payoff already in sight for the adjuvant programs.

With the next tumor, ovarian cancer, the opportunity to treat with drugs is also high, the cure potential with surgery is low, although the tumor can usually be resected. This is a relatively common tumor of young women and yet few studies have been launched until recently.

Perhaps of most interest is number 3, colon cancer; in the first column you can see that until recently, the cell kill potential with drugs in patients with advanced disease has been poor, but recent leads (the identification of the antitumor activity of the combination of drugs 5-Flouruoracil and

methyl-CCNU) have increased our capability to explore adjuvant studies considerably. The column under "cure potential for initial surgery" shows that for colon cancer, overall, this is not too bad but about 60% of those who undergo curative resection will eventually relapse; it can be seen in the column at the far right that this is the second leading cause of death from cancer for both sexes, and, overall, it has the highest incidence for any type of cancer. We have recently invested a considerable amount of funds in clinical trials in colon cancer to explore the effectiveness of adjuvant treatment programs. Since 47,000 patients die each year as a result of recurrent colon cancer, the impact of successful adjuvant treatment programs applied to these 47,000 people should be obvious.

Similar progress has been made in recognizing the opportunity in developing new treatments for stomach cancer.

Number 5 on the list - because of the identification of new drug combinations that are effective in patients with advanced disease, not only have the recurrence rates after surgery been reduced (clinical trials still ongoing) but the extent of surgery has now been reduced as well, so the lives of most patients can be salvaged without loss of their limbs. This is a step in the right direction since the operations for these diseases had been extremely mutilating in the past.

Item 7 on the list, lung cancer, offers a new opportunity for adjuvant therapy, particularly in epidermoid carcinoma, (the commonest type) when it is caught early; but it can be seen from the next column that only 25% are actually operated on for cure and the 5-year survival of those patients is low. Recently, immunotherapy has been identified as a potential way of controlling this disease, in resectable patients, and a large scale clinical trial to attempt to verify this observation has just embarked.

Number 8, bladder cancer, offers a unique opportunity since we have recently identified drugs with some effect, but this tumor has been poorly studied because of speciality competition.

Similar studies are in progress exploring the same opportunities for combined modality therapy in melanoma, prostate cancer, testicular tumors, and brain cancer. Many of the other tumors could be considered "unstudied" at this point in time and yet opportunities exist. These studies are expensive; there is a limitation on the resources available to us to be able to proceed to fully explore the opportunity for combined modality therapy.

Also, clear from the table is that some tumors rank high (Number 6 - pancreas) in terms of potential interest because of the frequency of the disease, but the interest is not yet matched with opportunity. In pancreas cancer, for example, there are very few chemicals that actually have an impact on the survival of patients with advanced disease; surgery cures an extremely small fraction of patients and yet it is a common tumor. For the latter reason alone, we are investing some time and money into trying to break the initial barrier to identify new drugs with activity against this disease.

National Cancer Institute

RANKING OF 16 NON-HEMATOLOGIC MALIGNANCIES
FOR COMBINED MODALITY PRIORITY

TUMOR	CELL KILL POTENTIAL AS DETERMINED IN PATIENTS WITH ADVANCED DISEASE	CURE POTENTIAL FROM INITIAL SURGICAL OR X-RAY THERAPY WITH LOCAL OR REGIONAL DISEASE	INCIDENCE OR IMPACT OF TUMORS
1. Breast	Very High 1. ≅60% response rate with combinations. 2. Good durations of remission. 3. Significant rates of complete remissions. 4. Many active drugs.	Excellent 1. Almost all patients are eligible to receive treatment of curative intent, i.e., the primary tumor is removed. 2. Criteria exist for separating good and poor risk for cure.	Most common cause of death in women.
2. Ovary	High 1. Single agents can give 50% response rates and 20% complete remissions. 2. Several agents active. 3. Combinations poorly tested.	Generally Poor 1. Overall 5-year survival is 20-25%. 2. 36-50% of women inoperable when first diagnosed.	High incidence. Attacks relatively young women.
3. Colon	Poor but recently improved 1. Several "active" agents but none exceeds 20% response rate. 2. Recent identification of more effective combination of 5-FU and MeCCNU.	Good 1. ≅ 75% of patients amenable to curative resection. 2. Cure rate ≅ 50% in those undergoing curative resection.	Second leading cause of death from cancer for both sexes. Highest incidence for both sexes.
4. Stomach	Poor-Fair but recently improved 1. Several active drugs but none highly active. 2. Successes with combinations, e.g., BCNU + 5-FU, offer some hope of useful adjuvant treatment.	Fair-Poor 1. 25% of patients resectable for cure. 2. 25% of resected patients live 5 years. 3. Overall 5-year survival 12%.	Although incidence is dropping, still ranks 6 as a cause of death in United States. 21,000 new cases yearly with 15,000 deaths.
5. Sarcoma	Fair-Good 1. Some degree of activity for the few drugs tested. 2. Combinations give 40-50% response rates. 3. Complete remissions possible in advanced disease.	Variable Depending on the many histologic types.	Generally rare.
6. Pancreas	Poor Two or three minimally active drugs with little impact on survival.	Dismal Overall only 7-10% amenable to curative resection with high surgical mortality rate and minimal survival (5-10%).	Ranks 4 among cancers in terms of mortality. Incidence is rising dramatically.
7. Lung	1. Small cell—Fair. 2. Adenocarcinoma and large cell—Poor. 3. Epidermoid—Poor. 4. While response rates are reasonably high, impact on survival (small cell) is minimal.	Poor 1. Only 25% operable for cure. 5-year survival for those undergoing surgery is 25%.	The single and most important cause of death from cancer in the United States.
8. Bladder	Recently Improved 1. Some activity for adriamycin, 5-FU and alkylating agents. No good data for other drugs. 2. Poorly studied tumor.	Fair-Good 56% overall 5-year survival	24,000 new cases yearly with 7,000 deaths.

NATIONAL CANCER PROGRAM

National Cancer Institute

RANKING OF 16 NON-HEMATOLOGIC MALIGNANCIES
FOR COMBINED MODALITY PRIORITY (CONTINUED)

TUMOR	CELL KILL POTENTIAL AS DETERMINED IN PATIENTS WITH ADVANCED DISEASE	CURE POTENTIAL FROM INITIAL SURGICAL OR X-RAY THERAPY WITH LOCAL OR REGIONAL DISEASE	INCIDENCE OR IMPACT OF TUMORS
9. Melanoma	Fair-Poor 1. Only a few active drugs with none greater than 20% response rate. 2. No successful combinations to date.	Good 61% overall 5-year survival	5,200 estimated yearly deaths.
10. Prostate	1. Little information available on chemotherapy. 2. Poorly studied tumor.	Generally Good 1. Dependent on stage. 2. 51% overall 5-year survival.	45,000 new cases yearly with 18,000 deaths.
11. Cervix Uteri	Fair-Good 1. Several active agents, many not tried. 2. No combination data. 3. Poorly studied tumor.	Good Cure rate dependent on stage: IA–100% Both surgery IB–90% and x-ray IC–70% curative. II–50% 60% overall III–30% 5-year survival. IV–5%	57,000 new cases yearly with 9,000 deaths.
12. Testicular	Excellent Curative potential against metastatic disease. Highly active combinations.	Good Both surgery and x-ray cure.	Rare overall, but most common tumor in young men age 28-32.
13. Head and Neck	Appears Good (data somewhat scarce) 1. Several active agents MTX with 50% response rate when optimally used. 2. Most drugs not studied. 3. Almost no combination data.	Good Both surgery and radiotherapy curative. 50% overall 5-year survival. Varies with location of primary lesion.	31,000 new cases yearly with ≅ 10,000 deaths.
14. Brain	Poor 1. One active class of drugs with minimal impact on survival. 2. Most drugs not studied. 3. No combination data.	Depends on Histological Type in Grade III or IV glioma, no curative potential with surgery or x-ray alone. Overall survival at 5 years of all types is 23%.	8,000 estimated yearly deaths from all types. Attacks the young.
15. Kidney	None Most drugs not tested.	Fair 36% overall 5-year survival.	Estimated 9,000 deaths per year.
16. Esophagus	None	Dismal	Relatively uncommon.

Mr. FLOOD. Because when we get the bill on the floor and don't forget when we go on the floor, you are sitting up there in the balcony picking your teeth after lunch, but Mr. Obey and Mr. Early and me are down there in the well. So anything you can give us to help us out on that, we will appreciate.

Dr. DEVITA. One comment: I think when you said there are 100 kinds of cancer, how many are controllable, that thinking of 100 different cancers is useful from the point of view of considering the variability of cancer, but if you look at the top 15 killers, they account for 90 percent of cancer deaths.

COMPREHENSIVE CANCER CENTERS

Mr. FLOOD. Last year, the General Accounting Office did a study of the whole comprehensive cancer center program. One of their recommendations was to clarify the role of the centers as the focal points for the demonstration programs. What have you done about the GAO recommendation?

Dr. NEWELL. Well, our advisory board has a subcommittee on centers. They took a look at the recommendation and made some comments and then we have made our own set of comments, and I believe they have been submitted. The essence of the report is with 19 comprehensive cancer centers, how can we ever be expected to cover a large part of the population?

Mr. FLOOD. That is a rhetorical question.

Dr. NEWELL. What we have learned is this: The criteria for comprehensive cancer center means that the center has to have all the components from good basic research, through clinical research, through outreach and application. But to get the good basic research components in a comprehensive cancer center is difficult, because good basic research expertise does not have an even geographic distribution.

But it is not that difficult to get good clinical research. Our belief is that in an institution that has good clinical research will have good clinical care including its surrounding sister hospitals.

Mr. FLOOD. I believe you mentioned this. Have you conducted your own evaluation of this cancer center program in the last 18 months in order to find out to what extent is there community participation?

Dr. NEWELL. Yes.

Mr. FLOOD. And the extent to which these centers we are talking about have developed affiliations with these community hospitals, with physicians, et cetera? That is what you are talking about.

Dr. NEWELL. We can provide that for the record. We do have some information on that.

Mr. FLOOD. You can give us that for the record.

Dr. NEWELL. Yes, sir.

[The information follows:]

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National Cancer Institute

Cancer Centers Affiliation With Community

The Nation's cancer centers, and particularly the Comprehensive Cancer Centers are a major resource and a major force in providing professional assistance to the community hospitals and the community physicians to enable them to provide quality cancer care to their patients. Every Comprehensive Cancer Center has as a primary characteristic, the responsibility to do everything possible to help the communities and physicians in its area to insure that the best knowledge and treatment technology is provided to patients within the community setting wherever possible, and when necessary, to expedite appropriate referral to a cancer treatment center. National Cancer Advisory Board site visits to all Comprehensive Cancer Centers will be carried out during the next 12 months to insure that this responsibility to communities is being met.

Although Comprehensive Cancer Centers are not uniformly distributed throughout the United States, they are in fact reaching a large portion of the Nation's community hospitals and citizens. The latest survey of 15 of the centers showed that they were directly providing professional service and assistance to about 1,000 community hospitals involving approximately 45,000 health professionals.

These cancer centers influence and assist the community in many ways. A few examples are illustrative. One cancer center alone provides: (1) bi-monthly professional training programs to 19 community hospitals in its state; (2) physician tumor conferences, nursing in-service and rehabilitation consultations; (3) monthly cancer-site-specific symposium for community physicians; (4) visiting physician program for interested community practitioners; (5) an area-wide tumor registry system for 37 community hospitals which includes analytic reports to each hospital on its own cancer data as well as regional data; (6) a clinical newsletter providing professional information for community cancer control programs; (7) a closed circuit telephone educational program; and (8) a system whereby rehabilitation services employed at the center can be provided and continued in the community setting.

Most Comprehensive Cancer Centers have developed an extensive public information service utilizing a toll-free telephone line or alternative system to enable every citizen in their areas to have easy access to the latest available information on all aspects of cancer.

Several Comprehensive Cancer Centers have assisted communities by developing a network of multidisciplinary cancer care clinics which make possible the providing of sophisticated cancer care within the community. Such care would normally be provided only in a cancer center.

Cancer centers have become directly involved with local neighborhoods and lay organizations to determine cancer education needs, set up cancer screening programs, and to carry out health assessment projects.

Many of the centers provide radiation therapy dosage computing services to community radiation therapy departments thereby making available to the community the best available dosage technology as utilized at the Comprehensive Cancer Center.

Without dominating community medicine, the Comprehensive Cancer Centers are in fact a primary and dominant force in transferring the best possible cancer care practices to the community setting through extensive systems of professional relationships.

SURVIVAL RATES

Mr. FLOOD. In your discussion you said there was no significant increase in the survival rate of certain kinds of cancer patients. You mentioned that in your statement and you mentioned it here in passing a few minutes ago.

If that is so, then what is the rationale behind increasing the amount of funds here to be spent for cancer therapy in this proposal you have before us? If what you say is so, shouldn't we take that money, shift that over to cancer biology, shift it to cause and prevention research; isn't that where it belongs?

Dr. NEWELL. I don't think so, Mr. Chairman.

Mr. FLOOD. No increase in survival rates.

Dr. NEWELL. Well, we have learned much from studying cancer in children. I remember some years back we were criticized for spending as much money as we did in studying leukemia because there weren't many children with leukemia. But we learned from that research information that is at the point of being put in clinical trials that will have effect on common cancer in adults. We are already seeing it in breast cancer, and we have the opportunity for colon and rectal the same kind of benefit, and this is the largest killer in both men and women.

We have it for ovary cancer in women and head and neck cancers. You take these four types, that is almost 50 percent of all cancer in adults, so the opportunity from what we have learned in the past has never been better for widespread clinical trial and application now.

Mr. FLOOD. You are going to stand by your guns on it?

Dr. NEWELL. Yes, sir.

MAJOR OPPORTUNITIES TO PREVENT CANCER

Mr. FLOOD. What is your opinion and that of your advisors in the National Cancer Advisory Board, as to what are the major opportunities to prevent cancer today and also, of course, how does this budget that you are talking about here help you take advantage of those opportunities? We always wind up with that budget.

Dr. NEWELL. Yes, sir, you know it has been said in the press and by many of us that it seems like somewhere between 60 and 80 percent of cancers are environmentally related, and we agree with that, so we have to find out what is in the environment, and we have to clean it up as best we can.

That involves testing of carcinogens, but just as importantly it involves improvement in our ability to test carcinogens, our ability to do it quickly, economically, and much more precise than we are able to do now. But that certainly is a very high priority area for us in the future.

Mr. FLOOD. Major opportunities to prevent cancer today, this is from you, this big council, and everybody wants to know that.

Dr. NEWELL. Well, the major opportunities are not availing one's self of tobacco, of proper nutrition, identifying individuals at high risk and educating them, cleaning up the chemicals in the workplace, educating individuals in the workplace as to what chemical hazards there may be. All of these things have to be done, Mr. Chairman.

Mr. FLOOD. That is a tough question to answer off the top of your head, and I hate to brush off a question and answer by saying put it in the record but questions like this get answered more completely when supplied for the record. You know how this record is observed especially on a point like that.

[The information follows:]

National Cancer Institute

Major Opportunities to Prevent Cancer

We believe the major opportunities for prevention of cancer today have to do with implementing what we know how to do. For example, we have evidence that 30-40 percent of all cancer burden is due to tobacco usage. This applies not only to primary lung cancer but to esophageal, nasopharyngeal, head and neck, bladder, and pancreas. If we could induce people not to smoke, lung cancer would virtually disappear in less than a generation. In addition, there would be a dramatic decrease in other diseases such as cardiovascular disease and emphysema. In the area of secondary prevention, we could practically eliminate deaths due to two of the major forms of cancer in women. While we do not as yet know the cause of breast cancer we could greatly reduce mortality due to the disease through proper education practices. This refers specifically to women in high risk groups and to the utility of self-breast examination. When detected early enough, the treatment of breast cancer practically eliminates death due to this disease. Another major form of cancer in women, cervical cancer, could also be secondarily prevented if we could assure that every woman, particularly those in the high risk groups, receives a Pap test on a regular basis. Here again, when detected early enough proper treatment for cervical cancer results in an almost total elimination of deaths due to this disease.

Additional opportunities in the prevention of cancer today have to do with the identification of high risk groups. That is, individuals who are at excess risk because of their genetic background, their life style, their occupation, etc. Once identified, these individuals could be singled out for special intervention procedures including alteration of lifestyle, etc.

The NCI would require $888,238,000 in FY 1978 in order to continue all ongoing projects and maintain the same program level as in FY 1977. With the current budget estimate, intramural research will be kept at approximately the same operating level. There will be reductions of up to 10 percent in the operating levels (both grant and contract) activities of the Institute. In order to maintain the momentum of the National Cancer Program, an increase of $136 million would be required over the budget request of $818,936,000. Specifically in the area of cancer cause and prevention, with the scientific base of information we now have, it is possible to exploit new leads. For example, with an additional $10 million we would be able to expand carcinogenesis research including viral-chemical co-carcinogenesis, i.e., research in how viral or chemical agents act as initiators or catalysts in transforming cells to a malignant state. An additional $9 million could be effectively used in stepping up the chemical testing program both by actually testing more chemicals and by developing new, faster, more inexpensive, and more accurate methods of testing chemicals for cancer-causing properties. An additional $4 million could be used to expand epidemiological programs to determine the distribution of cancer in the population and to identify the factors that increase the risk of populations and individuals for development of cancer. Additional funds could also be utilized to fund high priorty grants in these and other areas of research in the cause and prevention of cancer.

Dr. PETERS. I would like to add to what Dr. Newell has said. Primarily one of the greatest potential advantages for reducing the cancer burden depends on our ability to alter our lifestyle. I think Dr. Newell alluded to that. It is mostly what we eat, smoke and drink. We also must consider occupational exposure and environmental exposure. It has been estimated that 60 to 90 percent of all cancers are due to environmental factors. However, environment means different things to different people. There is external environment, and internal environment.

Mr. FLOOD. What does it mean to you?

Dr. PETERS. I would prefer to categorize internal environment as those things over which we as individuals, have, to a large degree, personal control such as the decision to smoke or not to smoke, whether to remain obese, whether to consume alcohol, I classify as external environment those things over which we as individuals have relatively little control, such as environmental pollution and occupational exposure.

Mr. FLOOD. To be obese, itself, induces cancer?

Dr. PETERS. There is a link between obesity and certain forms of cancer.

Dr. NEWELL. May I expand for a second?

Mr. FLOOD. Yes.

Dr. NEWELL. In terms of what is environmental carcinogenesis, I think we can think of it in four ways. One is the study of known environmental carcinogens. For example, we have mentioned some, radiation, sunlight, tobacco, chemicals; second, the screening for new carcinogens, the study of known carcinogens, the determination of new carcinogens, this is our bioassay program, and this is where we need better techniques, identifying patterns, third, the epidemiology studies we were talking about earlier, and, lastly, and very importantly, we have to determine the mechanism by which agents, chemicals or other agents, do in fact cause cancer because the mechanism may be the only way that we can successfully interfere with the process.

There will undoubtedly be some chemicals and other agents that are going to be of great benefit to society. We are going to need to use some of those chemicals, so we have to know the mechanisms to intervene in the process.

CONSTRUCTION

Mr. FLOOD. We have to touch on these things in these hearings. Your budget proposes a reduction in construction funds.

Dr. NEWELL. Yes, sir.

Mr. FLOOD. I would rather talk about what you are talking about; we have to talk about construction funds. Pretty obviously from the budget you have decided that construction gets a much lower priority than research. OK, that may be good. However, have you determined the course of all of this, that the communities now are going to pick up a greater share of construction whenever it is needed for the cancer centers?

Dr. NEWELL. I think we have been blessed in the past several years where we have been able to do most of everything that our advisers suggest we do. Here we have essentially no increase in budget for the first year. Unfortunately, it is me, but somebody would have necessarily had to be faced with the decision of if you can't do everything,

what do you not do. It seems to me if we can only pay 38 percent of approved regular research grants, and we have to put more money into carcinogenesis and bioassay program, we have an opportunity to conduct additional clinical trials; these are our highest priority areas.

I don't mean to say construction is not of high priority. It certainly is. We simply don't have the best of all worlds, and I think I would rather pay for people whose applications have been approved than I would to build new buildings at this time.

Dr. FREDRICKSON. I agree with what Dr. Newell said, but it is important to note, that the remainder of the construction funds is not only for building new buildings but for other important construction projects such as to upgrading facilities for biological containment and protection in dealing with more hazardous problems of research today. This is an important part of that residual.

Mr. FLOOD. Biohazard containment?

Dr. FREDRICKSON. Yes; biohazard containment.

Mr. FLOOD. All right; we have had people tell us that we should not be supporting the construction of centers and putting new beds in for cancer patients. You have heard that one, especially in the last year. Instead they suggest right along that we should be spending money to encourage the development of the program to take advantage of the existing beds in community hospitals or community centers and to encourage a backup of a highly competent team, as you know, in a region.

What do you think of this development?

Dr. NEWELL. I think that is certainly one approach. That is the approach, for example, that has been taken in northern California, the so-called northern California cancer program. At that location there is no construction for new beds but also there are some very fine institutions, Stanford University of California at San Francisco.

Mr. FLOOD. I mean community hospitals, too, not just cancer centers.

Dr. NEWELL. That is correct. And the approach taken there is to organize the community hospitals in such a way that they take advantage of the expertise that already existed in these superb institutions and at the same time educate physicians——

COMMUNITY HOSPITALS

Mr. FLOOD. What do you mean by community hospitals? Do you mean State hospitals as well as private hospitals?

Dr. NEWELL. That is correct.

Mr. FLOOD. Community hospitals?

Dr. NEWELL. Hospitals serving the population out there who are not generally in large academic research institutions.

LEUKEMIA RESEARCH

Mr. FLOOD. We have touched on this in passing, and I was going to ask you anyway. We talked in the past about your institute's efforts in leukemia research. A couple of years ago, we talked at great length about that. Can you give us an update about what you are doing in this area, and what you plan to do in the next fiscal year in leukemia research?

Dr. NEWELL. I am glad you asked me that, Mr. Chairman. We have testified to this committee in the past that at some point in time, maybe only 50 percent of children afflicted with leukemia would get the best in what is available in leukemia treatment—although it could

possibly be as much as 80 percent so we decided to take a closer look at this very question. Dr. Fink and her staff and our statisticians did a study—a survey, if you will—of leukemia that occurred for 1 year in the 10 percent of the U.S. population that we survey on an ongoing basis.

We found that in 1 year in the 10 percent 101 cases of leukemia occurred in children under the age of 15. We found that the average length of time from the onset of the first symptom to the onset of seeing a physician was 1 month. The average time from seeing a physician to being hospitalized was 1 week, and the average time from day of diagnosis to onset of therapy was 1 day. So it was 1 month, 1 week, 1 day in the sequence of the process.

We think this is very good. This is probably as good as can be expected.

The other thing that delighted us was that the survival data on these children, these 101 samplings throughout the country, survived only 1 month less than the children in the so-called acute leukemia group B clinical study. In other words, they got good diagnosis, good referral patterns, good treatment, and have good survival. I think virtually every child today gets good care for acute leukemia.

Mr. FLOOD. You hinted that last year.

TRAVEL

Now, travel requests, do you want to handle that?

Dr. NEWELL. Yes, sir.

Mr. FLOOD. All right, the travel request for the Cancer Institute, that is the biggest in the whole scheme out there; the biggest in the whole NIH.

Last year, Dr. Rauscher told us that this was in fact due to the Institute's special ambulatory care program. Can you tell us how much of your 1978 program is for this special ambulatory care program?

Dr. NEWELL. $1.9 million dollars is estimated for the ambulatory care service.

Mr. FLOOD. For the record, I want a table showing how much is spent for travel for the special ambulatory care program, how much is spent for monitoring your contracts and your grants, how much is spent for attending these professional meetings, how much is spent for international travel, and we would like the table to show that for the years 1976, 1977, and 1978.

(The information follows:)

NATIONAL CANCER INSTITUTE—TRAVEL

[In thousands of dollars]

	Fiscal year—		
	1976	1977	1978
Special ambulatory care program	$1,151	$1,151	[1] $1,900
Professional meetings	408	400	390
Contract and grant monitoring	651	660	690
International	275	280	285
Advisory committees and consultants	245	250	265
Scientific program travel	570	553	570
Total	3,300	3,294	4,100

[1] The special ambulatory care program has been expanding over the past few years, because we are growing increasingly successful in treating people on an outpatient basis, which is a benefit to patient morale, and a means of reducing the far more expensive impact of inpatient treatment.

Dr. NEWELL. I might say the only increase we project is in the ambulatory patients care category——

Mr. FLOOD. That table should be very eloquent.

Dr. NEWELL. May I also point out that we instituted the Clearinghouse on Environmental Carcinogenesis this year. This is a group of outsiders who advise us on selecting chemicals to be in a test, helping decide the protocols, and evaluating data. The support of the Clearinghouse is going to cost us about $80,000 in travel that we didn't have last year. So if there is any kind of crunch on travel, I would like to see that viewed as an exception because it is a very specific and high priority item. Those are the only two increased categories.

Mr. FLOOD. Mr. Obey?

CONTRACT REVIEW

Mr. OBEY. Thank you, Mr. Chairman. I want to clear up the answer to a question I asked earlier, and I wasn't quite sure I understood the response, frankly.

When I asked you about your process for reviewing contract research proposals, did you tell me that there was or was not an internal review, in-house review, as well as a review by outside sources?

Dr. NEWELL. There usually is. There are usually two levels of review for contracts. One is the level of relevance priority and need, that is, does it fit within the program; is it something that we want done; part of a plan, and so forth? This is usually done in-house, and then once that is done and we advertise for proposals from the community and we get in the proposals, then we conduct a technical level review, and it is usually this technical level where you actually pick individual respondents to a request for proposal that is conducted by outsiders and outside committees.

Some contracts, resource contracts, as I say, when we go buy cells, or tissue culture, or something, we may do that with an in-house review.

Mr. OBEY. I am talking about research contracts. Would you describe for me again what the process is?

Dr. NEWELL. The general rule, and I suppose there may be exceptions, but not many, is that in the development of the plan for the program area, whatever it is, the internal staff will review the need, the relevance priority and need for any one project. Then we advertise for respondents and when we get the responses in, we conduct a technical level of review. This technical level is where you actually choose, if you have six proposals and you can only take two, you want the best two of the six, that would be done through the outside chartered committee with outsiders.

CARCINOGENESIS PROGRAM

Mr. OBEY. Last year, Dr. Rauscher and I discussed some of the people involved in making a lot of critical decisions in your operation.

Dr. Saffiotti was head of the carcinogenesis program. He is now gone and the program has been divided into two areas; is that correct?

Dr. NEWELL. That is correct. He is not gone from the Institute.

Mr. OBEY. I mean from that slot.

Dr. NEWELL. Yes.

Mr. OBEY. But one is bioassay and the other is the carcinogenesis research; is that right?

Dr. NEWELL. Yes.

Mr. OBEY. Who heads those?

Dr. NEWELL. The bioassay is headed by Dr. Richard Griesemer, who just came with us the first of February. Prior to that, it was Dr. Robert Squire, who left for personal reasons. We think we have a very good person in Dr. Griesemer, and he is taking hold of that quickly.

In terms of the research area, Dr. Peters is pretty much heading that up, and we have a search committee out to look for an associate director for research. This is an area I mentioned earlier and said we let one person pay more attention——

Mr. OBEY. You say Dr. Peters is in charge of that at the divisional level?

Dr. PETERS. Actually, I have asked Dr. Gori, my Deputy Director, to assume those responsibilities on an acting basis, until we can find a permanent associate director for that program.

Mr. OBEY. At the division level, what is your role?

Dr. PETERS. Both of those programs are in the division of which I am the Director.

CANCER ADVISORS

Mr. OBEY. Last year, Dr. Rauscher said one of his key advisors was Dr. Shubik. Is that still true now as far as you are concerned?

Dr. NEWELL. Dr. Shubik is a member of the National Cancer Advisory Board appointed by the President.

Mr. OBEY. That Board is rather unique, isn't it? It is appointed directly by the White House. In fact, some people have argued that the Board and the Panel are considerably more broad than just advisory. Wouldn't you say that is true?

Dr. NEWELL. They give a lot of advice, if that is what you mean.

Mr. OBEY. Dr. Shubik is a member of the Board, and he is chairman of the Subcommittee on Environmental Carcinogenesis; isn't he?

Dr. NEWELL. Yes, sir.

Mr. OBEY. So Dr. Shubik is the man who is in charge of looking over the shoulder of the Division of Cancer Cause and Prevention, so to speak. Would that be an accurate description?

Dr. NEWELL. Well, I think the role of the advisory committee has been a bit broader than that. I don't think they delve very much into the operational aspects of any division. I think they have been broadened in the sense——

Mr. OBEY. I understand it is broader. But one of the functions for them is to sort of oversee in a general way, isn't it?

Dr. NEWELL. Yes.

Dr. PETERS. Historically, if you go back 3 or perhaps 4 years ago, to the time when that subcommittee of the Board was established, you will find that it was established by the chairman of the Board for a specific purpose. To the best of my knowledge there have been only two specific charges to that subcommittee, both of which have been completed. I do not believe that the degree of their overseeing the direct operations of the carcinogenesis program is that great.

Mr. OBEY. Well, nevertheless, it would be helpful for you or anyone else working that area if you had good relations and good communication with Dr. Shubik, would it not?

Dr. PETERS. With all members of the committee.

Mr. OBEY. Isn't it extremely important that any dealings that take place between the Institute and the Division of Cancer Cause and Prevention and Dr. Shubik and the research organization over which he presides be handled with the most open, regular and rigorous possible review?

Dr. PETERS. Yes, sir.

Mr. OBEY. The Eppley Institute is one of the largest recipients of NCI money of any organization in the country, isn't it? What did it receive last year?

Dr. PETERS. About $3 million, but that——

Mr. OBEY. Over the last 8 years?

Dr. PETERS. I don't have that figure.

CONTRACT REVIEW

Mr. BROWNING. About $20 million to $25 million.

Mr. OBEY. Let's take 1 year in those 8; take 1973, what kind of review took place both internally and externally? Let's take internally first. You say there would have been no internal review of the Eppley contract?

Dr. NEWELL. I am going to turn that to Dr. Peters.

Dr. PETERS. I cannot be sure for any specific year, including 1973, but to the best of my knowledge there has always been an internal review.

Mr. OBEY. OK, was there in-house review of the Eppley contract in 1973?

Dr. PETERS. I would assume so. I see no reason for there not to have been. I would have to go back and check the record; that is four years ago. I was not at that time in the position I am in now.

Mr. OBEY. Could you provide for the record what scientists in your shop participated in that review?

Dr. PETERS. Yes.

[The information follows:]

NATIONAL CANCER INSTITUTE

INTERNAL REVIEW OF EPPLEY INSTITUTE CONTRACT

There was an internal review of the Eppley contract in 1973. It was reviewed by the Carcinogenesis Contract Program Management Group (CCPMG) on April 24, 1973.

The members of the CCPMG (all NCI personnel) who reviewed the Eppley contract on April 24, 1973 were: Dr. Saffiotti, chairman; Drs. Bates, Peacock, Kraybill, Berg, Weisberger, Domanski, Cooper, Rapp, Sporn, Gori, and Heim.

Mr. OBEY. What kind of outside review of that contract did you have:

Dr. PETERS. For several years that contract was reviewed by special ad hoc review groups; as have other contracts of a large multidisciplinary nature. This was because the activities within these contracts were such that we felt that no one individual review group could adequately provide a review.

Mr. OBEY. Did any standing advisory committee in your operation review that? The answer would be no?

Dr. PETERS. That is correct.

Mr. OBEY. So a special committee was appointed to review that; is that right?

Dr. PETERS. That is right.

Mr. OBEY. Who was responsible for collecting the names of people who served on that special advisory committee?

Dr. PETERS. This was done in conjunction with the project officer and the senior investigator in the program area. I'm sure Dr. Saffiotti, as Program Director, had input.

Mr. OBEY. Any idea who else?

Dr. PETERS. Dr. Gori was the project officer.

Mr. OBEY. Would you have had any responsibility in that area?

Dr. PETERS. I would have had approval responsibility for the selection.

Mr. OBEY. Could you tell us who served on that committee and give us the dates they met to discuss the contract?

Dr. PETERS. I can provide that.

Mr. OBEY. Do you have any idea now?

Dr. PETERS. No; but I can provide the information.

Mr. OBEY. Do you know if they, in fact, ever met?

Dr. PETERS. They may have conducted a mail ballot; that is frequently done.

Mr. OBEY. Did they ever meet?

Dr. PETERS. I don't know. For that particular year I will have to check the record and provide that information.

Mr. OBEY. If they had met, would that have been or not have been a violation of HEW regulations? What I am trying to get at is, was this, in fact, a duly constituted advisory committee under HEW regulations?

Dr. PETERS. As far as I know, we have always operated within the regulations. I am not aware of any operation outside the regulation.

Mr. OBEY. It was not one of the nine standing committees, but you say you think that committee could have met without being in violation of HEW regs?

Dr. PETERS. No; I said I think it may have been an ad hoc committee, but I am not sure, and I said it may have conducted its business by mail ballot. I am not sure about that either, but I can provide it for the record.

Mr. OBEY. Could that committee have met under HEW regulations seeing that it was an ad hoc rather than a regular committee?

Dr. PETERS. I don't think so. I don't know exactly what the stipulation was or when the Committee Management Act came into being. I just don't remember.

Mr. OBEY. I would like you to provide whatever information you can for the record.

Dr. PETERS. Certainly.

[The information follows:]

National Cancer Institute

Review Committee - Eppley Institute Contract

The technical review of the Eppley Institute contract was accomplished in the following manner.

A number of professionals with diverse expertise in the field of carcinogenesis were sent the Eppley proposal to evaluate the technical aspects of the contract. On an individual basis each sent their written comments to Dr. Saffiotti, who then formulated the technical recommendation from these individual responses. A mail ballot was not used. The Project Officer, Dr. Gio Gori and the Program Director, Dr. Saffiotti were responsible for collecting the names of the people who participated in the technical review.

The individuals who evaluated the technical aspects of the Eppley Institute proposal were the following:

Dr. Leon Goldberg
Albany Medical College

Dr. Harold C. Grice
Food & Drug Directorate
Canada

Dr. Paul Harris
(Retired, Indianapolis, Ind.
formerly Eli Lilly Company)

Dr. Martin Lipkin
Sloan Kettering Inst. for
Cancer Research

Dr. J. A. Swenberg
The Upjohn Company

Dr. I. B. Weinstein
Columbia University

Dr. Gerald Wogan
Massachusetts Institute of
Technology

Dr. John Berg
NCI

Dr. Luigi De Luca
NCI

Dr. Thaddeus Domanski
NCI

Dr. Herman Kraybill
NCI

Dr. Jerry Rice
NCI

Dr. James Selkirk
NCI

Dr. Carl Smith
NCI

Dr. Michael Sporn
NCI

Dr. Friedrich Wiebel
NCI

The above individuals were not required to meet because of the procedure by which the technical evaluation of the contract was accomplished. This was not a chartered DHEW committee, therefore there was no violation of DHEW regulations.

Mr. OBEY. Once the contract was awarded, what effort was made by the Institute to monitor the progress of the Eppley Institute during the year? And I am talking about 1973. Do you have any idea?

Dr. PETERS. I feel sure there were routine site visits. I can find out for you as to how many and who went on them.

Mr. OBEY. Any progress reports which are sent to you for something like that?

Dr. PETERS. Yes; quarterly progress reports and an annual report,

Mr. OBEY. Quarterly or semiannual?

Dr. PETERS. At that time, they may have been semiannual. I will have to check.

Mr. OBEY. Can you tell us which in-house scientist at NCI would have read and reviewed those semiannual reports in 1973?

Dr. PETERS. The project officer and the senior staff of the operating program.

Mr. OBEY. If you could for the record tell us who they would have been.

Dr. PETERS. All right.

[The information follows:]

NATIONAL CANCER INSTITUTE

PROGRESS REPORTS REVIEW—EPPLEY INSTITUTE CONTRACT

Once the contract was awarded it was monitored by the project officer, Dr. Gio Gori. During the course of the contract year that began May 15, 1973, Dr. Gori site visited Eppley Institute twice: (1) July 26–27, 1973, (2) February 11–12, 1974. In each case Dr. Gori completed an extensive review of specific projects with the investigators responsible for the particular research effort.

The annual progress report was submitted by Eppley Institute dated February 22, 1973. This document also served as the technical part of the 1973 renewal proposal. There was a thorough documentation of the previous year's accomplishments as well as the plans for the succeeding year. In addition, another progress report was provided the Institute, dated December 15, 1973, which served as a semiannual report.

The semiannual reports were reviewed by the program director, Dr. Saffiotti and the project officer, Dr. Gori. In addition, the annual report was reviewed by the carcinogenesis contract program management group (CCPMG).

Mr. OBEY. You don't have any idea right now?

Dr. PETERS. Other than the project officer and the senior staff of that program area I do not know. That would be the normal procedure for that or any other contract report.

Mr. OBEY. Now, this year I understand the Institute will be handling that contract a little differently.

Dr. PETERS. That is correct.

Mr. OBEY. They will receive the normal in-house and standing advisory committee review that everybody else gets?

Dr. PETERS. That is correct.

Mr. OBEY. How will you go about that? You will break down the contract into its constituent parts?

Dr. PETERS. That is correct; four major areas.

Mr. OBEY. Given the ability to do that this year, why wasn't it done that way in the past?

Dr. PETERS. The reason that it was not done in prior years is that we were working closely with the people at the Eppley Institute in order to provide them an opportunity to come in for grant support, which they did.

Mr. OBEY. I guess I still don't understand that response. My point is, given the position that Dr. Shubik occupies, given the relationship he has to the Institute, wouldn't it have been more appropriate if you had used the same procedure which you plan to use from now on in previous years to review that contract?

Dr. PETERS. It would have. I indicated a moment ago that because of the multidisciplinary nature of that contract, it, and others of that type are frequently reviewed by special ad hoc groups because there is not sufficient expertise on any one committee to evaluate all facets of that type contract.

Mr. OBEY. Why is it possible to do it now?

Dr. PETERS. Because we split it into four areas of effort, each of which will be reviewed by a contract review committee.

Mr. OBEY. Why couldn't that have been done before, is my question?

Dr. PETERS. We were in the process of attempting to do that. It took time.

ADDITIONAL SPACE REQUIREMENTS

Mr. OBEY. Just one other question. Last year, this committee asked NCI to provide adequate space to the carcinogenesis program to house the additional scientists. Would you tell the committee what the status is of the Institute's efforts to comply wih that directive?

Dr. NEWELL. I think we have made some good progress along those lines. We will be occupying a new block of space in a building called the Landow Building. This is space, I believe, the National Heart, Lung, and Blood Institute was in, and they are consolidating. That is some 8,000 square feet of space.

Dr. FREDRICKSON. Let me take the responsibility for that reply. The Cancer Institute has requested space for this increase in its activity and the problem at NIH has been twofold. One is that the contemplated move of the Health Resources Administration to Prince Georges County has been delayed for many months. That move, which will take place in April will free space on the NIH Campus now occupied by HRA and will help us provide more space for the Cancer Institute. The second problem has been that we have had a great deal of difficulty in procurement of a particular building in Rockville, but we are now again moving forward, I think——

Mr. OBEY. How are you coming with GSA?

Dr. FREDRICKSON. It looks like we will be able to come to closure. We are optimistic that we will be able to get that building.

Mr. OBEY. That is all the questions, Mr. Chairman. I do have some additional questions I would like to submit for the record.

Mr. FLOOD. Without objection, that will be done.

Mr. FLOOD. Mr. Early?

UTERINE CANCER

Mr. EARLY. On the uterine cancer program, you suggest you have reached one-half million of those hard-to-reach women in the program. How many do you estimate are out there that fall in that category?

Dr. NEWELL. It is hard to know. I think that we probably have reached as many as we can reach given finite resources. We are picking up about 1 cancer per 1,000 in these women, and its costs about $6 to do one Pap test. We do follow the women; we like to follow them.

And the other thing we like to do is be assured that once we have detected a cancer that they are put in the health care delivery system so that they get that cancer removed, or initiate whatever treatment is appropriate. Usually it is surgery if it is in situ. We have determined and we are very careful about not paying for health care delivery. That is not what we get our dollars for. On the other hand, we did decide in this program that we would pay to the point where the woman had a definitive diagnosis made, because in order to get a definitive diagnosis, she has to be in the delivery health care system.

BREAST CANCER

Mr. EARLY. So with the breast cancer your statistics show a great number of new cases, 88,700 new cases. Do you identify that to your crash program last year, or TV, or at-home testing, a woman testing herself?

Dr. NEWELL. We don't have a self-test for the breast cancer except for self-breast examination.

Mr. EARLY. Didn't I see TV ads in the past year or so?

Dr. NEWELL. Yes, sir, you are talking about the screening projects, I believe. Yes, sir, those are the 27 so-called breast cancer detection projects.

A couple of things happened which have made women more aware of breast cancer, and I think it is good that women are more aware. Certainly the experience that Mrs. Ford and Mrs. Rockefeller had, and then the business recently that I discussed with the chairman about mammography and the radiation dose being delivered and whether we should be screening asymptomatic women or not. These have really created quite an awareness among women.

One out of seven women during a lifetime will develop breast cancer, which is a large number. It is widespread disease. The 27 units that we jointly fund with the American Cancer Society were designed to be demonstration projects, to see if we could solicit into each 1, 10,000 women, screen them by 3 methods, history, physical, and mammography, and if we could detect early breast cancer by doing this, could we eventually prolong their survival? We do plan to follow these 270,000 women for the next 10 or more years.

Mr. EARLY. In that program in connection with the American Cancer Society, is there any duplication there?

Dr. NEWELL. No; not really. Not at all.

Dr. FINK. Is your question related to the duplication between the cervical cancer program and the breast cancer program?

Mr. EARLY. No; the breast cancer. You say you are working with the American Cancer Society, in partnership with.

Dr. FINK. We do fund the 27 breast cancer units with the American Cancer Society.

Mr. EARLY. Togetherness is just cofunding?

Dr. FINK. The National Cancer Institute and the American Cancer Society are jointly funding this project. It is not only this cofunding. It is also the technical support of the program and really joint management, if you will, on the part of the Federal agency being the National Cancer Institute and the voluntary agency, the American Cancer Society. For example, project officer visits and moni-

toring of these contracts is jointly done by the American Cancer Society and the National Cancer Institute.

Mr. EARLY. I see. Along that same line, the television testing, advertising program you ran in the past year, how effective was that? Did it help?

Dr. NEWELL. Mr. Early, I am sorry. I can't focus in on the television program you are talking about.

Mr. EARLY. It seemed to get great emphasis right after the Mrs. Ford and Mrs. Rockefeller thing.

Dr. FINK. There have been a number of programs, and again I am sorry I don't know which you are referring to directly. With the opening of most of the breast cancer detection units there was a publicity campaign which included discussions about methods for detecting breast cancer, such as breast self-examination (BSE). In addition, American Cancer Society runs regular spots on BSE and several have been shown in the local area.

CHILDHOOD SCREENING

Mr. EARLY. How about with regard to children? Are we satisfied we are doing enough on screening and early detection with children?

Let me ask this, what would be the total cost to screen one child for as much cancer detection as possible?

Dr. NEWELL. The total cost would probably not be that great. I think that in the area of children, we probably are doing much better in screening than we are in adults, the reason being most children see pediatricians often because they have to get immunizations before they go to school, so the way we are set up tends to put children in contact with pediatricians and therefore they are seen, whereas many adults don't do this.

I think the fact they are followed and in contact with physicians means that they are getting screened to the best of our ability to detect early cancer in children.

Mr. EARLY. I have several children, and I don't know whether they have been tested or screened any place as far as Massachusetts is concerned. I don't see any expenditure of cancer money for early detection in children.

Dr. NEWELL. You probably don't, because I don't think we have any dollars specifically earmarked for that bit of work.

Mr. EARLY. Is that something we should be doing that we are not doing?

Dr. DEVITA. I think the problem is that there are less than 10,000 children a year that develop cancer. Although it is a common cause of death in children, it is not a common disease. The best screening examination is to go to a pediatrician when they have illness and many cancers are discovered in the course of examination for what is suspected to be a virus infection. Actually, most children are being screened by that method.

INCIDENCE OF CANCER IN CHILDREN

Mr. EARLY. Do we have anything in any study historically that tells us roughly what is the average start of a cancer?

Dr. DeVita. One cancer that I think causes the most fear in children is leukemia.

Mr. Early. I would like you to address the 15 types of cancer that you addressed to the chairman that you suggested constitutes 90 percent of the cancer.

Dr. DeVita. Cancers that start in children?

Mr. Early. Of the 100 that Mr. Flood referred to, you suggested 15 cancers constituted roughly 90 percent of the cancer.

Dr. DeVita. The question?

Mr. Early. Which of those 15 would be in children?

Dr. DeVita. Leukemia is on the list. Leukemia, as a group, adults and children, is on the list of 15. But childhood leukemias only make up one-third of those patients.

Dr. Fink. In addition, I might say as far as childhood cancer goes, the business of Pap smears in late teenagers, we have had contacts with family planning, maternal child and health groups that would deal with this problem. Breast cancer is a disease of older women, so mammography, say, in the teenage group is not fruitful or indicated. We do have programs, however, dealing with young girls who have had exposure to the problem of DES during their mother's pregnancy and trying to elucidate the kind of examination and followup these girls should have that can then be translated to the family practitioner who might come in contact with the girl. In general, early screening in children we have limited to very specific groups, such as DES.

Mr. Early. Are we satisfied that the private sector is doing enough of that health screening with regard to cancer? I am thinking of a couple of very progressive companies in my area that have the mobiles that give these physicals. Is there enough approach to cancer?

Dr. Newell. It is difficult, Mr. Early, for me to say I am satisfied that there is enough. We can always do more. It is a dangerous disease to get. I am not sure exactly how much of that is being done.

I do know that we have a subcommittee of Dr. Fink's advisory committee that is looking at the way the insurance industry is paying or can be persuaded in some way to pay for preventive measures for early screening measures.

NATIONAL HEALTH INSURANCE

Mr. Early. As we get the national health proposal, is the Cancer Society going to be able to show where some expenditure can actually be a savings in money in early detection and prevention?

Dr. Fink. That is exactly one of the problems we are tackling through the activity we have going on with Blue Cross. Can you develop a screening package that an insurer, like Blue Cross, can take on and make widely available throughout the country? At the current time, they are evaluating screening programs determining how to set up a program. Then we will be field testing the screening programs in several settings designated by Blue Cross. This is a beginning to get into this whole question of how do you reimburse preventive medicine. It is a tough area.

Mr. Early. It is very hard to assess a value to preventive medicine; it is really a direction I think we should be going.

ANTICANCER DRUGS

Doctor, you said you were going to have a speedup in the implementation of new drugs with regard to cancer. Have you gone too slow with trying these drugs?

Dr. DEVITA. No; I think we are using a different method of developing compounds now. We used to use primarily random screening, and we are putting more new structures in with some biochemical rationale, and then earmarking a group of drugs with high priorities, using a system where we identify an advocate with a compound to try to move more high priority compound drugs through the program quicker; we are trying to get a higher quality compound with greater speed.

Mr. EARLY. Haven't malpractice suits, et cetera, delayed us beyond where we should have started to implement these?

Dr. DEVITA. No, sir.

Mr. EARLY. Finally, Doctor, what year do you suggest that you will be coming before this committee saying that you have developed so much in cancer research you are asking for less money? Will Mr. Flood still be here?

Dr. NEWELL. Absolutely; no question about that.

Mr. EARLY. Thank you.

Mr. FLOOD. Thank you very much. Good show.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. PATTEN

CANCER ATLASES

Mr. PATTEN. Dr. Newell, the National Cancer Institute has produced two cancer "atlases"; one each for white and nonwhite populations. I believe that any such data serves a great purpose in helping to identify different cancer sites that are more prevalent in certain regions of the country. It appears, however, that since the issuance of the first atlas, various States and regions have been labeled "cancer alley" and other things which have served more to frighten people and sell newspapers than to enlighten professional persons with responsibilities in the area of the public health. It is hoped that the following questions, when answered, will help clear the air on a number of matters.

Please advise the subcommittee what data is used in what way in preparation of the atlases.

Answer. The data which were used in the preparation of the atlases were comprised of all death ascribed to cancer which were reported to the National Center for Health Statistics for the period 1950–69 and populations for individual counties taken from the 1950, 1960, and 1970 censuses of population. Utilizing these data, age adjusted rates for specific sites of cancer were calculated and compared to corresponding rates for the total United States. The results of these comparisons were subsequently presented in the form of maps.

Mr. PATTEN. How reliable is the data?

Answer. The data are believed reliable from the standpoint that the geographic patterns for a number of sites of malignancy provide information consistent with known associations such as sunlight and skin cancer, high rates of stomach cancer among Scandinavians and excesses of gallbladder cancer among American Indian females. This does not imply that there are no problems.

Mr. PATTEN. Are there any inherent problems or weaknesses in using that data?

Answer. There are weaknesses in using the data. Regional differences in diagnosis will affect the comparability of reported mortality from one part of the country to another. There is no evidence, however, that this is a major factor. Also, there are reports from the Bureau of the Census concerning the underestimation of the resident population. The age groups which are most af-

fected are those for which mortality due to cancer is not the major cause of death, e.g. nonwhite males between 20 and 30 years of age.

Mr. PATTEN. Are there figures in the atlases that rank, or enable one to rank States or their subdivisions according to incidence of death by cancer? Is there any information in the atlases which would enable one to numerically rank the States in terms of cancer mortality?

Answer. The atlases are companion volumes to an earlier NCI publication U.S. Cancer Mortality by County: 1950–1969 (NIH 74–615). This publication presents rates for the total United States, individual States as well as counties. When the three publications are used jointly one can rank States and/or counties by referring the mortality rate in question to the appropriate table given in the back of each atlas.

Mr. PATTEN. In your professional opinion, are there any figures (non-NCI) that can reliably rank States or their subdivisions on cancer morbidity and/or mortality?

Answer. In addition to the above mentioned NCI publications one can utilize the annual publications of the National Center for Health Statistics and/or contact the States directly in order to accomplish the desired ranking on cancer mortality. A comparable ranking on morbidity could only be accomplished by utilizing data from cancer registries, and there is not a reliable registry in each State.

COOPERATION WITH OTHER AGENCIES

Mr. PATTEN. Finally, on a separate matter, do you support the concept of joint funding as authorized by the Intergovernmental Cooperation Act? Has the NCI successfully coooperated with other agencies on joint funding applications?

Answer. The National Cancer Institute fully supports concepts embodied in the Intergovernmental Cooperation Act of 1968 to achieve the fullest cooperation and coordination of activities among levels of government in order to improve the operation of our Federal system in an increasingly complex society.

NCI currently provides funding at a level of approximately $17,000,000 annually for active agreements to approximately 20 sister agencies in support of 63 cancer research and cancer control projects, including over $3 million to the National Institute for Occupational Safety and Health to support investigations into cancer-causing chemicals in the workplace.

Joint problem solving and costsharing project activities are continuing in many areas. A collaborative epidemiologic study is currently underway involving the State of Michigan, Food and Drug Administration and National Institute of Environmental Health Sciences and NCI at policy and program planning levels. Establishing priorities for selection of chemicals to be tested in the carcinogenesis bioassay program is under the purview of the DHEW Committee to Coordinate Toxicology and Related Programs. This committee is constituted of officials from National Cancer Institute, Food and Drug Administration, National Institute for Occupational Safety and Health, Center for Disease Control, National Institute of Environmental Health Sciences, Environmental Protection Agency, Consumer Product Safety Commission, Energy Research and Development Administration, Department of Defense, U.S. Department of Agriculture, and Department of Labor. Aspects of the Stanford Research Institute program "A Research Program to Acquire and Analyze Information on Chemicals That Impact on Man and His Environment," which relate to specific pesticides continue to be conducted under a costsharing agreement with an office of the Environmental Protection Agency (EPA).

The Interagency coordinating groups organized by the National Cancer Institute include the Interagency Coordinating Committee on the National Cancer Program, the Interagency Coordinating Committee on Cancer Control and the Interagency Collaborative Group on Environmental Carcinogenesis.

Finally, and very importantly, the NCI Clearinghouse on Environmental Carcinogenesis consists of 26 members and includes representatives from academia, the commercial sector, the general public, and the scientific community.

MR. MICHEL

CANCER DEATH RATES

Mr. MICHEL. You mention in your statement that cancer death rates have decreased for the types of cancers in age groups under 35. Can you provide us with the specific rates in this regard?

Answer. The following table provides the age specific death rates for various age groups under 35. The figure shows the decreasing trends from 1961 through 1973.

TRENDS IN THE AGE SPECIFIC CANCER DEATH RATES (PER 1,000) UNDER AGE 35 IN THE UNITED STATES, 1961–73

Age group	Death rates		Absolute differences	Percentage decrease in death rates
	1961	1973		
Under 1	0.069	0.042	0.027	39.1
1 to 4	.104	.064	.040	38.5
5 to 9	.078	.060	.018	23.1
10 to 14	.061	.048	.013	21.3
15 to 19	.078	.067	.011	14.1
20 to 24	.090	.084	.006	6.7
25 to 29	.138	.119	.019	13.8
30 to 34	.242	.200	.042	17.4

Mr. MICHEL. Above age 55, the cancer death rates are increasing. Does that suggest that the cancer-causing elements for this age group are increasing?

Answer. This does not necessarily mean that cancer-causing elements are increasing for this age group because of the 20- to 30-year latent period. Also trends vary for different sites, for example, stomach cancers are decreasing while lung cancers are increasing, and it is possible that exposure to certain cancer-causing elements (which vary by cancer site) is changing over time. As an example, the increase of lung cancer rates among women may be due to the changing (increasing) smoking habits among women which began more than 20 years ago. In contrast, the decreases in stomach cancer over time may be due to changing diets or refrigeration usage, or changes in exposure to suspected or known carcinogenic agents.

CIGARETTES AND CANCER

Mr. MICHEL. There has, of course, been a major campaign during the past several years warning people of the danger of cigarettes. Has that campaign had any impact on the incidence of lung cancer?

Answer. Public antismoking campaigns have developed progressively since the 1964 Surgeon General's report. Because of the long latent period before diagnosis of lung cancer (10–15 years), it is too early to determine if changes in smoking patterns brought about by these campaigns have been effective. Current information indicates that lung cancer incidence has not declined. In addition, there is evidence that suggests changing smoking patterns for certain groups. The proportion of young people, white women, and black men, who smoke may be increasing while the proportion of older (45 and over) white men who smoke may be decreasing.

Mr. MICHEL. You refer to the development of a less hazardous cigarette. Are they just of one type or under one brand name, or do they cut across the spectrum?

Answer. Less hazardous cigarettes are not of one type. The objective of the smoking and health program is to identify the extent to which various cigarette components are hazardous and determine practical methods for controlling the more hazardous components. Many parameters are descriptive of less hazardous cigarettes and these may be combined in various ways to produce cigarettes that are less hazardous than in currently available commercial brands. Thus, there may be several different types of cigarettes that could properly be considered as being "less hazardous."

Mr. MICHEL. Are you trying to convince the tobacco companies to substitute these cigarettes for others, and if so, what kind of success have you had?

Answer. Yes; one goal of the smoking and health program is to provide research data to commercial firms and encourage them to decrease the amount of hazardous materials in their particular brands of cigarettes. Our preliminary success is suggested by the fact that every major cigarette producer has introduced low tar/low nicotine cigarettes, a first step in developing less hazardous cigarettes.

CHEMICAL TESTING RESULTS

Mr. MICHEL. Regarding your carcinogenesis testing program, what do you do with the results when chemicals have fully gone through the testing process?

Answer. A formal mechanism has been developed for the release and dissemination of information about the results of testing when a chemical has gone through the carcinogenesis testing process. The Federal regulatory agencies are notified and provided with a report that includes the data on which the interpretation of the National Cancer Institute (NCI) is based. The exchange of information frequently results in ad hoc conferences with representatives of the Federal agencies to assist them in making regulatory decisions. Other Government agencies are notified through the DHEW Committee to Coordinate Toxicology and Related Programs. The various sectors of industry, labor, consumers, and academia are notified of the results of carcinogenesis testing through the Clearinghouse on Environmental Carcinogens. Technical reports describing the experiments, the results and their interpretation are published and distributed by NCI. A summary of the report is published in the Federal Register. An announcement is made through the press to inform the public that the report is available. Through the Office of Cancer Communications at NCI, inquiries from the public receive a prompt reply. Data of interest to the scientific community are published in the scientific literature. The results of carcinogenesis testing are also sent to the International Agency for Research on Cancer for incorporation in a worldwide data bank on chemical carcinogenesis.

COOPERATION WITH NIOSH

Mr. MICHEL. How do you distinguish between your efforts in this regard and those of the National Institute for Occupational Safety and Health?

Answer. The difference between NCI efforts in carcinogenesis and those of NIOSH are as follows:

NCI's efforts are directed towards identifying carcinogens, conducting research into the mechanisms of carcinogenesis, and conducting research in carcinogenesis testing, that, is developing new and improved methods for testing, better animal models, improved protocols, and so forth. NIOSH on the other hand conducts research primarily through the epidemiological studies in the occupational environment. NIOSH, in addition, has right-of-entry so that they have accessibility to the workplace. NCI, of course, has no regulatory or enforcement activity.

Mr. MICHEL. Reference is made in your statement to an interagency agreement with NIOSH providing $3 million to support 21 projects. Is that Cancer Institute money or NIOSH money?

Answer. The $3 million to which I referred is money which the NCI has provided to the National Institute for Occupational Safety and Health. These funds were contained in the National Cancer Institute appropriation and an interagency agreement was written with NIOSH.

Mr. MICHEL. Are these joint projects, or are they solely undertaken by one agency or the other?

Answer. The monitoring and evaluation of these particular projects are being done under the immediate auspices of the National Institute for Occupational Safety and Health. The National Cancer Institute staff reviewed these projects for cancer relevance prior to effecting the interagency agreement and, as such, they are considered joint projects.

Mr. MICHEL. What do these projects involve?

Answer. All of the projects—in one way or another—involve either the surveillance of, or testing for, possible dangers to people in the workplace as a result of exposure to substances which could be toxic or carcinogenic. For areas where danger is found to exist we would then, of course, try to provide or recommend practical control and prevention methods.

Mr. MICHEL. How do you distinguish between your efforts in the carcinogenesis field and those of NIOSH?

Answer. As I mentioned previously, NIOSH conducts research primarily through the epidemiological studies in the occupational environment. I might add that within the last year we have transferred nearly $4 million to NIOSH in order to support epidemiology studies that are important to the mission of both institutes.

ENVIRONMENTAL FACTORS

Mr. MICHEL. There have been a great variety of reports as to the extent to which cancer is caused by environmental factors. The World Health Organization, for instance, recently came out with a report stating that 75 percent to 80 percent of all cancer cases are caused by environmental factors. Do you agree with that analysis?

Answer. Estimates regarding the percentage of cancer cases due to environmental factors have varied from 60–90 percent. We believe that these figures do, in all likelihood, bracket the actual amount. Certainly, the World Health Organization figures of 75–80 percent is within the range. We are admittedly working with incomplete data and given the present state of knowledge, cannot be any more accurate.

It is important to define the term environmental carcinogenesis. To many, environmental carcinogenesis means occupational exposure to, and environmental pollution by, chemical carcinogens. We view environmental carcinogenesis as including other exogenous factors such as those over which we have some degree of personal control. These include things that we eat, things that we smoke and things that we drink. It is certainly well-documented that tobacco is responsible for some 30–40 percent of the total cancer burden. This is in addition to its tremendous impact on cardiovascular disease and emphysema. In addition, we are now accumulating extensive evidence linking certain dietary factors including alcohol with several forms of cancer. While the problem of environmental pollution and occupational exposure is important, we believe that it contributes no more than 5–10 percent to the total cancer burden.

Other factors which play a role in cancer causation include genetic susceptibility and other endogenous factors relating to the host. It is not possible to estimate the exact contribution of those cofactors to the total disease burden but there is increasing evidence that they do contribute. Another cofactor that is as yet unqualified is the role of viruses or viral components including those transmitted both vertically and horizontally.

LAETRILE

Mr. MICHEL. The drug "Laetrile" has been a source of controversy for some time, and it still remains so. Is it still the position of the Cancer Institute that this drug has no scientific value?

Answer. Yes, sir, it is. The NCI has supported extensive tests of Laetrile in animal tumor systems. In none of these tests has Laetrile shown any reproducible evidence of activity. In contrast, drugs which have demonstrated effectiveness against several forms of human cancer all were active in one or more of these animal screening systems. In other words, experience has shown that drug activity in a variety of animal tumors predicts for activity in human cancers. Since Laetrile is not active in these systems, there is no reason to believe it would benefit patients with cancer.

Mr. MICHEL. Have there been any recorded instances where it has helped in the treatment of cancer?

Answer. There are few if any objective reports which serve to substantiate the claim made for the effectiveness of Laetrile in patients with cancer. For the most part proponents of Laetrile rest their case on anecdotal or testimonial evidence. Due to the difficulties in establishing precise diagnosis and extent of disease and due to the extreme variability of the course of different cancers in different people, it is impossible to attach any significance to such anecdotal claims which have not been validated in terms of diagnosis, previous or concurrent treatment, extent of disease and duration of survival. The kind of carefully planned and monitored studies necessary to objectively establish the effects of any cancer treatment over a significant period of time has never been carried out by those using Laetrile to treat cancer patients. Thorough analysis of a small number of cases in which beneficial effects of Laetrile were claimed failed to substantiate the claims.

Mr. MICHEL. Why has there been such a desire to use this drug on the part of some elements of the population? Do you have any explanation?

Answer. Laetrile, the subject of an extensive national, promotional effort, is represented as a nontoxic, natural material ("vitamin B–17"). While claims for its "curative" powers are often played down publicly by its proponents, the idea of cure is much in the minds of those who accept it as a simple alternative to surgery, X-ray and chemotherapy—treatment modalities often attended by unpleasant side effects.

The promotional effort is frequently in terms of "freedom of choice"—where the choice expressed is between a simple, effective, harmless treatment and a harsh, expensive and often ineffective course of action. Not without reason cancer is probably the most feared of the dread diseases. It is a very human trait to hope that the serious problems posed by cancer can be solved in a simple fashion without recourse to treatment that may be painful, expensive, tedious

and sometimes disfiguring. To an increasing number of people Laetrile is being portrayed as that simple solution.

Mr. MICHEL. If people feel so strongly about using this drug, why don't we just let them do so?

Answer. There are several reasons. First, because the proponents of Laetrile have not submitted satisfactory evidence of Laetrile's safety and efficacy to the FDA, the material has not been approved for interstate distribution. Second, as mentioned previously, there is no objective evidence that Laetriel is of actual or potential clinical value. Third, if access to Laetrile were uncontrolled, Laetrile usage would to an increasing degree tend to supplant the use of treatments of demonstrated effectiveness. The argument is sometimes made that patients should be allowed to receive Laetrile if they reach the stage where "nothing else can be done." This idea has a superficial appeal which does not bear careful examination. To illustrate, it is always difficult to determine that point at which nothing more can be offered; if the concession is made to allow Laetrile to be given at a terminal stage in a patient's course, inevitably other patients who have a good chance for cure or effective palliation through the use of orthodox treatment will end up taking Laetrile instead. Thus, the time during which true benefit could have been achieved may be irretrievably lost. To provide free access to Laetrile would serve to legitimize the idea that its proponents have some special insights into the problems of cancer, that these insights are being suppressed, and that the proponents could therefore flout accepted procedures for drug development and testing. Unfortunately, cancer is not a simple problem that lends itself to a simple solution. Although cancer arouses highly emotional responses among those directly involved, the search for preventive and curative techniques must be conducted on a rational scientific basis. Thus, the development, testing and certification of drugs is one area in which large institutions such as the Government must legitimately play a leading role. No citizen can do this for himself and no citizen or group can declare himself exempt from the requirements society has established for its own protection. The tenor of Laetrile promotion tends to mislead and to create false hope among those whose need is great and who are uniquely vulnerable to exploitation. To provide ready access to Laetrile would only serve to magnify this situation. Moreover, to open the door to Laetrile would serve to open the door to a succession of unproven and fraudulent panaceas-measures that would imperil the real progress that has been made in effectively treating an increasing number of patients with cancer.

CANCER RESEARCH FUNDS

Mr. MICHEL. Last year, I asked you to provide the total amounts being spent on cancer research in NIH as a whole, by Institute, and also for the total amount being spent nationwide, public and private. Would you update those figures for us this year?

Answer. Yes, sir, I am submitting a table showing the fiscal year 1976 obligations by the National Institutes of Health on cancer research and, in addition, our best estimates of the amounts spent nationwide by the public and private sectors:

National Institutes of Health

	Amount
National Cancer Institute	$760, 751, 000
National Institute of Allergy and Infectious Diseases	7, 375, 000
National Institute of Child Health and Human Development	1, 517, 000
National Institute on Aging	630, 000
National Institute of Dental Research	555, 000
National Institute of Environmental Health Sciences	6, 893, 000
National Institute of Neurological and Communicative Diseases and Stroke	1, 167, 000
National Eye Institute	1, 914, 000
Total NIH obligations	780, 802, 000
Other Federal agencies	62, 949, 000
State and local governments	95, 000, 000
Volunteer agencies	85, 000, 000
Private institutions	40, 000, 000
Industry	31, 000, 000
Total nationwide	1, 094, 751, 000

BASIC RESEARCH

Mr. MICHEL. How much of your budget is being spent for "basic research"?

Answer. In FY 1978, it is estimated that the NCI will obligate approximately $398,976,000, or 48.7 percent of the President's Budget of $818,936,000 for basic research. This includes all regular research grants and cancer research emphasis grants (CREG); appropriate portions of: (1) the other grant programs including cancer centers, training, and construction; (2) contracts; and (3) intramural research.

Mr. MICHEL. What percentage of all the cancer research grant applications are funded? Secondly, what percentage of the applications approved by the study sections (peer review panels) are funded?

Answer. In fiscal year 1976, there were 2,016 competing (new and competing renewal) regular research grant applications received and 646 of these were funded. This represents 32.0 percent. The study sections approved 1,286 competing grants with 646 being funded, or 50.2 percent. The comparable number of grants and percentages are estimated as follows for fiscal year 1977 and fiscal year 1978:

	1977 estimate	1978 estimate
A. Total received	2,354	2,393
Total funded	583	605
Percentage of those received to be funded	24.8	25.3
B. Total approved by study sections	1,585	1,586
Percentage of those approved to be funded	36.8	38.2

CONTROL GROUP PATIENTS

Mr. MICHEL. I note that for colon-rectal cancer, some 15,000 people will be in a control group. How are these people selected?

Answer. It is necessary, in testing new drug treatments, to insure that a new therapy is actually useful and significantly better than no treatment or at least as effective as any currently available therapy. Thus, it is important to compare it to a control, untreated population or population treated with a standard drug or other agent. Control patients are selected at random as they enter a clinical study in order to eliminate any study bias which would be introduced by subjective selection.

Mr. MICHEL. In a general sense, how are people selected to receive special treatment in your various treatment centers, clinical trials, et cetera? Is there any basic criteria here?

Answer. Clinical trials of new therapies represent the search for more effective treatment of cancer for which there is no satisfactory means of control. Patients who would thus be eligible include those whose tumors have not responded to conventional therapy or who might benefit from a treatment which shows more promise than the standard therapy.

MR. CONTE

LEUKEMIA

Mr. CONTE. What is the 5-year remission rate for children with acute lymphocytic leukemia (ALL)? Have there been any recent developments in treatment methodology?

Answer. The 5-year survival rate for children with acute lymphocytic leukemia has approached 50 percent in clinical studies. Research continues on the use of immunotherapy. Prophylactic treatment of the central nervous system has proven to be a key factor in prolonging disease-free survival.

CARCINOGENESIS TESTING

Mr. CONTE. Could you outline the major problems encountered in the carcinogenesis testing program? How are they being overcome?

Answer. A major problem in the carcinogenesis bioassay program has been inadequate staff to conduct and monitor the program. This has resulted in a backlog of chemicals for which the experiments have not been completed. The lack of staff has been corrected by the allocation of new positions by Congress to the bioassay program. A plan of attack has been developed for handling the backlog of chemicals and all available resources have been concentrated on this problem, so that the majority of the backlog will be completed during this fiscal year.

Another problem has been the selection of chemicals for testing. Since the available resources have not permitted testing of all chemicals that may be hazardous to human health, two advisory mechanisms have been established to assist in the selection of chemicals—the DHEW Committee to Coordinate Toxicology and Related Programs through which chemicals can be nominated for testing from all of the governmental agencies, and the Clearinghouse on Environmental Carcinogens through which chemicals can be nominated from the various public and private sectors.

Mr. CONTE. You mentioned a national shortage of individuals who have been trained in this area. What sort of training program do you have in the carcinogenesis field? Is this exclusively postdoctoral?

Answer. The National Cancer Institute research training program is conducted under the authority of the National Research Service Act. Both predoctoral and postdoctoral training is offered in carcinogenesis to individuals. This area continues to be one of our highest piority areas for training of cancer researchers.

Mr. CONTE. Do you have adequate numbers of researchers to maintain the carcinogenesis program at budgeted levels? Or would it be better to pull back slightly and let the manpower catch up to the research programs?

Answer. Currently, there are reasonable numbers of researchers to maintain the carcinogenesis program at budgeted levels. There is concern, however, about whether the program can be adequately sustained in the future. It is apparent that increased emphasis in environmental carcinogenesis and on the role of nutrition will require an augmented pool of trained investigators in these areas. It requires about 8 years following the baccalaureate degree to train an investigator to do high quality independent research in these areas. Emphasis should be put into this category of manpower rather than limit our research programs.

LESS HAZARDOUS CIGARETTE

Mr. CONTE. Would you tell me more about the National Cancer Program's development of a less hazardous cigarette. What makes them less hazardous? Does it seem to satisfy those who are hooked on smoking? How is it distributed, and how is it competing with ordinary commercial cigarettes?

Answer. The primary objective of the program is to reduce the morbidity and mortality of smoking-related diseases in human beings. Projected estimates indicate that further increases in smoking related mortality can be expected, unless the hazards of smoking can be eliminated or reduced. One of the program approaches toward this objective involves the modification of smoking products for the purpose of producing a less hazardous cigarette. This entails the following sequence of events:

Tobacco blends are analyzed to determine their chemical constituents, and the chemical composition of experimental cigarettes is determined.

Cigarette smoke condensate, whole smoke, and chemical constituents are bioassayed to identify levels of tumorigenicity and other evidence of biological activity. Several animal models are used to test biological parameters.

Flavor components are identified to determine acceptability levels.

Bioassays are conducted to assess whether toxicity results from the reintroduction of flavor characteristics.

Chemical, bioassay, and flavor results are correlated, and decisions are then made for further modification of tobacco products. Such modifications should eventually result in a tobacco product and/or experimental blend that is both less hazardous and more acceptable to the smoking population.

A cigarette is considered less hazardous when the smoke and condensate contain less of the known tumor producing ingredients and laboratory experiments indicate a significant decrease in tumor incidence rate when compared to standard cigarettes.

Smokers' satisfaction with the cigarette is considered through studies of acceptability that adjust flavorings, nicotine levels, and so forth. The proper additions of approved flavors should make even a bland, less hazardous cigarette acceptable to the smoking public.

Data derived from the program are made readily available to commercial producers who utilize the information to produce their own brands. All major cigarette industries in the U.S.A., and several around the world, have been marketing several new cigarette brands during the last 10 months, which incorporate many of the findings from the research conducted by the smoking and health program of the NCI. It is expected that our research will continue to stimulate vigorous market competition and consumer interest in less hazardous cigarettes.

NUTRITION

Mr. CONTE. You mentioned your nutrition program as applied to more effective cancer patient management. Are you working with any of the other Institutes in this area? How about the National Center for Health Services Research?

Answer. The diet, nutrition, and cancer program works, at this time, on demonstration projects and applied research in the areas of: (1) Host-tumor competition and food intake determinants; (2) anorexia—behavioral and food modification intervention; (3) differential nutritional requirements by host and tumor as the basis for dietary treatment of cancer; (4) gustatory taste evaluation of cancer patients; (5) diet and colon cancer in a low-risk population; and (6) studies on differential nutritional requirements by host and tumor as the basis for dietary treatment of brain tumors.

The diet, nutrition, and cancer program of the National Cancer Institute coordinates its efforts in nutrition research through the NIH Nutrition Coordinating Committee which includes the following institutes: National Heart, Lung, and Blood Institute; National Institute of Arthritis, Metabolism, and Digestive Diseases; National Institute of Child Health and Human Development; National Institute of Dental Research; National Institute on Aging; National Eye Institute; and the National Institute of Neurological and Communicative Disorders and Stroke.

We have established contact with the officials of the National Center for Health Services Research to discuss data acquisition and exchange of information in the nutrition field.

LUNG CANCER

Mr. CONTE. Are current methods of lung cancer detection really practical for large-scale screening efforts? Are there ways of identifying high-risk populations for more intensive screening?

Answer. Current screening methods for lung cancer including chest X-rays and sputum analysis are being tested in clinical trials to determine their effectiveness. When these trials are completed, we should be able to determine whether the methods are really practical for large-scale screening efforts. There is no question that if they are proven effective then they will be very practical methods for detecting lung cancer. Sputum analysis can be done on self-obtained specimens; however, failing this, an induced specimen can generally be obtained. Some populations have already been identified as being at high risk, for example, males over age 45 who are heavy smokers. Epidemiological studies of lung cancer victims will be pursued so that if there are other populations at high risk to lung cancer, they will be identified.

Mr. CONTE. Can you tell me what sorts of discoveries have been made about lung cancer biology through increased use of bronchoscopy?

Answer: The increased use of bronchoscopy is demonstrating the relationship between areas of precancerous changes, areas where the tumor cells have not traveled beyond the original site, and areas where the tumor has metastasized. It has also shown that these lesions are not focused in one spot. It is hoped that as usage of this technique increases, diseases of the lung can be detected earlier and treated more effectively.

BREAST CANCER

Mr. CONTE. How widely used is the reduced radiation dosage for breast cancer screening to which you referred? Is the technology readily available for this new technique?

Answer. The radiation exposures in mammography have been reduced to less than 1 radiation absorbed dose (rad) per examination in the 27 breast cancer detection centers supported by the National Cancer Institute. Dosage levels are periodically monitored by radiation physicists employed under a series of independent contracts established specifically to provide this service. The technology for measurement of radiation exposure utilizing a mailed thermoluminescent dosimeter has been perfected; and through an interagency agreement with the Bureau of Radiological Health, Food and Drug Administration, this system is being offered to State health departments. Measurements have been completed on machines in 4 States and an additional 12 States will be surveyed during this year. Monitoring of all States is expected to be completed by the end of next year. This technology is readily available, and the primary goal of the interagency agreement is to increase its use throughout the Nation.

LAETRILE

Mr. CONTE. There has been a fair amount of publicity lately in the newspapers about the drug laetrile. Has the Cancer Institute done any work with that drug?

Answer. The National Cancer Institute has supported extensive testing of laetrile in animal tumor systems. Laetrile has not shown any evidence of activity in any of these tests. It is useful to point out here, however, that drugs which have demonstrated effectiveness against several forms of human cancer were all active in one or more of these animal screening systems. In other words, experience has shown that the activity of a drug in a variety of animal tumors is indicative of that drug's probable activity in human cancers.

CLINICAL ONCOLOGY

Mr. CONTE. What can you tell me about your new clinical oncology program? How far along is it? How much will you be spending on it this year?

Answer. The clinical oncology program of the Division of Cancer Treatment encompasses all intramural as well as collaborative cancer treatment research. The reorganization of this program has been completed, and it is fully operational. The clinical oncology program budget for fiscal year 1977 is $13,470,000, including intramural and collaborative support.

Highlights of the completed reorganization include:

(*a*) The assignment of the Surgery branch and Radiation Onocology branch to the Division of Cancer Treatment, clinical oncology program, in order to facilitate a multimodal approach to therapy.

(*b*) The selection of the chief for the Pediatric Oncology Branch and section chief within the branch to head up the new and redirected efforts in experimental hematology.

(*c*) The selection of the new associate director for the clinical oncology program.

(*d*) A new emphasis in biologic markers has been initiated, particularly as it relates to breast cancer.

(*e*) The initial clinical studies in whole body hyperthermia have been accomplished and are very promising.

BASIC RESEARCH

Mr. CONTE. How much money will you spend this year for projects which are technically outside of the Cancer Institute but which impact on cancer research—basic molecular/biological research, for example?

Answer. All research that is supported by the Cancer Institute certainly relates to the cancer problem. We estimate that approximately 48 percent of the total NCI budget is spent on basic research. This includes our regular research grants and basic research in cancer centers, organ site programs, contracts, intramural research, as well as portions of our training and constuction programs. The largest portion of our basic research can be identified with our research thrusts, for example, cause and prevention research, detection and diagnosis research, and treatment research. There is other research that we term "cancer biology" that has application to all research thrusts but is very basic research and therefore difficult to identify with each of the research thrusts. This area of cancer biology, which totaled $117,709,000 in fiscal year 1976, includes basic research in epidemiology, carcinogenesis (physical and chemical), viral oncology, nutrition, tumor biology, and immunology. This research is also beneficial to the other institutes of NIH, and conversely the research of the other institutes is very

beneficial to the work of the National Cancer Institute. There is excellent coordination among the various institutes in exchanging research information.

RECOMBINANT DNA

Mr. CONTE. Does the Cancer Institute fund or propose any research in conjunction with work on recombinant DNA?

Answer. In fiscal year 1978, it is estimated that the NCI will be supporting recombinant DNA research at a level of approximately $5,041,000. This amount is comprised of applicable portions of research grants and contracts, training activities and intramural efforts. Because facilities requirements are rather stringent to insure human and environmental safety, major efforts have not been instituted in this area. As you are aware there has been considerable activity recently in this area of research. Guidelines have been developed which must be adhered to prior to receiving NCI (and NIH) support for recombinant DNA research. Therefore, construction funds, predominantly for alteration and renovation of facilities, are required in order to renovate existing space to make it suitable for this type of research. Approximately $2 to $3 million is included in the construction portion of the budget for this program in 1978.

IMMUNOTHERAPY

Mr. CONTE. Would you tell me about the work the Institute is doing in the area of immunotherapy and the application of immunotherapy to cancer treatment?

Answer. Currently the majority of studies on immunotherapy are still on the level of animal models. The experimental variables studied include strains of the organism, optimum dose, schedule and method of administration. Other preclinical studies include studies on the effects of an immunologic agent known as MER, utilization of RNA to increase the immunity to specific tumors, and immunotherapy with cells which are chemically treated and reinjected into the body. As far as human studies are concerned, early trials have been directed toward the most promising areas of melanoma and myelogenous leukemia. Very recent results in treatment of localized lung cancer suggest that introduction of another agent known as BCG into the pleural space after removal of the primary lung tumor prolongs significantly the disease-free interval. Although the immunotherapy has not produced dramatic results as yet, the work in melanoma, myelogenous leukemia, and lung cancer indicates that this approach to cancer therapy is becoming established as a fourth modality of treatment.

HEREDITY

Mr. CONTE. The August 21, 1976, National Observer had an article concerning the "two hit" theory, that relates to the idea that a second genetic mutation is needed for a hereditary predisposition to lead to cancer. What is being done on the hereditary aspects of cancer; and is there anything to support the "two hit" theory?

Answer. It is believed that carcinogenesis is a multistep process and considerable information is developing which supports this contention. The "two hit" theory is a simplified version of the "multistep theory." It basically states that the first genetic mutation converts a cell or some cells to a preneoplastic state and that if a second mutation follows, the same cell will become neoplastic or cancerous. If the first mutation occurs in a germ cell, then the embryo that develops therefrom may only require one additional hit to develop cancer, whereas embryos that have developed from germ cells that were not mutated before conception would require two hits.

There is considerable emphasis being placed on somatic cell genetic studies and somatic cell hybridization studies to ascertain whether neoplasia is a dominant or recessive trait and whether it is the result of one genetic change or many. All of these studies relate directly and indirectly to the problem of how many genetic changes occur before the neoplastic state is established. Furthermore, there are basic studies being supported in the genetics of the immune system to determine what contributions deficiencies of the immune system add to predisposing individuals to cancer. Epidemiological studies are being encouraged to ascertain the validity of theories that contend predisposition to cancer is hereditary. All of the above currently supported efforts are intended to clarify the contributions of direct genetic alterations and heredity to the cancerous process.

Mr. CONTE. A recent NIH report indicated that certain forms of cancer strike some races with greater frequency than others. Can you give me some examples, and is research being done on this effect?

Answer. Compared to other nonwhite groups, cancer mortality among blacks was high for cancers of the mouth and throat, esophagus, stomach, pancreas, larynx, lung, bladder, cervix and multiple myeloma. American Indians had increased mortality for cancers of the biliary passages and liver (primarily gallbladder cancer in females). Mortality among Chinese-Americans was very high for cancers of the nasopharynx, and Japanese-Americans experienced excessive mortality from stomach cancer. These findings are not new, but rather are consistent with a number of earlier reports documenting excessive rates of malignancy among specific racial groups. Investigations of factors related to these racial differences are included in a number of ongoing studies which are following up on leads found in the atlases.

LUNG CANCER

Mr. CONTE. If you have found such close correlations between smoking and lung cancer, why does the Federal Government continue to grant price supports to tobacco growers? Why isn't some stronger action taken on smoking by the appropriate health officials?

Answer. The Institute recognizes the very close correlation between cigarette smoking and lung cancer. We cannot, however, regulate what the Federal Government does in terms of granting price supports to tobacco growers. The institute is, of course, pursuing its efforts to minimize the dangers of smoking.

In 1974, the National Cancer Advisory Board, in a resolution on smoking sent to President Ford, stated that:

"While the opportunity for preventive medicine is technically available, its implementation will require a social decison. The Natonal Cancer Advisory Board, charged with the task of furthering the national effort against cancer is compelled to point out the importance of this issue and recommends that Government take all steps possible to reduce cigarette smoking and to protect the smoker".

"The National Cancer Advisory Board recommends that the regulatory authorities of the Federal Government be examined for their application and adequacy to reduce health hazards from smoking cigarettes, and that the Congress enact and the President support new legislative amendments, if appropriate, to strengthen these powers".

Also as I mentioned in my opening statement, a less hazardous cigarette has been developed through efforts under the National Cancer Program. It is hoped this will help reduce the risk of developing lung and other cancers. In addition, the National Cancer Program is continuing and expanding its efforts to promote dissemination of information and knowledge about cancer of all sorts to all who can benefit—physicians, patients, and the general public.

PESTICIDE EFFECTS

Mr. CONTE. Some scientists are predicting that a sharp increase in the cancer death rate will begin within 5 years, when the long-term effect of some agricultural pesticides and other chemicals begin to take hold. Is this likely? Are there indications now of such an effect?

Answer. It is not possible to predict with certainty whether cumulative exposures to environmental chemicals such as agricultural pesticides will lead to a sharp rise in the incidence of cancer. We do know that heavy exposure to certain chemicals such as in the workplace can produce cancer, but only limited data are available to evaluate the carcinogenic effects of agents entering the general environment through air, water, and food. Although there is no evidence that cancer rates are now rising in the general population as a result of these substances, the threat of a future problem is real and calls for close epidemiologic monitoring of cancer risk in the population-at-large and in various groups with greater-than-usual exposure to suspect chemicals.

CARCINOGENS

Mr. CONTE. Last June the GAO reported that there was a serious lack of overall Federal policy on carcinogenesis research and regulation. Examples include

cases where the Food and Drug Administration has banned a substance from food but EPA allows the same chemical in drinking water. Or cases where the Cancer Institute issues a report on a carcinogen but no action is taken by the regulatory agencies. What is being done to see that these types of things don't occur, that carcinogens don't slip between the bureaucratic cracks?

Answer. It is recognized that the legislative statutes which provide authority to Federal regulatory agencies differ from agency to agency and within agencies, depending upon the nature and vehicle of human exposure to chemical substances. For instance, the Food and Drug Administration may ban a chemical where the enabling legislation, in this case the Delaney clause, provides the authority for them to do so. This same chemical, however, found elsewhere in the environment would be subject to other statutes, for example the Toxic Substances Control Act, where the legislative requirement is that risk-benefit assessment be made. Therefore, given the present legal structure, a given chemical found to be cancer-producing in animals will be dealt with in different ways by different regulatory agencies. This is not necessarily inconsistent with the best interests of public health nor does it necessarily interfere with the generation of uniform scientific approaches to cope with chemical carcinogens.

From an operational standpoint we have recently instituted a mechanism for hand-delivery of reports from NCI to all of the Federal regulatory agencies. In addition, availability of the report is announced in the Federal Register, a press release is prepared announcing the availability of the report and the report is distributed widely by the National Cancer Institute's Office of Cancer Communications. In addition, we have cross-linking memberships between the various advisory groups within and among the Federal regulatory agencies, such as Environmental Protection Agency, Food and Drug Administration, and National Institute for Occupational Safety and Health. Third, we have recently established the National Clearinghouse on Environmental Carcinogens which has representatives and observers from all of the Federal agencies involved and meets regularly in public forum.

Mr. CONTE. What is being done by the Cancer Institute to clear the backlog of reports on long-term animal testing programs?

Answer. A program has been developed and implemented to eliminate the backlog of chemicals being tested for carcinogenicity. It is anticipated that nearly all will have been completed and the results made public by the end of the fiscal year. Reassignment of National Cancer Institute (NCI) staff has made it possible to expedite the monitoring of the various stages of completing the backlog research and writing of reports. At present, 82 percent of the backlog of chemicals are proceeding as scheduled or ahead of schedule. The others lag behind schedule a few weeks, but the surveillance mechanisms has served to identify the problems in the flow of experimentation making it possible to correct them as they arise. All of the resources available to the bioassay program have been concentrated on this problem, which has been given the highest priority. A new NCI project officer has been assigned to the prime contract. The principal investigator on the prime contract has been replaced. Several consulting groups have been added in pathology, toxicology, and report writing to expedite the completion of the backlog of carcinogenesis testing and reporting.

PEER REVIEW

Mr. CONTE. There have been critical reports that the Cancer Institute's advisory peer review panels are too conservative and/or too self-interested in their own grants to be objective about the review process. Do you think there is any basis in such criticisms? Would there be any justification in including scientists, perhaps researchers from other fields, to participate in the review process?

Answer. I do not feel that such criticisms are justified. The overall record of NCI peer review is a good one. Neither the biomedical community nor NCI staff would tolerate a lesser standard of review than that of the generally accepted NIH standard. The review committee members' expertise is very frequently augmented by the use of additional consultants, many of whom have expertise in such scientific specialties as cell biology, genetics, molecular biology, virology and biochemistry, which are applicable to the specific cancer proposal under evaluation. The "self-interest" of the review committee is thus offset by these specialists from other fields. This is especially true at site visits where most of the reviewers are not review committee members. Even for reviews of applications for center core support where experienced site visitors knowledge-

able of this support mechanism are essential, site visit teams rarely contain as much as 50 percent of the reviewers who are members of the regular review committee. The members of the review committee are invariably very strongly influenced by the outside reviewers' opinions and comments. Thus, we recognize the merits of including scientists from other fields to participate in the review process and have done this as a standard practice. The question of "conservatism" has been asked about most initial review groups at NIH. However, as is evidenced by the types of investigator-initiated research grants approved by the review groups and later awarded by the NCI, new and innovative research is continually the hallmark of our grants basic research program. Therefore, new research is not at a disadvantage in the evaluation and review process, and accordingly it is not being sacrificed for the continuation of the same type of research.

RESEARCH GRANTS

Mr. CONTE. In your research grants, why do you have such a decrease in regular noncompeting categories?

Answer. There is a $2.3 million decrease in the amount being funded for noncompeting regular research grants in fiscal year 1978. The NCI is funding all of the noncompeting requirements. The noncompeting requirements are less in 1978 because a smaller number of new grants were awarded in 1977 than in the prior year. The new grants funded in 1977 become noncompeting grants in 1978.

TRAINING

Mr. CONTE. Why are you requesting almost a reversal of your priorities for individual training awards between competing and noncompeting categories?

Answer. The National Research Service Act, which authorizes training awards and fellowships was passed in 1974. New awards were made in 1975 and 1976. Because the awards generally cover from 2 to 5 years of support, the number of noncompeting awards made each year has cumulatively increased. Since we give a high priority to the payment of our "moral commitment" noncompeting continuation grants, then the requested funds for new grants is reduced. This determination is based on an earlier decision to fund approximately $18 million in training grants of a total appropriation request of $818,936,000.

CONSTRUCTION

Mr. CONTE. You are requesting $12 million for construction. What will that be used for, and why is it $10 million less than last year?

Answer. The grant construction program will fund biohazard containment projects needed by the recombinant-DNA, environmental carcinogenesis, and viral oncology research programs. These projects will be primarily renovation work but new construction work may be required. Contracts for construction will be used to update and modify laboratories and other cancer research support areas on the NIH reservation and the Frederick Cancer Research Center.

The decrease in the construction program was the result of a decision on priorities, that is, to utilize more of the requested 1978 funds to meet immediate research needs in such research programs as epidemiology, carcinogenesis, nutrition, and clinical trials.

POSITIONS

Mr. CONTE. You are requesting nine fewer positions for program management. Will that permit you to effectively administer the tremendous program you have? Would you explain why there is a slight increase of funding for program management along with the decrease in positions?

Answer. The budget request reflects a decrease in positions from 2,031 in 1977 to 2,022 in 1978. Manpower shortages in the National Cancer Institute have been a problem throughout the expansion of the National Cancer Program. Additional positions would be very helpful, particularly in the management of grants and contracts, as well as in the clinical trials program. The increase in funding for program management is attributed predominately to necessary personnel costs including within-grade increases and the Federal pay raises as well as increased costs for program operations.

AUTHORIZATION

Mr. CONTE. Are you supporting a particular level of authorization in the legislation for the extension of the National Cancer Act? Do you believe that a 15-percent increase above the previous year's appropriation would be adequate as proposed by the Health Subcommittee?

Answer. The National Cancer Advisory Board has recommended an authorization level for fiscal year 1978 of $1.3 billion. This level is well above what would be anticipated that Congress will appropriate. However, there are some uncertainties about several research areas, and the Board would like to have the authorization ceilings sufficiently high to take care of new opportunities and increased requirements. Some of these are as follows:

(*a*) In the future we will have to spend more construction money to permit laboratories around the country to have the minimum essential biohazard containment.

(*b*) It may become desirable in the relatively near future to propose several trial installations of radiation therapy equipment utilizing stripped nuclei protons or pi-meson beams.

(*c*) With the multitude of compounds in the environment, and the new ones entering at the rate of 900–1,000 per year, there needs to be a significant gearing up of bioassay activities and carcinogenesis research. Also, depending on how the division of responsibility develops under the Toxic Substances Control Act, NCI may have to substantially increase its activities in this area.

(*d*) A closely related area which will have to be stepped up is in diet and nutrition research. There is a need for much more research in the causative properties of diet as well as maximizing the role of nutrition in therapy.

The total authorization level in the National Cancer Act for fiscal year 1977 is $1,073.5 million. I would recommend that figure as the minimum level of authorization for fiscal year 1978, but support the recommendation of the Board $1.3 billion to allow for new opportunities, and expansion of programs. A 15-percent increase above the previous year's appropriation could be a deterrent in the conduct of research and cancer control activities. The scientific base is available now which can and should be more fully exploited. It is logical, therefore, that authorization levels will be sufficient to take care of current opportunities available to us and to allow rapid exploitation of new opportunities in both cancer research and cancer control.

PROGRAM LEVEL

Mr. CONTE. What level of funding would have to be provided in order to permit a genuine continuation of all ongoing projects and the maintenance of this year's program level?

Answer. The NCI would require $888,238,000 in fiscal year 1978 in order to continue all ongoing projects and maintain the same program level as in fiscal year 1977. This figure represents no increase in the number of grant and contract awards over the fiscal year 1977 level. It would not be possible to provide significant expansion to such vital areas as development of rapid testing methods for carcinogens, clinical trials, community activities and research in the effects of diet and nutrition on cancer cause and cancer therapy. In order to maintain the momentum of the National Cancer Program, an increase in the budget request of $136 million to a level of $955 million would be required, as recommended by the National Cancer Advisory Board over the budget request of $818,936,000.

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JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Amounts Available for Obligation[1/]

	1977	1978
Appropriation	$815,000,000	$818,936,000
Comparative transfers to:		
"Health Services Administration" (for transfer of one position to establish linkage between research activities in NIH and operating Health Services Administration programs)	-38,000	---
"General Departmental Management" (for support of Grants Appeal Board function)	-26,000	---
Subtotal, budget authority	814,936,000	818,936,000
Unobligated balance, start of year	1,000	---
Total, obligations	$814,937,000	$818,936,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 estimate - $136,000; 1978 - $136,000.

National Cancer Institute

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	No.	FTE 1/	Amount	No.	FTE 1/	Amount
Research Grants						
Regular:						
Non-competing	1,418		$110,151,000	1,205		$107,878,000
Competing	(583)		(52,149,000)	(605)		(57,923,000)
Renewal	263		26,090,000	257		27,961,000
New	320		19,871,000	348		22,978,000
Supplemental	(187)		6,188,000	(186)		6,984,000
Subtotal	2,001		162,300,000	1,810		165,801,000
Specials:						
Cancer research centers	188		138,553,000	184		139,569,000
Task forces	158		14,300,000	151		14,300,000
Research career program	129	129	3,081,000	125	125	3,000,000
Clinical education program	85		8,996,000	77		9,000,000
Radiation development program	19		4,060,000	17		4,000,000
Cancer research emphasis grants	119		9,471,000	129		10,200,000
Subtotal	698	129	178,461,000	683	125	180,069,000
Total research grants	2,699	129	340,761,000	2,493	125	345,870,000
Training Programs:						
Individual awards:						
Non-competing	146	146	1,635,000	207	207	2,960,000
Competing	(189)	(189)	(2,924,000)	(115)	(115)	(1,640,000)
Renewal	---		---	---		---
New	189	189	2,120,000	115	115	1,640,000
Supplemental	(268)		804,000	(---)		---
Subtotal	335	335	4,559,000	322	322	4,600,000
Institutional awards:						
Non-competing	112	718	15,441,000	88	650	13,563,000
Competing	(---)		(---)	(---)		(---)
Renewal	---		---	---		---
New	---		---	---		---
Supplemental	(---)		---	(---)		---
Subtotal	112	718	15,441,000	88	650	13,563,000
Research and development contracts	976		222,814,000	963		221,291,000
Intramural research			79,891,000			84,771,000
Direct operations			61,488,000			67,846,000
Program management			7,357,000			7,762,000
Cancer control			60,625,000			61,233,000
Construction			22,001,000			12,000,000
TOTAL			$814,937,000			$818,936,000

1/ Full-time equivalent.

DHEW - National Institutes of Health

CROSSWALK - 1977 COLUMN 1978 JUSTIFICATION

National Cancer Institute
(In thousands of dollars)

Program	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Direct Operations	Program Management	Cancer Control	Construction	Total
	Regular Program	Specials: Cancer Centers	Specials: Other	Individual	Institutional							
1977 Appropriation												
A. Research												
1. Cause and prevention research	$36,299	$18,449	$14,268			$106,136	$24,274	$13,993	$2,370			$215,789
2. Detection and diagnosis research	6,905	723	4,319			19,972	7,683	8,389	861			48,852
3. Treatment research	69,149	44,437	9,005			80,897	29,998	20,926	2,222	$2,523		259,157
4. Cancer biology	49,947	17,044	239			15,809	17,936	12,742	1,449			115,166
Subtotal	162,300	80,653	27,831			222,814	79,891	56,050	6,902	2,523		638,964
B. Resource Development												
1. Cancer centers support		57,900						1,501	88			59,489
2. Research manpower development			12,077	$4,559	$15,441			1,367	66			33,510
3. Construction								821	51		$22,001	22,873
Subtotal		57,900	12,077	4,559	15,441			3,689	205		22,001	115,872
C. Cancer Control								1,749	250	58,102		60,101
Total obligations	$162,300	$138,553	$39,908	$4,559	$15,441	$222,814	$79,891	$61,488	$7,357	$60,625	$22,001	$814,937
Standard level user charge								(1,225)				(1,225)

DHEW - National Institutes of Health

CROSSWALK - 1978 COLUMN 1978 JUSTIFICATION

National Cancer Institute
(In thousands of dollars)

Program	Research Grants			Training Programs		Research and Development Contracts	Intramural Research	Direct Operations	Program Management	Cancer Control	Construction	Total
	Regular Program	Specials: Cancer Centers	Specials: Other	Individual	Institutional							
1978 Estimate												
A. Research												
1. Cause and prevention research	$36,877	$17,972	$15,107			$110,733	$24,480	$15,981	$2,491			$223,641
2. Detection and diagnosis research	7,045	746	4,007			19,245	8,556	8,939	908			49,446
3. Treatment research	71,861	45,450	9,141			76,540	32,025	22,975	2,352	$2,662		263,006
4. Cancer biology	50,018	17,401	245			14,773	19,710	14,025	1,537			117,709
Subtotal	165,801	81,569	28,500			221,291	84,771	61,920	7,288	2,662		653,802
B. Resource Development												
1. Cancer centers support		58,000						1,663	94			59,757
2. Research manpower development			12,000	$4,600	$13,563			1,414	70			31,647
								849	46		$12,000	12,895
3. Construction												
Subtotal		58,000	12,000	4,600	13,563			3,926	210		12,000	104,299
C. Cancer Control								2,000	264	58,571		60,835
Total obligations	$165,801	$139,569	$40,500	$4,600	$13,563	$221,291	$84,771	$67,846	$7,762	$61,233	$12,000	$818,936
Standard level user charge								(1,405)				(1,405)

Summary of Changes

1977 Estimated Obligations	$814,937,000
1978 Estimated Obligations	818,936,000
Net change	+3,999,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	---	$70,000	---	+$104,000
2. Bureau of Employees Compensation	---	75,000	---	+86,000
3. FTS rate increase	---	580,000	---	+47,000
4. Service and Supply Fund	---	2,735,000	---	+155,000
5. Payment for centrally furnished services	---	26,940,000	---	+3,732,000
(Standard level user charge)	---	(1,225,000)	---	(+180,000)
Subtotal		30,400,000		+4,124,000
B. Program:				
1. Research grants				
a. Regular program	---	162,300,000	---	113,866,000
(1) Non-competing continuations converting from competing status	---	(110,151,000)	---	(+55,943,000)
(2) Competing (new, continuations and supplementals)	---	(52,149,000)	---	(+57,923,000)
b. Special programs	---	178,461,000	---	+1,608,000
2. Individual training awards	---	4,559,000	---	+4,600,000
a. Non-competing continuations converting from competing status	---	(1,635,000)	---	(+2,960,000)
b. Competing (new, continuations and supplementals)	---	(2,924,000)	---	(+1,640,000)
3. Intramural research	1,524	77,579,000	---	+4,836,000
4. Direct operations	266	33,732,000	---	+2,488,000
5. Program management	183	7,131,000	-9	+388,000
6. Cancer control	58	60,519,000	---	+602,000
Subtotal	2,031	524,281,000	-9	+128,388,000
Total, increases	2,031	554,681,000	-9	+132,512,000

Summary of Changes--Continued

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Built-in:				
1. One less day of pay.....	---	---	---	-$187,000
Subtotal.....	---	---	---	-187,000
B. Program:				
1. Research grants				
a. Regular program.....	---	$162,300,000	---	-110,365,000
(1) Non-competing completed or converted to competing status.....	---	(110,151,000)	---	(-58,216,000)
(2) Competing completed or converting to non-competing	---	(52,149,000)	---	(-52,149,000)
2. Individual training awards.....	---	4,559,000	---	-4,559,000
a. Non-competing completed or converting to non-competing status.....	---	(1,635,000)	---	(-1,635,000)
b. Competing completed or converting to non-competing....	---	(2,924,000)	---	(-2,924,000)
3. Institutional training awards.....	---	$15,441,000	---	-1,878,000
a. Non-competing completed or converted to competing status	---	(15,441,000)	---	(-1,878,000)
4. Research and development contracts.....	---	222,814,000	---	-1,523,000
5. Construction.....	---	22,001,000	---	-10,001,000
Subtotal.....		427,115,000		-128,326,000
Total, decreases.....		427,115,000		-128,513,000
Total, net change.....	---	---	-9	+$3,999,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
34	Research						
	(a) Cause and Prevention Research....	661	$215,789,000	659	$223,641,000	-2	+$7,852,000
	(b) Detection and Diagnosis Research.....	233	48,852,000	232	49,446,000	-1	+594,000
	(c) Treatment Research	612	259,157,000	610	263,006,000	-2	+3,849,000
	(d) Cancer Biology....	388	115,166,000	386	117,709,000	-2	+2,543,000
47	Resource Development						
	(a) Cancer Centers Support.....	23	59,489,000	23	59,757,000	---	+268,000
	(b) Research Manpower Development.....	18	33,510,000	18	31,647,000	---	-1,863,000
	(c) Construction.....	15	22,873,000	14	12,895,000	-1	-9,978,000
54	Cancer Control						
	(a) Cancer Control....	81	60,101,000	80	60,835,000	-1	+734,000
	Total obligations.....	2,031	$814,937,000	2,022	$818,936,000	-9	+$3,999,000
	(Standard level user charge).....		(1,225,000)		(1,405,000)		(+180,000)

DHEW - National Institutes of Health

Research Programs Summary

National Cancer Institute

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
RESEARCH PROGRAMS						
Epidemiology	146	$31,234,000	146	$32,115,000	---	+$881,000
Carcinogenesis (Physical & Chemical)	266	102,965,000	267	112,029,000	+1	+9,064,000
Viral Oncology	327	98,836,000	325	97,756,000	-2	-1,080,000
Nutrition	7	7,389,000	7	7,640,000	---	+251,000
Tumor Biology	252	61,168,000	249	61,963,000	-3	+795,000
Immunology	201	77,216,000	199	78,326,000	-2	+1,110,000
Diagnostic Research	132	28,052,000	132	28,541,000	---	+489,000
Preclinical Treatment Research	275	108,236,000	274	106,247,000	-1	-1,989,000
Clinical Treatment Research	288	121,335,000	288	126,380,000	---	+5,045,000
Rehabilitation Research	---	2,533,000	---	2,805,000	---	+272,000
Total	1,894	638,964,000	1,887	653,802,000	-7	+14,838,000
RESOURCE DEVELOPMENT	56	115,872,000	55	104,299,000	-1	-11,573,000
CANCER CONTROL	81	60,101,000	80	60,835,000	-1	+734,000
Total NCI	2,031	$814,937,000	2,022	$818,936,000	-9	+$3,999,000

National Cancer Institute

Fiscal Year 1977

CROSSWALK - Research Programs

RESEARCH PROGRAMS	Cause and Prevention Research		Detection and Diagnosis Research		Treatment Research		Cancer Biology		Total	
	Pos.	Amount	Pos.	Amount	Pos.	Amount	Pos.	Amount	Pos.	Amount
Epidemiology	71	$17,952,000	41	$9,175,000	34	$2,776,000	---	$1,331,000	146	$31,234,000
Carcinogenesis (Physical & Chemical)	259	91,446,000	---	---	---	---	7	11,519,000	266	102,965,000
Viral Oncology	325	93,908,000	---	---	---	---	2	4,928,000	327	98,836,000
Nutrition	2	5,153,000	---	---	5	1,354,000	---	882,000	7	7,389,000
Tumor Biology	---	---	---	---	---	---	252	61,168,000	252	61,168,000
Immunology	4	7,330,000	60	11,625,000	10	22,923,000	127	35,338,000	201	77,216,000
Diagnostic Research	---	---	132	28,052,000	---	---	---	---	132	28,052,000
Preclinical Treatment Research	---	---	---	---	275	108,236,000	---	---	275	108,236,000
Clinical Treatment Research	---	---	---	---	288	121,335,000	---	---	288	121,335,000
Rehabilitation Research	---	---	---	---	---	2,533,000	---	---	---	2,533,000
Total	661	$215,789,000	233	$48,852,000	612	$259,157,000	388	$115,166,000	1,894	$638,964,000

National Cancer Institute

Fiscal Year 1978

CROSSWALK - Research Programs

RESEARCH PROGRAMS	Cause and Prevention Research		Detection and Diagnosis Research		Treatment Research		Cancer Biology		Total	
	Pos.	Amount	Pos.	Amount	Pos.	Amount	Pos.	Amount	Pos.	Amount
Epidemiology	71	$18,998,000	41	$8,930,000	34	$2,669,000	---	$1,518,000	146	$32,115,000
Carcinogenesis (Physical & Chemical)	260	99,044,000	---	---	---	---	7	12,985,000	267	112,029,000
Viral Oncology	323	92,657,000	---	---	---	---	2	5,099,000	325	97,756,000
Nutrition	2	5,240,000	---	---	4	1,343,000	1	1,057,000	7	7,640,000
Tumor Biology	---	---	---	---	---	---	249	61,963,000	249	61,963,000
Immunology	3	7,702,000	59	11,975,000	10	23,562,000	127	35,087,000	199	78,326,000
Diagnostic Research	---	---	132	28,541,000	---	---	---	---	132	28,541,000
Preclinical Treatment Research	---	---	---	---	274	106,247,000	---	---	274	106,247,000
Clinical Treatment Research	---	---	---	---	288	126,380,000	---	---	288	126,380,000
Rehabilitation Research	---	---	---	---	---	2,805,000	---	---	---	2,805,000
Total	659	$223,641,000	232	$49,446,000	610	$263,006,000	386	$117,709,000	1,887	$653,802,000

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	2,031	2,022	-9
Full-time equivalent of all other positions	380	390	+10
Average number of all employees	2,395	2,412	+17
Personnel compensation:			
Permanent positions	$40,504,000	$41,639,000	+$1,135,000
Positions other than permanent	6,576,000	7,121,000	+545,000
Other personnel compensation	1,693,000	1,828,000	+135,000
Subtotal, personnel compensation	48,773,000	50,588,000	+1,815,000
Personnel benefits	7,378,000	7,670,000	+292,000
Travel and transportation of persons	3,294,000	4,100,000	+806,000
Transportation of things	330,000	390,000	+60,000
Rent, communications and utilities	3,120,000	3,450,000	+330,000
Printing and reproduction	1,490,000	1,680,000	+190,000
Other services:			
Project contracts	273,038,000	269,724,000	-3,314,000
Payment for centrally furnished services	26,940,000	30,672,000	+3,732,000
Other	37,923,000	41,463,000	+3,540,000
Supplies and materials	17,350,000	18,114,000	+764,000
Equipment	6,310,000	6,552,000	+242,000
Grants, subsidies and contributions	388,991,000	384,533,000	-4,458,000
Total obligations by object	$814,937,000	$818,936,000	+$3,999,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1977 House Report	
Environmental Epidemiology	
1. The Committee is quite concerned that adequate study be done to examine the relationship between cancer rates in population groups and their exposure to various chemical and environmental factors. The Committee, therefore, provided 17 new positions for the Environmental Epidemiology Branch and the Institute is directed to provide the necessary additional space for this activity. (page 25)	1. 17 additional positions have been allocated to the Environmental Epidemiology Branch, and recruitment is being handled on a priority basis. Additional space will be provided for this activity.
Carcinogenesis	
2. The Committee directs the National Cancer Institute (NCI) to place greater emphasis upon research on identifying carcinogenic agents. The Committee, therefore, provided 60 new positions for the Carcinogenesis Program, and the Institute is directed to provide the necessary additional space for this activity. (page 25)	2. 60 additional positions have been allocated to the Carcinogenesis Program and recruitment is being handled on a priority basis. Additional space will be provided for this activity.
Occupational Carcinogenesis Program	
3. The Committee directs the National Cancer Institute to continue its participation with the National Institute for Occupational Safety and Health (NIOSH) in the Occupational Carcinogenesis program and has provided $3 million for that program. (page 25)	3. An inter-agency agreement has been finalized which provides $3 million to NIOSH.

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act:		
Section 301 - Research and Investigation...		
Title IV, Part A -- National Cancer Institute.....	1/	$801,050,000 2/
Section 409 (b) -- Cancer Control.....	1/	
Section 410C. -- Research.....	1/	
Title IV, Part I -- National Research Service Awards.....	1/	$17,886,000 3/

1/ Authorization expires September 30, 1977. Extension legislation is proposed.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $277,000 for old training programs.

National Cancer Institute

(Comparable)

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$176,246,000	$176,246,000	$183,941,000	$176,225,000
1969	180,869,000	175,754,000	184,754,000	178,311,500
1970	173,887,000	173,887,000	191,703,000	174,615,963
1971	197,404,000	220,651,000	228,651,000	223,651,000
1972	369,063,000	371,479,000	391,469,000	372,881,000
1973	427,422,000	485,505,000	485,505,000	485,505,000 1/
1974	500,000,000	523,183,000	580,800,000	528,286,000 2/
1975	600,882,000	480,388,000 3/	755,882,000	692,548,000
1976	605,920,000	704,484,000 4/	804,484,000 4/	762,647,000 5/
1977	687,670,000	773,348,000	849,936,000	814,936,000
1978	818,936,000			

The figures presented in this table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of general research support grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

1/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by Public Law 93-192.

3/ Excludes contracts not considered by House due to lack of authorization.

4/ Excludes fellowships and training grants--not considered due to pending legislation ($18,163,000).

5/ Includes $18,163,000 authorized by the continuing resolution.

National Cancer Institute

(Actual)

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	180,725,000	200,000,000	181,454,000
1971	202,383,000	227,383,000	235,383,000	233,160,000
1972	334,338,000	337,531,000	358,233,000	378,794,000
1973	432,205,000	492,205,000	492,205,000	492,205,000
1974	500,000,000	522,383,000	580,000,000	527,486,000[1/]
1975	600,000,000	479,506,000[2/]	755,000,000	691,666,000
1976	605,000,000	703,564,000[3/]	803,564,000[3/]	761,727,000[4/]
1977	687,670,000	773,412,000	850,000,000	815,000,000
1978	818,936,000			

1/ Appropriation after reduction as authorized by Public Law 93-192.

2/ Excludes contracts not considered by House due to lack of authorization.

3/ Excludes fellowships and training grants--not considered due to pending legislation ($18,163,000).

4/ Includes $18,163,000 authorized by the continuing resolution.

Justification

National Cancer Institute

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research	1,894	$638,964,000	1,887	$653,802,000	-7	+$14,838,000
Resource Development	56	115,872,000	55	104,299,000	-1	-11,573,000
Cancer Control	81	60,101,000	80	60,835,000	-1	+734,000
Total	2,031	$814,937,000	2,022	$818,936,000	-9	+$3,999,000

General Statement

The goal of the National Cancer Program (NCP) is to develop the means to significantly reduce the incidence, morbidity and mortality of cancer in man and ultimately to develop the means to eliminate all human cancers. As stated in the National Cancer Act of 1971 and reiterated in the National Cancer Act Amendments of 1974, the National Cancer Program is to "...plan and develop an expanded, intensified, and coordinated cancer research program encompassing the programs of the National Cancer Institute, related programs of other research institutes, and other Federal and non-Federal programs." (National Cancer Act, Section 407. (b) (1).)

The National Cancer Institute (NCI) is the responsible Federal agency for the implementation and coordination of the NCP and is a principal source of financial support to organizations throughout the world involved in cancer research. Research efforts of the NCP are directed to developing the means, the knowledge and the techniques necessary for controlling and eliminating this dread disease.

A National Cancer Program Plan (NCPP) evolved as a result of the efforts of leading cancer experts throughout the United States. A Strategic Plan, the result of the continuous planning process of the NCPP, has been developed and provides a series of recommendations for research and control activities. The major research objectives are organized into the research thrusts of: cause and prevention research; detection and diagnosis research; treatment research; and cancer biology. Control objectives are organized into major intervention areas of: prevention; detection, diagnosis and pretreatment evaluation; and treatment, rehabilitation and continuing care. Complementary to the research and control activities are support components consisting of cancer centers support, research manpower development, and construction.

Research Thrusts

Cause and prevention research is concerned with the identification of those factors which cause cancer in man and with the development of mechanisms for preventing cancer in man.

Detection and diagnosis research is directed toward the identification of cancer in patients early enough and precisely enough so that the latest methods of treatment can be applied for maximum effect toward control of the disease.

Treatment research enhances the development of methods to cure as many cancer patients as possible and to maintain control of the cancerous process.

Cancer biology is essential to each of the other research thrusts and constitutes a basic research nucleus which is critical to the implementation of the National Cancer Program. The Cooperative Minority Biomedical Program will continue to receive support to further implement and foster cancer research through minority programs. Efforts will be directed in the research thrusts of the Program as well as training programs.

Research Programs

During the past year, the Institute has identified 10 research programs which encompass all research funded by the National Cancer Institute. This common language was needed in order to reduce or eliminate confusion between similar or related program activities, ambiguous description of existing programs which could result in program overlaps, and misinformation throughout the Institute on program concepts and task force activities.

The 10 research programs within the four basic research thrusts which span the NCI organizational units are: Epidemiology, Carcinogenesis (Physical and Chemical), Viral Oncology, Nutrition, Tumor Biology, Immunology, Diagnostic Research, Preclinical Treatment Research, Clinical Treatment Research, and Rehabilitation Research. Priority is being given to Epidemiology, Carcinogenesis, Nutrition and Clinical Treatment Research.

Resource Development

Complementing the research and control activities of the National Cancer Program Plan are the supporting activities of cancer centers support, research manpower development, and construction.

Cancer Centers Support - This activity provides funds for developing centers which can generate new knowledge about cancer and accelerate the transfer of this knowledge into improved practices for cancer prevention, diagnosis, treatment, and rehabilitation.

The NCI has recognized 19 cancer centers which have met or nearly meet the criteria established by the National Cancer Advisory Board to be comprehensive centers.

Research Manpower Development - The research manpower needs in specific disciplines important to the fulfillment of the National Cancer Program are met by providing individual and institutional fellowships, training grants, and education grants. Programs included are: National Research Service Awards; the Clinical Cancer Education Awards; Research Career Development Awards; and Research Career Awards.

Construction - Within the provisions of the National Cancer Act of 1971, as amended in 1974, the NCI is authorized to support new construction, modernization and renovation of outdated research facilities and construction of new biohazard containment facilities. Through construction grants, the National Cancer Institute provides up to 75 percent of eligible construction costs with at least 25 percent being provided by the grantee from non-Federal sources. Construction funds are also used to modernize and renovate facilities on the NIH campus and at other Federal facilities including the Frederick Cancer Research Center.

Cancer Control

The Cancer Control Program, as established under the National Cancer Act, has the responsibility for conducting a national effort to facilitate the dissemination of the latest proven and practical research knowledge or technological advancements to the health community and the public. In meeting these responsibilities, program activities are coordinated with those of State and Territorial Health Departments, and health care delivery institutions, as well as with other governmental agencies, societies and associations involved in all phases of controlling cancer.

In this role the Cancer Control Program serves as an intermediary between the research laboratory or clinic and the general health care delivery systems of the U.S. The Program does not deal directly with the entire population at risk or afflicted by cancer, but instead develops prototype projects which, if successful, serve as models to be used by the various organizations involved in cancer control.

Support Activities

Other activities which serve to support the Research, Resource Development and Cancer Control Programs of the National Cancer Institute include: international activities; dissemination of information; and interagency coordination of Federal programs concerned with cancer research.

International activities implemented by the NCI and as specified in the National Cancer Act include: the establishment of the International Cancer Research Data Bank (ICRDB); support for cancer research outside the United States by highly qualified foreign nationals; support for collaborative research involving both American and foreign scientists; and maintenance of close liaison and joint scientific endeavors with international organizations having well defined interests and programs in the cancer field.

The NCI, to assure the dissemination of cancer information, is actively involved with other governmental agencies, private and voluntary groups and organizations. The Institute conducts a variety of activities which communicate research and cancer control information to physicians. Conferences are held in strategic locations throughout the United States to assist health professionals update their knowledge of advances in cancer through the communication activities of the cancer centers and programs. The clinical cooperative research groups and organ-site programs provide important avenues for channeling research and cancer control information to physicians and health professionals.

The NCI continues to broaden its involvement with other Federal organizations in cancer, cancer-related and other categorical or noncategorical health activities. Included in this area of interagency cooperation are the Interagency Committee for the National Cancer Program, and the Interagency Coordinating Committee for Cancer Control. The NCI is also responsible for coordination of the NCP's Environmental Carcinogenesis Program with other governmental agencies.

Nine administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

The narrative justifications and the Program Purpose and Accomplishment statements provide additional insight into these programs.

Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cause and Prevention Research	661	$215,789,000	659	$223,641,000	-2	+$7,852,000
Detection and Diagnosis Research	233	48,852,000	232	49,446,000	-1	+594,000
Treatment Research	612	259,157,000	610	263,006,000	-2	+3,849,000
Cancer Biology	388	115,166,000	386	117,709,000	-2	+2,543,000
Total Research	1,894	638,964,000	1,887	653,802,000	-7	+14,838,000
Budget Mechanism:						
Research Grants:						
Regular		162,300,000		165,801,000		+3,501,000
Non-competing		(110,151,000)		(107,878,000)		(-2,273,000)
Competing		(52,149,000)		(57,923,000)		(+5,774,000)
Specials		108,484,000		110,069,000		+1,585,000
Cancer Research Centers		(80,653,000)		(81,569,000)		(+916,000)
Other Specials		(27,831,000)		(28,500,000)		(+669,000)
Research and Development Contracts		222,814,000		221,291,000		-1,523,000
Intramural Research	1,524	79,891,000	1,524	84,771,000	---	+4,880,000
Direct Operations	199	56,050,000	199	61,920,000	---	+5,870,000
Program Management	171	6,902,000	164	7,288,000	-7	+386,000
Cancer Control		2,523,000		2,662,000		+139,000
Total	1,894	$638,964,000	1,887	$653,802,000	-7	+$14,838,000

Cause and Prevention Research

Program Purpose

Cause and Prevention Research is concerned with the identification of factors, such as specific physical, chemical and biological agents, life styles and genetic factors, which contribute to human cancer. With the development of knowledge concerning the biological processes by which cancer occurs, the ultimate goal of this research is preventing or interrupting the carcinogenic process in man. It is well documented that much of the cancer occurring in the U.S. today is preventable. World-wide statistics show that different countries can have very different cancer experiences. Additional evidence suggests that such differences are primarily due to environmental factors, diet and life-styles.

The major programs of Cause and Prevention Research include the following:

Epidemiology studies generate and test hypotheses concerning environmental and host factors in the causation of cancer. This research includes identification of individuals who are susceptible or resistant to cancer, and includes exploration of possible reasons for susceptibility or resistance. A major component of the research is identification of

peculiarities in the patterns of cancer among people in families, ethnic groups, occupations or different geographic settings. Additional studies support the evaluation of treatment and diagnostic research along with general statistical support of various research projects at NCI and other components of the NIH.

Carcinogenesis (Physical and Chemical) research emphasizes the identification of cancer-causing chemicals (carcinogens) in the environment. Included are an extensive chemical testing effort; research to develop rapid and less expensive laboratory testing methods; a carcinogenesis information system to collect and disseminate human exposure and carcinogenicity data concerning environmental chemicals; work on the biological metabolism of carcinogens; studies of the combined action of viruses, physical agents, and environmental carcinogens; a Smoking and Health program directed toward reducing risk of disease among smokers; and a recently established Clearinghouse on Environmental Carcinogens.

Viral Oncology research seeks to identify the role which viruses or subviral components may play in cancer causation. Research is being conducted into the nature of both RNA- and DNA-containing tumor viruses. Studies also involve the co-factor mechanism whereby viruses may interact with environmental carcinogens changing a normal cell into a cancerous one.

Nutrition research focuses on the development and dissemination of information on relationships between diet and nutrition and the causes of cancer. Included are studies relating dietary and nutrient excesses, deficiencies or imbalances to cancer susceptibility or resistance, and attempts to define the optimum role of dietary nutrients in the treatment and rehabilitation of the cancer patient.

Immunology efforts place major emphasis on the role of the immune system through study of immunologic abnormalities and immune surveillance.

Program Plans

The 1978 budget estimate for Cause and Prevention Research of $223,641,000 and 659 positions represents an increase of $7,852,000 and a decrease of 2 positions from the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Epidemiology - a 1978 estimate of $18,998,000 and 71 positions.

Studies are underway and will continue to identify environmental and other factors responsible for clusters of high-risk communities in the United States, and to determine the interactions between inherited and environmental factors in the development of cancer. Other research will attempt to correlate the hormone-binding characteristics of breast cancer tissue with epidemiologic risk factors, as well as to further elucidate the relationships between occurrence rates of breast cancer and exposure to hormonal drugs or other environmental agents. Several studies are intended to determine whether smoking and alcoholism are high-risk factors in head and neck cancer by examination of the effectiveness of anti-smoking and anti-drinking clinics in reducing risk and to identify populations exposed to known and suspected

occupational carcinogens for bladder cancer.

Carcinogenesis (Physical and Chemical) - a 1978 estimate of $99,044,000 and 260 positions.

In the area of carcinogenesis bioassay, the quality of the animal studies will continue to be upgraded. The program will attempt to bring up to date a backlog of studies in the area of pathology and supporting information systems. Emphasis will be directed toward body burden and metabolism studies. This information for substances stored in the body will permit comparison of effects in animals with those anticipated in man.

Selected in vitro testing systems are now sufficiently far advanced in their development that they will be further assessed for reproducibility and reliability, which will permit more rapid and economical conduct of a broad spectrum of investigations in carcinogenesis.

Intensified interest in environmental carcinogenesis has resulted in increased collaboration with regulatory agencies such as the Food and Drug Administration and the Environmental Protection Agency, as well as other interested agencies including the National Institute of Occupational Safety and Health and the National Institute of Environmental Health Sciences. Increased communications and collaboration in this area will be fostered by the recently established Clearinghouse for Environmental Carcinogens which will serve as a focal point in matters concerning the identification, evaluation and assessment of risk of chemical carcinogens.

In accordance with the newly legislated Toxic Substances Control Act, the Institute will be providing assistance to EPA in the areas of: development of standards for carcinogenicity testing; review and evaluation of test data; periodic review of the adequacies of the standards; providing representation to the Administrator's interagency committee for selecting substances for testing; determination of the extent of human exposure; development of research on testing programs; complying with new requirements for the standardization of reported data; and centralizing and making accessible all pertinent information within NCI information storage systems.

Continued studies of the chemistry, metabolism and toxicity of carcinogens will provide a greater understanding of their mechanisms of action in animals. An understanding of these mechanisms is needed to form the basis for developing methods to interrupt the carcinogenic process before the development of cancer. Studies of compounds called synthetic retinoids will continue in an effort to demonstrate their potential application to limit or possibly reverse the development of cancers of the lung, bladder, breast and skin.

The carcinogenesis information systems will continue to be developed to make data on human exposure and carcinogenicity of environmental chemicals more rapidly available to all segments of our society. Further efforts to determine the mechanism of carcinogenic action responsible for human tumor development will be conducted. Research will be continued to provide the basis for greater acceptability of cigarettes with a much lower level of risk for cancer and other respiratory damage.

Viral Oncology - a 1978 estimate of $92,657,000 and 323 positions.

The emphasis in cancer virology has moved from the search for cancer-causing viruses to the study of mechanisms by which viral genetic material might influence the composition and functions of host cells. Viruses appear at present to be among the best and most useful tools for studying the cancerous process. To that end, studies of cell growth are planned to determine whether cellular mechanisms are involved in the initiation of cancer by viral material. Such studies may lead to specific natural or synthetic products that may control this process.

Efforts will be increased to define the interaction of viruses with biological, physical and chemical factors resulting in the transformation of cells to a cancerous state.

Of special interest are chemicals and biological agents that affect virus expression, thus providing a rational basis for prevention and treatment of human cancer.

Studies will continue to be conducted to adapt biochemical and immunological tests for viral substances to the detection of early breast cancer. Similar tests have proven useful in predicting the occurrence of tumors in animals.

Continued effort will be made to counteract or suppress the cancerous properties of transformed cells so that they are once again subject to normal growth control. One approach would use chemicals (natural or synthetic) that induce differentiation of immature cells to the mature cells of adults.

Human cancer cells will be examined for viral DNA (deoxyribonucleic acid, the hereditary material of genes) which may be integrated into cellular DNA. While the search for new RNA viruses (ribonucleic acid, which can direct the synthesis of DNA under certain conditions) from non-human primates is continued, greater emphasis will be placed on determining whether DNA viruses can play a role in causing human cancer. Scientists have learned that certain DNA viruses, which are found in association with several human cancers, will change normal cells in laboratory cultures into cancerous cells.

A comprehensive survey of human cancers for the presence of herpes viruses will be intensified. Viruses from this group are widespread in the population and may be causally linked to cancers of the nasopharynx (inner passages of the nose) and uterine cervix.

Nutrition - a 1978 estimate of $5,240,000 and 2 positions.

Research will further explore dietary factors linked to cancer and their mechanisms of action, the definition of desirable food intake for health maintenance, and the role of nutrition in cancer therapy and patient rehabilitation.

For optimal nutritional support of the cancer patient, alternatives to

intravenous procedures need to be developed and tested. Studies will be initiated to identify deficiencies in nutrient solutions which are administered orally, and to define the competitions between host and cancer cells for nutrients.

Laboratory studies of certain dietary components will be pursued to clarify the possible role of carbohydrates in carcinogenesis to determine the effect of dietary antioxidants on spontaneous and chemically induced cancers in animals and to elucidate the effects of nutrients on enzymes that metabolize known carcinogens. Other studies will explore the effects of selenium and dietary fiber on the development of cancer and the effect of carcinogens on rats fed varying diets.

In studies of humans, the focus initially will be on evaluating current methods used to survey dietary intake in large populations so that improved methods may be developed for analyzing the effects of nutrition on human cancer.

Immunology - a 1978 estimate of $7,702,000 and 3 positions.

Studies will be pursued to determine the basis for increased incidence of lymphomas and certain other types of tumors in immunologically abnormal animals.

Studies to examine the mechanism underlying increased tumor incidence following viral infection of immunosuppressed animals will be continued.

Detection and Diagnosis Research

Program Purpose

In the natural history of cancer there is a period, usually long, in which a tumor has started to grow, but causes few or no symptoms. If the tumor can be found at this stage the chances of long-term survival are extremely good. Early diagnosis for cancer of every site is the goal of research in the detection and diagnosis of cancer. There are three main areas of research: epidemiology, immunology and diagnostic research. Epidemiology is concerned with the identification of groups of people at high risk to cancer. In immunology, because of the great specificity of immunologic reactions, it is hoped that immunodiagnostic tests can be developed that will indicate the presence of cancer. If these tests are successful, many cancers could be detected earlier than is possible with x-rays. Diagnostic research has two approaches. The first is histological, the standard diagnostic method of examining tissue under a microscope. This includes cytology, the microscopic examination of cells as in the Pap smear. The second is radiology, the visual identification of cancerous growths using x-rays.

Programs Plans

The 1978 budget estimate for Detection and Diagnosis Research of $49,446,000 and 232 positions represents an increase of $594,000 and a decrease of 1 position from the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Epidemiology - a 1978 estimate of $8,930,000 and 41 positions.

The SEER (Surveillance, Epidemiology, End Results) program will be continued and expanded to follow national cancer incidence, identify high risk groups, and estimate national treatment results. This work identifies problem areas and indicates trends in disease patterns. Many cases of cancer are far advanced when first seen, in spite of symptoms being present for some time and in spite of the past efforts to educate the public concerning the cancer symptoms and the importance of annual checkups. Research will be continued in order to discover the reasons for this and what must be done to make patients see a doctor sooner.

The most common cancer among women is breast cancer. In spite of many years of epidemiological studies, many questions remain unanswered, while new ones have been generated (possible diet effects, wide use of estrogens), so that this area in particular requires a special effort. Some of the newly identified potential factors in cancer causation will be studied epidemiologically.

Immunology - a 1978 estimate of $11,975,000 and 59 positions.

The highly sensitive reactions of the body's immune defense system potentially may be used for early detection of cancer with tests for antigens, substances which stimulate immunologic responses. Research will continue to develop and improve tests for several cancer-associated antigens,

including ferritin, in the blood of breast cancer patients and blood in the feces of patients with cancers of the intestinal tract. The assay for fecal blood will undergo a wide clinical evaluation.

Investigators have been concerned with the problem of nonspecificity of the assays. The immunologic reactions have been directed toward antigens that at times occur with noncancerous conditions or fail to occur in some cancer patients. To improve such assays, new cancer antigens will be sought, isolated and identified, and used to produce antibodies for new tests. The blood of patients with early stages of cancer then will be tested for the presence of antigens. Blood banks have been organized where, under carefully controlled conditions, blood specimens with proper clinical information are stored to be used for evaluating newly developed tests.

The complex reactions of cell-mediated immunity will be explored further for new immunologic approaches to cancer detection and diagnosis.

Diagnostic Research - a 1978 estimate of $28,541,000 and 132 positions.

The detection program relies heavily on methods using x-rays which in recent years made great strides in improving the images while lowering the exposure doses to ionizing radiation. This has been achieved in several ways. Equipment has been modified to give a better focusing of the x-ray beams, more sensitive films have been developed, and recognition of specific picture patterns has improved as has the performance of technical personnel. The questions to be addressed now are how often one should be screened, how many different views are required, and what other effective methods might exist that do not require exposure to x-rays. Ultrasound is now being tested for tumor visualization and its practical application will be evaluated. New and more detailed algorithms will be developed and applied in Computerized Axial Tomography (CAT) in which an x-ray scanner produces highly defined cross-sectional pictures of the body. Additional computer methods for CAT will also be worked out to localize internally administered radioisotopes. New techniques will be further developed for mammography to reduce the dosage of radiation. Additional methods of cell separation will be explored so that machines can be used to read samples from Pap smears.

The clinical trial assessing the effect of early diagnosis on survival from lung cancer will have completed patient enrollment. The project will continue in the follow-up stage to monitor the screenees - about 30,000 men, all middle-aged cigarette smokers. Even at this early stage it appears that close surveillance with chest x-ray and sputum cell samples can find cancer at a much earlier stage than surveillance by annual x-ray. Another experimental method of cancer detection requiring no ionizing radiation is thermography which measures the heat emitted by the body. Studies must now be carried out to gain some understanding of bodily processes of heat production to make better use of this non-invasive method.

Imaging techniques can also be developed and improved through the use of radioactive isotopes generated by cyclotrons. Few cyclotrons are available and those are devoted principally to atomic energy studies. A project is to be carried out to develop a small, hospital-based cyclotron devoted to clinical use.

Treatment Research

Program Purpose

The goal of the National Cancer Program in treatment research is to develop the means for providing maximum benefit to the cancer patient, the ultimate objective being to enable the patient to live a normal life span free of cancer. As cancer treatment has evolved, emphasis has been placed successively on individual methods, namely: surgery; radiotherapy; chemotherapy; and recently immunotherapy. In recent years, however, there has been a growing realization that cure of the various disseminated cancers will probably require use of some or all of these modalities in combination. Much of the present and future program emphasis will be directed toward exploitation of new discoveries in each of the modalities separately and their optimal integration.

Treatment Research includes the following research programs:

Epidemiology research is principally concerned with statistical analysis of disease trends in ongoing clinical trials. Nutrition research involving clinical trials will be concerned with hyperalimentation studies of cancer patients. Immunology research will primarily concern studies utilizing the patients' immune system to manage the disease. Preclinical Treatment research includes the acquisition of material and screening for antitumor agents, pharmacology and toxicology tests in animals, preclinical combined modality research, and the production and formulation of agents for clinical trials. Clinical Treatment research is the testing of new treatment in people and includes chemotherapy, radiotherapy, surgery and immunotherapy, as well as other approaches such as hyperthermia. Rehabilitation research is concerned with the investigation of methods for the most proper rehabilitation of the cancer patient. Areas of investigation include pain and nutrition, as well as reconstructive methods and techniques.

Program Plans

The 1978 budget estimate for Treatment Research of $263,006,000 and 610 positions represents an increase of $3,849,000 and a decrease of 2 positions from the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Epidemiology - a 1978 estimate of $2,669,000 and 34 positions.

In clinical trials, efforts will be directed on the use of concomitant or prior patient information for the selection of "best" treatments. There is a continual need to provide computer support, a more involved design of trials for more forms of cancer, and for analysis of large sets of data. More emphasis will also be placed on developing programs to facilitate comparisons of data collected in different clinical trials using sophisticated biostatistical techniques.

The use of a vaccine to prevent viral hepatitis (this disease is associated with liver cancer in Africa) will be studied to determine if a reduction in hepatitis will be associated with a diminished incidence of liver cancer.

Nutrition - a 1978 estimate of $1,343,000 and 4 positions.

Hyperalimentation has been identified as a high priority research area. Chemotherapy and radiation therapy tend to seriously affect the gastro-intestinal tract, causing severe vomiting and diarrhea. Patients are also not able to take medication which further aggravates their condition. Hyperalimentation is a method to maintain the patient's weight and overall physical condition in order to strengthen patients against infection and to bolster their ability to receive medication. It is felt that if the physical condition of the patients can be maintained they will have a better response to therapy. These studies are primarily in support of patients with head and neck cancer and lung cancer as well as those with gastrointestinal tumors.

Immunology - a 1978 estimate of $23,562,000 and 10 positions.

Studies in animal models will be expanded to determine the best ways of stimulating the natural immunities against cancer. It is intended that these animal applications will be transferred for use in human clinical trials.

Phase I trials (studies to determine the tolerated dosage and toxicity in man) of selected new immunotherapeutic procedures will be conducted on selected patients with advanced cancer of various types.

Preclinical Treatment Research - a 1978 estimate of $106,247,000 and 274 positions.

The drug development area will continue to be a major thrust of this program. A spectrum of experimental animal tumors and xenografts (human tumors grown in animals) is being established as a secondary screen after biologic activities of drugs have been identified. Efforts in this area will facilitate more rapid and efficient evaluation of these systems as potential predictors of clinical activity of new agents for cancers of specific organ systems in man.

Comprehensive drug development projects will be supported under the Cancer Research Emphasis Grant (CREG) mechanism to bring together several research activities--development of new screening methods with new drug synthesis, and pharmacology with biochemical studies on drug action and resistance. Bringing together these disciplines is designed to create an optimal scientific environment leading to rational drug synthesis and evaluation.

A program on the design of radiation sensitizing drugs will exploit recent findings that such drugs do exist and may indeed provide increased clinical benefit when used to supplement radiation therapy.

Clinical Treatment Research - a 1978 estimate of $126,380,000 and 288 positions.

With the establishment of a new screening panel, increased emphasis will be placed on the evaluation of new agents in the clinical program in order to determine as rapidly as possible the predictive value of those systems. These studies will principally involve Phase II studies which concern the initial evaluation and efficacy of single agents, combination of agents, or combined modalities in specific types of cancers.

Chemotherapy regimens recently developed for large bowel cancer and stomach cancer will continue for the treatment of patients with advanced metastatic disease. Based on the successful results, studies have been initiated utilizing these regimens immediately after surgery and such protocols will be extended to include the use of immunotherapy in addition to chemotherapy. Adjuvant studies will also be initiated in other major cancers where surgery alone fails to cure a meaningful number of patients. Particular emphasis will be placed on early stages of lung cancer, head and neck cancer, and genitourinary cancers.

The use of drugs and hormones in the treatment of breast cancer will be continued because of the recent ability to specifically identify hormone responsive patients by the presence of estrogen binding proteins. In addition, ongoing studies involving chemotherapy after mastectomy continue to demonstrate a significantly lower recurrence rate for women whose breast cancer has spread to the lymph nodes. It is intended to modestly expand these studies to include the use of drugs with other modalities, such as immunotherapy, in order to increase survival and at the same time reduce the necessity for radical surgery.

The Clinical Cooperative Group Program will continue to place emphasis on the creation of new, smaller, geographically oriented groups. Further resources will be required to expand the character of the existing large multidisease groups from a chemotherapeutic approach to a multidisciplinary one including surgery, radiotherapy and immunotherapy.

Clinical trials with whole body hyperthermia (use of heat to treat cancer) and with regional hyperthermia combined with radiotherapy will be initiated. Clinical trials will be continued involving new drugs, immunotherapy, combined modalities, high LET radiation, and new studies of radiation time-dose-volume fractionation. The use of markers will also be extended to more clinical trials programs.

Rehabilitation Research - a 1978 estimate of $2,805,000.

Rehabilitation research projects will continue to be funded to investigate rehabilitation methods and techniques with emphasis on the psychosocial aspects of cancer rehabilitation; the development of means to deal with specific impairments suffered by cancer patients and problems involved in rehabilitation of childhood cancer patients. Specific fields include those of reconstruction of facial defects, voice change after radiotherapy, the provision of sensory feedback in a leg prosthesis, the rehabilitation of oropharyngeal cancer and investigations into the development of an electronic pharyngeal prosthesis.

Cancer Biology

Program Purpose

Cancer Biology is fundamental to all other research thrusts of the National Cancer Program. Its purpose is to generate basic knowledge which will advance our understanding of the uncontrolled growth and spread of cancer cells. These major areas of concern, loss of growth control and metastasis, or spread, must be studied at the biochemical, molecular and structural level of the cell if a rational and effective basis for dealing with the problems of cancer diagnosis, treatment and prevention is to be developed and refined. During loss of growth control, a normal functioning cell becomes drastically altered and prone to rapid, repeated and uncontrolled divisions. Cancerous growth occurs because of one or more alterations in the complex regulatory biochemistry of the cell. These changes can be induced by chemical, physical and biochemical carcinogens, by viruses or by combinations of these. Nutritional and genetic factors may also contribute to the susceptibility, development and control of cancer, but how these factors might interact with carcinogens and viruses is unknown. While learning to understand growth is a primary focus, the most devastating and killing effects of cancerous growth is due to the spread of cancer cells to multiple sites in the body where growth is reinitiated. During metastasis, cancer cells invade the surrounding tissue, reach the blood stream and somehow avoid destruction by the immune system.

A complete understanding of growth control and metastasis requires a thorough examination of regulatory mechanisms that occur both within and between cells. Nearly all of the basic biological disciplines are involved in studying these processes. These include pathology, cell biology, biochemistry, developmental biology, histology, immunology, virology, genetics, molecular biology, and epidemiology. Cancer Biology is important to each of the other cancer program thrusts and represents research to expand basic information which is essential to the implementation and progress of the National Cancer Program. Research programs within Cancer Biology include epidemiology, carcinogenesis (physical & chemical), viral oncology, nutrition, tumor biology and immunology.

Program Plans

The 1978 budget estimate for Cancer Biology of $117,709,000 and 386 positions represents an increase of $2,543,000 and a decrease of 2 positions from the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Epidemiology - a 1978 estimate of $1,518,000.

Biological and medical research efforts will continue to develop ways to identify populations of people who are at high risk of developing cancer through analyses of abnormalities in human populations and the assessment of biological factors contributing to increased risk to cancer in certain groups.

Carcinogenesis (Physical and Chemical) - a 1978 estimate of $12,985,000 and 7 positions.

The action of carcinogens may be considerably more complex than originally believed. Evidence is accumulating that nutritional factors and other chemicals which are not causes of cancer by themselves may actually act together to become carcinogens. It has been reported that in some cases when exposure to a promoter substance is followed by exposure to a known carcinogen, the amount of carcinogen required to cause cancer is much lower than if the carcinogen were acting alone. Thus, in identifying carcinogens and determining their mode of action, it is also important to consider the multiple effects of promoter substances. Research will be continued and expanded to identify the cellular sites of action and mode of action of cancer causing agents (e.g., carcinogens and viruses).

Viral Oncology - a 1978 estimate of $5,099,000 and 2 positions.

There is evidence that only a small part of cancer virus genetic material directs or controls tumor induction. Continuing investigations will seek an understanding of the excision of viral genes and their integration into host cell control mechanisms which will aid in understanding the transformation of normal cells into tumor cells. Further studies will explore the meaning by which gene expression is regulated in cancer viruses.

Nutrition - a 1978 estimate of $1,057,000 and 1 position.

The role of dietary fat and fat metabolism in the development of cancer will be further investigated to determine the effect of nutritional factors on the molecular structure in normal and cancerous individuals and animals.

Tumor Biology - a 1978 estimate of $61,963,000 and 249 positions.

As an essential element in the development of more effective procedures for cancer diagnosis, cancer treatment and cancer cure, research studies will be conducted to determine and evaluate critical differences between normal and cancer cells.

It has been demonstrated that uncontrolled growth in certain kinds of breast cancer is regulated by two different hormones. This discovery is important because it begins to explain why all breast cancers, while displaying similar symptoms, are not responsive to the same endocrine therapies.

Future emphasis will continue to concentrate on changes that occur in the cell surface. Recent advances in technology have clearly shown that the cell surface is not a separate entity but is highly integrated with internal cellular regulatory processes. The appearance, disappearance and alteration of cell surface components may very well account for the ability of cancer cells to grow uncontrollably, invade surrounding tissue and escape the immune system. It is expected that new developments in the field of genetics will be invaluable in defining which of the many different cell surface components contribute to cancer cell behavior. Once these components are identified developments should follow in the design of biochemical and immunological therapies.

Continuing efforts will be made to elucidate which factors control gene expression, and which chromosomal genes are significant to the development and maintenance of cancer.

At the Frederick Cancer Research Center efforts will be continued to include cell biology and biochemistry studies in order to determine the role of cell membrane antigens in tumor development.

Immunology - a 1978 estimate of $35,087,000 and 127 positions.

Immunological research will continue in order to seek ways in which the body's natural defenses can be mobilized against cancer cells. In the past few years the complexity and lack of uniformity of the cancerous process has been firmly established through immunological research. For example, it has been demonstrated that patients with plasmacytoma (any benign or malignant tumor of plasma cells) who exhibit the same symptoms actually produce different immune responses. Thus, the cancerous process occurs at many different sites.

These kinds of discoveries further emphasize the importance and necessity of developing a complete understanding of cellular regulatory processes if we are to establish how changes on these processes can produce different degrees of abnormality.

Resource Development

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cancer Centers Support	23	$59,489,000	23	$59,757,000	---	+$268,000
Research Manpower Development	18	33,510,000	18	31,647,000	---	-1,863,000
Construction	15	22,873,000	14	12,895,000	-1	-9,978,000
Total Resource Development	56	115,872,000	55	104,299,000	-1	11,573,000
Budget Mechanism:						
Research Grants:						
Specials		69,977,000		70,000,000		+23,000
Individual Training Awards		4,559,000		4,600,000		+41,000
Institutional Training Awards		15,441,000		13,563,000		-1,878,000
Direct Operations	50	3,689,000	50	3,926,000	---	+237,000
Program Management	6	205,000	5	210,000	-1	+5,000
Construction:						
Grants		16,000,000		9,000,000		-7,000,000
Contracts		6,001,000		3,000,000		-3,001,000
Total	56	$115,872,000	55	$104,299,000	-1	-$11,573,000

Cancer Centers Support

Program Purpose

The Cancer Centers Support activity provides funds for the development and support of centers which can generate new knowledge about cancer cause and prevention, diagnosis, treatment, and rehabilitation and enhance the dissemination of this knowledge to those responsible for the health care in the surrounding communities.

Cancer centers serve as national research resources and promote effective interaction between basic and clinical scientists. They bring together the surgeon, radiation therapist, medical oncologists, and many others as a research team to provide improved treatment and management of the cancer patient.

The cancer centers support (core) grant is a mechanism to support those elements of a cancer center that are required for the planning, development, evaluation, administration, and maintenance of an active and unified center in order to consolidate and focus cancer-related activities into a single administrative and programmatic structure. Through this mechanism, funds may be provided to support center activities. It provides support for professional staff, centralized services and resources, and shared equipment. Research is not supported by the core grant except for small developmental projects which are limited to three years.

Exploratory grants provide support for planning new cancer centers or cancer programs as well as for planning expansion, modification, or strengthening of existing centers and programs.

Program Plans

The 1978 budget estimate for Cancer Centers Support of $59,757,000 and 23 positions represents an increase of $268,000 over the 197/ estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Cancer centers continue to play a highly visible and important role in the National Cancer Program. They serve as a focus for research in all aspects of the cancer program. Centers also provide a base for cancer control activities through their outreach programs, e.g., cancer information services have been established in 17 of the comprehensive centers.

Nineteen cancer centers have now been recognized by the National Cancer Institute as meeting or rapidly approaching the criteria set down by the National Cancer Advisory Board to be considered comprehensive centers.

During calendar year 1977, evaluations will be conducted under the auspices of the National Cancer Advisory Board of each of the 19 recognized comprehensive centers. The purpose of the visits is to measure progress and further evaluate each center's program in terms of the established criteria. These visits will be an essential part of the continuing overall evaluation of the Centers Program.

Cancer Centers continue to serve as an important and solid base for the development, implementation and evaluation of numerous efforts by the National Cancer Institute in the attack on cancer. Without a strong base the development and coordination of a variety of cancer programs within an institution or community would often be difficult or impossible.

While support for the development of data and statistical capability is not limited to comprehensive centers, the NCI is especially promoting this activity in these centers. This is in keeping with the recommendations of the National Cancer Advisory Board (NCAB) and the National Cancer Program. A minimum cancer patient data base for a Centralized Cancer Patient Data System (CCPDS) has been defined. Continued development and increased funding for this program are important. The information contained in the Centralized Cancer Patient Data System will provide certain basic administrative as well as scientific data which will help to describe and to evaluate the function and performance of participating cancer centers. CCPDS will also provide the means to supply data designed to fit the needs of the International Cancer Research Data Bank (ICRDB) program. In addition, a Statistical Analysis and Quality Control Center (SAQC) will be funded. SAQC will be mainly a mechanism for cancer centers to set up a cooperative reporting system on clinical cancer data and will serve as a platform for a fruitful interaction among centers and between centers and NCI.

Community outreach or cancer control activities will continue as a vital component of cancer centers. The centers will provide leadership in developing programs and a base from which to operate. Programs presently being developed and those currently underway are targeted to make the knowledge acquired by research in centers more readily available to community physicians as well as the lay public. It is increasingly important to develop high quality diagnostic and treatment procedures in the community since it is not practical to refer all cancer patients to a cancer center or

cancer hospital. Eventually, except for the more serious and complicated cancer cases, quality cancer therapy should be made available at the local level.

Medical, surgical and radiation oncologists are now located in a large number of communities. Many of these oncologists were trained in cancer centers and are aware of the importance of a team effort in the diagnosis and treatment of cancer. The team approach needs to be expanded to additional communities throughout the nation.

In FY 1978, the cancer centers will continue to serve as national resources for research, education, training and community outreach. Since the National Cancer Act of 1971, there has been increasing emphasis on centers of broad scope to provide a comprehensive attack upon cancer in geographically and demographically strategic areas across the nation. There are, however, many other centers receiving cancer center support funds whose scope is less extensive. Such centers may specialize in radiation, medical, surgical or pediatric oncology. Others focus on cancer immunology, pharmacology, epidemiology, virology or carcinogenesis. Regardless of the scope of a cancer center all contribute to the efforts of the National Cancer Program.

Research Manpower Development

Program Purpose

Highly specialized professional personnel are urgently needed to continue and expand the concerted attack on cancer. Needs for personnel in specific disciplines to support important areas of the National Cancer Program are identified through a continuous process of assessment with the scientific community. It is well recognized that both basic and clinical researchers are needed. The work of the clinical researchers is directly based upon fundamental knowledge of cancer developed by basic researchers. The need for manpower, both short term and long range, can only be met by organizing dynamic research training, education and fellowship programs. The research manpower development programs of the National Cancer Institute include the following:

The National Research Service Awards Program supports clinical and fundamental research training in fields identified by the NCI as areas of crucial manpower needs. Institutional grants are the mainstay of any manpower development system. They not only stabilize the manpower development program by strengthening institutions' capabilities for excellent and up-to-date training, but also provide the coordination necessary for goal-oriented programs responding to scientific and educational needs. Individual fellowships are a valuable adjunct to the institutional program. Individually tailored training complements institutional grants and amplifies the effectiveness of the total manpower development program by increasing the availability of scientists in needed disciplines.

Clinical Cancer Education Grants assist medical and dental schools and other selected institutions to improve the quality and scope of their clinical cancer teaching activities directed toward undergraduate and graduate students and practicing physicians and dentists. These grants have enabled institutions to define their teaching objectives relative to cancer, to plan core cancer curricula, to offer additional cancer electives, to develop new teaching materials, and to provide a broad, coordinated, and multidisciplinary approach to undergraduate cancer education. Both undergraduate and graduate students have been exposed to specialized learning experiences that have attracted many of them to careers in oncology. Practitioners have learned to use the best available detection, diagnostic and therapeutic techniques in dealing with their cancer patients and have expert consultation made freely available to them.

Research Career Development Awards provide support for young scientists who show potential for developing into outstanding independent investigators in the cancer-related sciences. High quality, independent research will be pursued in such areas as carcinogenesis, epidemiology, tumor biology, immunology and viral oncology.

Research Career Awards, which are slowly being phased out, provide lifetime salaries to accomplished cancer research specialists.

Program Plans

The 1978 budget estimate for Research Manpower Development of $31,647,000

and 18 positions represents a decrease of $1,863,000 below the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

National Research Service Awards Program - a 1978 estimate of $17,886,000.

This will allow the awarding of approximately 319 individual awards and 88 institutional awards. These awards will continue to support training in three broad research areas. The first area is the cause, nature and prevention of cancer. Extensive research is needed to determine how viruses relate to the host's ability to resist infection and to the presence of environmental carcinogens. At the same time, every effort must be made to learn whether the transformation of normal cells to cancerous cells can be prevented and whether cancerous cells themselves can be prevented from spreading through the body. The second area of manpower training encompasses the detection and diagnosis of cancer. It is imperative that procedures be developed to accurately assess the risk of any particular person having cancer and to determine the presence and probable course of cancer in those who have the disease. The third area includes the treatment and cure of cancer as well as restoration of patients to normal and productive lives. Chemotherapy, immunotherapy, surgery and radiotherapy must be extensively developed alone and in combination. Laboratory discoveries must be translated more rapidly into application at the local medical level through improvements in the processes of technological transfer. Also, rehabilitative activities directed towards the physical, emotional and socio-economic aspects of the patient's needs must be vastly improved. Examples of the types of research specialists that will be trained for performing short-range and long-range clinical and non-clinical cancer research are:

Biochemists	Radiation Oncologists
Medical Oncologists	Pathologists
Epidemiologists	Surgical Oncologists
Biostatisticians	Immunologists
Nutritionists	Pyschologists

Clinical Cancer Education Program - a 1978 estimate of $9,000,000.

This will allow the awarding of 77 institutional awards which will include 6 new awards. These awards will continue to support coordinated and innovative cancer teaching in schools of medicine, dentistry, osteopathy, and public health, in major hospitals affiliated with medical schools, and in specialized cancer institutions. There are more than 300 eligible institutions for clinical cancer education awards.

It has been estimated that cancer morbidity and mortality could be reduced by 25 to 50 percent if existing and newly developed diagnostic and therapeutic measures were applied promptly. One way to help bring this about is to broaden the education of physicians and dentists at all levels relative to cancer. Even the most sophisticated teaching institutions can, with supplemental support, provide a better quality of cancer teaching to more individuals.

Research Career Program - a 1978 estimate of $3,000,000.

Research Career Development Awards will support 116 individuals who show outstanding research potential for careers of independent research of high quality in the sciences related to cancer. Awards are made to research and academic institutions to provide all or part of the salary of the awardee, based on training, experience, and demonstrated potential for health-related research productivity. Nine Research Career Awards will continue to provide salary support to finance established cancer investigators of high competence, although the program itself is being phased out.

A total of $277,000 will be required to continue the phase-out of the Graduate and Clinical Training Programs.

The resources of the Research Manpower Development Program supported by the NCI are summarized in the following table:

Research Manpower Development Program	(In thousands) 1977 Estimate	1978 Estimate
National Research Service Awards	$18,236	$17,886
Clinical Cancer Education Program	8,996	9,000
Research Career Development Awards	2,805	2,718
Research Career Awards	276	282
Graduate & Clinical Training Program	1,764	277
Staff and Other Support	1,433	1,484
Total	33,510	31,647

Construction

Program Purpose

The National Cancer Act of 1971, as amended in 1974, authorizes the National Cancer Institute to renovate, modernize, and construct new facilities for basic research, clinical research, and biohazard containment. Each application for funding undergoes review for scientific merit, evaluation of the competence of the investigator of the research program which will be housed in the proposed space, and analysis of its role in the National Cancer Program. Only after passing this extensive review is a construction project approved and funded. Therefore, funds to improve cancer research space are committed only where there is a demonstrated need for modern and safe laboratories - safe with respect for proper containment of hazardous materials to protect the community and the environment. The NCI can provide up to 75% of eligible construction costs, with the prospective grantee providing at least 25% from non-federal sources.

The continuance of funding high priority construction projects has been strongly advocated by both the President's Cancer Panel and the National Cancer Advisory Board. Their recommendations have been based on three factors: (1) basic research has supplied promising new information which now needs specialized clinical research facilities for patient trials; (2) new and encouraging research leads now being developed will require more research space; and (3) there is a need for biohazard containment research facilities to meet new laws and DHEW regulations.

Program Plans

The 1978 budget estimate of $12,895,000 and 14 positions represents a decrease of $9,978,000 and 1 position below the 1977 level for construction. The need for adequate and safe laboratories to conduct experiments on potentially hazardous compounds remains one of the highest priorities in the NCI construction program. As an example, the NIH has launched a major research program involving recombinant DNA material. The program will study the genetic regulation of cell growth and thereby will yield a more complete understanding of cancer cell growth patterns. The hazards of this work are of varying degrees but most of these projects will require specialized containment facilities in order to prevent accidental harm to the environment and the community. The NCI will participate in the support for some of these efforts. The 1978 construction funds will also improve clinical research space and laboratories relating to virology, carcinogenesis, immunology, chemotherapy and radiation therapy. A portion of the total funds will be used to support contract construction at NIH and other Federal facilities, including the Frederick Cancer Research Center. It is estimated that these funds can support the construction needs of selected institutions for a total of approximately 93,000 square feet.

Cancer Control

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cancer Control.....	81	$60,101,000	80	$60,835,000	-1	+$734,000
Total Cancer Control....	81	$60,101,000	80	$60,835,000	-1	+$734,000
Budget Mechanism:						
Direct Operations.....	17	1,749,000	17	2,000,000	---	+251,000
Program Management.....	6	250,000	5	264,000	-1	+14,000
Cancer Control:	58	58,102,000	58	58,571,000	---	+469,000
In-house.....	(58)	(4,172,000)	(58)	(4,300,000)	(---)	(+128,000)
Contracts.....		(44,223,000)		(45,433,000)		(+1,210,000)
Grants.....		(9,707,000)		(8,838,000)		(-869,000)
Total.....	81	$60,101,000	80	$60,835,000	-1	+$734,000

Cancer Control

Program Purpose

The Cancer Control Program was established to undertake a national effort to assist in the transfer of the latest proven and practical research knowledge and technological advances to the health community and the public of the United States. The Program is defined in terms of the three major intervention areas of Prevention; Detection, Diagnosis, and Pretreatment Evaluation; and Treatment, Rehabilitation, and Continuing Care. The implementation of these activities within the intervention areas to achieve the program's goal is a technology transfer process. To carry out this transfer process, the following steps are taken: (1) identify the current technology state-of-the-art and establish the "readiness" for control implementation; (2) identify the current community needs and gaps; (3) determine the resources available within the National Cancer Program to effect the transfer of needed and available technology; and (4) establish mechanisms for facilitating the technology transfer process.

The selected cancer control activities are implemented using three approaches: (1) the traditional or single intervention approach directed at a specific site in a limited community setting; (2) the community based approach focusing on the combined cooperative efforts of a community to carry out control activities in a large community setting in a coordinated manner encompassing all interventions available for each disease site selected by the community; and (3) the center outreach approach using experienced cancer centers as the focal point for reaching out and responding to a community's needs for education, consultation, and assistance in applying cancer control interventions. Technology transfer is facilitated within the Program in the following ways: (1) the control technology field tested and demonstrated within each of the approaches is transferred to and incorporated in other related program supported activities; (2) the members of the biomedical/clinical community and the public directly involved in the control activities supported by the Cancer Control Program act as transfer agents who can promote the current technology learned to other parts of their community and other communities.

Program Plans

The 1978 budget estimate for Cancer Control of $60,835,000 and 80 positions represents an increase of $734,000 and a decrease of 1 position from the 1977 estimate. The program plans for 1978, along with expected accomplishments, are as follows:

Prevention - a 1978 estimate of $7,609,000 and 9 positions.

The objective of this intervention area is to make practical and effective methods and techniques of cancer prevention available and encourage their use by health professionals and the public. To this end, ongoing and proposed new activities will be focused on: (1) occupationally associated cancer; (2) cancer associated with tobacco, alcohol, drugs and food consumption; (3) cancer associated with ionizing radiation; and (4) prevention health education directed toward medical professionals, populations at risk and the public-at-large.

Efforts will continue in the identification of those carcinogenic agents that warrant specific prevention activity. These efforts are and will consist of state-of-the-art workshops, conferences, and monograph development projects which will focus on particular proven chemical or physical carcinogens such as asbestos, diethystilbestrol (DES) and vinyl chloride. These monographs will delineate the risks resulting from exposure as well as community strategies for developing prevention control programs for those agents which occur in a particular community.

In 1978, several initiatives are planned for interceding in the occurrence of lung cancer through its causal relationship with smoking. A major effort will be undertaken to develop smoking withdrawal programs and advise the public of the consequence of smoking and especially of the hazards of starting the smoking habit at an early age. Also, information will be generated and disseminated regarding the synergistic increase of the hazard posed by smoking and environmental or occupational situations.

Cancer associated with ionizing radiation is largely preventable. Estimates by the Bureau of Radiological Health (BRH), FDA, DHEW, indicate that 130 million Americans receive diagnostic x-rays yearly. X-rays are a source of over 90 percent of man's exposure to radiation in the United States. In addition to increasing the risk of leukemia, it has been established that radiation can induce a number of human cancers, such as leukemia, skin, thyroid, breast, lung and bone cancers. Among the areas which the Cancer Control Program will emphasize in 1978 is its program for the close monitoring of women undergoing mammography in mass screenings for breast cancer. The six radiological physics centers will continue to review dosimetry and act as a resource in consultation and continuing education for medical physicists throughout the country. Through Cancer Control interagency support, BRH will continue to monitor equipment in states to reduce exposures down to "safe" levels without jeopardizing the effectiveness of the diagnostic techniques.

Detection, Diagnosis and Pretreatment Evaluation - a 1978 estimate of $28,549,000 and 33 positions.

Much of the impact from cancer would be reduced if the public and health care professionals had available, and made full use of, the present knowledge about the detection of cancer, the proper diagnosis of cancer and advanced skills in the pretreatment evaluation of cancer.

The goal of the breast cancer detection demonstration project is providing an increase in the awareness of breast cancer through the demonstration of four methods or techniques of early detection: mammography; thermography; patient history; and physical examination. The uterine cervix cancer screening project is being conducted with state health departments with a primary focus on motivating high-risk persons to seek these services. Both of these projects will provide models for future large-scale screening projects by determining the best methods to be used, and optimum population size, and testing intervals. Also, it is planned to initiate a project to field test and evaluate a prescreening approach for use with large populations so that appropriate clinical followup can be recommended for persons at higher risks.

A cost-reimbursement study is being conducted through the Blue Cross Association. The study will be directed toward determining whether screening techniques for cancer can be organized in an economically acceptable manner to third party reimbursers. If the optimum package can be developed in such a way that third party payers would provide reimbursement for screening, it could result in considerable savings for the public and federal, state and local governments.

Pathology Reference Centers will be ready for implementation to demonstrate quality control in pathology for cancer diagnosis in the general hospital community.

Treatment, Rehabilitation, and Continuing Care - a 1978 estimate of $24,677,000 and 38 positions.

The program will continue to emphasize the field testing and demonstration of the most recent treatment techniques in a multidisciplinary management approach at the community level, where 80% of all cancer patients are seen and treated, with networks of hospitals and practitioners.

Separate networks have been established for acute leukemia, Hodgkin's disease, lymphoma, breast cancer and head and neck cancer. The networks organize community hospitals and community physicians to develop multidisciplinary cancer treatment approaches which include the new treatment methods.

The Community Clinical Oncology Program will continue to create mechanisms in the community for field testing new methods and techniques to implement cancer control activities relating to diagnosis, pretreatment evaluation and treatment and continuing care for most cancer sites. This is to be achieved by developing multidisciplinary teams of clinical oncologists practicing in three community hospitals per project. Nine clinical oncology projects will be providing input for testing the concept of community cancer centers.

Another community-level outreach program has been established using the resources of NCI's Clinical Cooperative Groups in cancer control. This effort is utilizing already identified leaders in oncology and "cancer-experienced" treatment facilities in the implementation of cooperative alliances with community oncologists to promote wider use of the latest, proven patient management protocols.

A patterns-of-care study is being conducted by the American College of Radiology to assess the practices in radiation therapy throughout the United States. This study will continue in 1978 to complete reviews of practices in all types of institutions. Medical schools, cancer centers, community hospitals, and free standing clinics will initiate analyses of results of patient treatment in relation to radiation therapy practices.

The rehabilitation and continuing care segment of the program includes a variety of projects that provide field tests and demonstrations of a full range of rehabilitation and continuing care interventions. Programs provide systematic approaches to early and continued rehabilitative support during: (1) hospitalization; (2) post-hospitalization through out-patient clinics and at-home services; and (3) when under continuing, supportive care, through "hospices."

Integrated rehabilitation in cancer centers, medical centers and community hospitals involves the development of model rehabilitation programs covering the entire course of a cancer patient's illness. These rehabilitation models will continue to demonstrate multidisciplinary rehabilitation protocols that can be easily disseminated to and used by, other major hospitals and community hospitals.

Projects for at-home rehabilitation service are developing, field testing and evaluating approaches to provide a full spectrum of rehabilitation resources in the non-hospital settings and include: (1) the identification of physical, psychological, vocational, nutritional, and continuing care needs of the discharged oncology patient; (2) education of rehabilitation teams and discharged patients and families; and (3) evaluation of project design and its impact in terms of physical restoration, psychosocial adjustments, vocational re-entry and program efficacy.

The hospice, a relatively new concept of care for the terminal cancer patient, will be continued in 1978. Hospice advocates the quality of life survival. Consequently, project emphasis will be on effective symptoms management and host maintenance during advanced stages of cancer.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cause and prevention research (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
661	$215,789,000	Pending *	659	$223,641,000

Purpose: Cause and Prevention Research is concerned with the identification of those factors which cause cancer in man and with the development of mechanisms for preventing cancer in man. The four main objectives of this research thrust are: (1) to develop the means to reduce the effectiveness of external agents; (2) to modify individuals in order to minimize the risk of cancer development; (3) to prevent transformation of normal cells to cells capable of forming cancers; and (4) to prevent progression of precancerous cells to cancer, the development of cancers from precancerous conditions, and spread of cancers from primary sites.

Explanation: Research in this thrust is conducted in government laboratories and in academic and private institutions through the use of research grants, contracts and intramural efforts. Efforts in this area are concerned with epidemiology, carcinogenesis (physical and chemical), viral oncology, nutrition and immunology research.

Accomplishments in 1977: (1) A series of correlation analyses studies were carried out to formulate hypotheses regarding the factors responsible for the geographic variation in cancer within the United States; (2) establishment of a series of chemical resources, including a centralized repository, now provides for the acquisition, synthesis, storage, and distribution of well-characterized reference materials to collaborative projects requiring them; (3) a Clearinghouse for Environmental Carcinogens was established; (4) in mice with breast cancer it has been determined that the level of a certain viral protein in the blood correlates well with the tumor burden of the animal; (5) a reduction of lung cancer risk has been identified with the use of low tar filtered cigarettes; and (6) the Advisory Committee for the Diet, Nutrition and Cancer Program recommended specific courses of action to follow regarding both causative and therapeutic aspects of nutrition.

Objectives for 1978: Research efforts in this thrust will be continued to include: Continued expansion of the role of environmental carcinogenesis in human cancers through the completion of pathology backlogs of compounds; greater emphasis will be placed on determining whether DNA-containing viruses are causally related to human cancer; research will be directed toward studies of dietary components linked with cancer and of their mechanisms of action, and studies directed towards identification of environmental and other factors responsible for clusters of high-risk communities in the U.S.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Detection and diagnosis research (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation			1978		
				Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
233	$48,852,000	Pending *	232	$49,446,000

Purpose: Detection and diagnosis research involves two major goals. The first is to develop an accurate method for determining and identifying individuals and population groups at a high risk of developing cancer. Secondly, research in this activity focuses on developing methods and techniques to determine the presence, location and extent of existing cancer, pre-cancerous conditions and/or factors indicative of possible future cancer.

Explanation: Research in this area is conducted in government facilities and in academic and private institutions through the use of research grants, contracts and intramural efforts. Detection and diagnosis research has three principle objectives: (1) early determination of persons or groups at a high risk of developing malignancy; (2) improved means by which to recognize and locate the exact location (or locations) of an existing cancer; and (3) better ways of predicting an individual's response to treatment of cancer, as well as the growth and spread of the disease.

Accomplishments in 1977: (1) A major contribution was the publication of cancer rate by county, obtained from the 10% sample of the U.S. population in the Third National Cancer Survey; (2) application of immunologic techniques has resulted in the development of promising methods of testing feces for blood, an important means of detecting possible bowel cancer at an early stage; (3) new methods have been developed for the utilization of ultrasound as a diagnostic technique for breast and other types of cancer, which until now depended upon the use of ionizing radiation; and (4) accurate and early diagnosis of pancreatic cancer is more promising now than ever before due to the use of a combination of x-ray duodenography and duodenopancreatic cytology.

Objectives for 1978: Major areas of emphasis will include: Research on the development of mathematical models for determination of frequency of screening. These models will give the mortality, morbidity and financial cost of various frequencies and combinations of cancer screening tests. A clinical trial on the cause and effect of close surveillance and cure of lung cancer will continue. The close surveillance is achieved through chest x-ray and sputum cytology, both of which make possible the very early detection of lung cancer. A clinical test will soon begin on a Computerized Axial Tomography (CAT) scanner that can produce a highly defined cross-sectional picture of the body in less than five seconds.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Treatment research (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
612	$259,157,000	Pending *	610	$263,006,000

Purpose: The goal of the National Cancer Program for research in the treatment of patients with cancer is to "develop the means to cure as many patients as possible and to maintain control of the cancerous process," the ultimate objective being a survival rate for the cancer patient equal to that of the general population.

Explanation: Research in this area is conducted in governmental facilities and in academic and private institutions through the use of research grants, contracts and intramural efforts. Identified with goals of this research are three general areas of investigation: preclinical treatment research, clinical treatment research, and rehabilitation research.

Accomplishments in 1977: (1) Clinical trials have been initiated with maytansine, a new antitumor agent demonstrating a high degree of activity in a variety of experimental tumor systems; (2) clinical trials with the new non-marrow toxic drug chlorozotozin have been initiated; (3) combination chemotherapy has brought about significant improvements in small cell carcinoma of the lung, as reflected in the rate of remissions and in survival at one year following treatment; (4) research sponsored on hyperalimentation has resulted in the wider use of this supportive nutrition therapy in host maintenance; and (5) the first successful growth in tissue culture of normal human T-cell lymphocytes has been accomplished. This achievement has major implications for basic immunology research and immunotherapy.

Objectives for 1978: Research efforts in this area will be continued to include: further development of drugs active against the slow-growing, common tumors; and clinical trials involving both single and combined-modality treatment, determination and testing for markers, and pharmacology and toxicology relating to clinical trials.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer Biology (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
388	$115,166,000	Pending *	386	$117,709,000

Purpose: Cancer Biology has application to all of the research thrusts of the National Cancer Program. Its overall goal is to generate basic knowledge of the fundamental biochemical, molecular, and structural changes which occur during the growth and development of normal and malignant cells which is essential to understanding the cause of cancer.

Explanation: Research in this area is conducted in governmental facilities and in academic and private institutions through the use of research grants, contracts and intramural efforts. The focus of Cancer Biology encompasses two major areas of concern. The first is loss of growth control, during which a cell which normally does not divide develops the property of persistent growth. Cancerous growth can be induced by such factors as: chemical carcinogens, oncogenic viruses, and radiation working alone or in combination with other influences. The second area of concern is that of metastasis - the invasion by cancer cells of the surrounding tissue and entrance into the blood stream by somehow avoiding destruction by the immune system of the host.

Accomplishments in 1977: (1) It has been demonstrated that the inner surface of the outer cell membrane has a new level of organization consisting of contractile components. These components appear to exert control over the distribution and mobility of cell surface molecules. (2) Genetic mutant cultures of mammalian cells are available which lack specific cell surface components. This will help to ascertain the role of these components in such processes as: virus infection, cellular aggregation, tumorigenicity and drug sensitivity. (3) A method for measuring the effects of a few cancerous cells on normal embryonic cells has been developed and may serve as an excellent model system for investigating the interaction of tumor cells and normal cells. (4) Estrogen and prolactin have been identified as responsible for regulating the growth of mammary tumors in rats. This is important because it begins to explain why certain breast cancers are not responsive to current endocrine therapies. (5) At the Frederick Cancer Research Center, a model has been developed for studying the effect of immunotherapy in established tumors which have metastasized.

Objectives for 1978: Research will be continued and expanded to include: (1) studies to determine the mechanism of action of chemical carcinogens; (2) efforts to assess the key role of the cell surface in tumor growth, invasiveness and metastasis; and (3) the identification of growth and developmental regulation processes that differ in normal and tumor cells.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer centers support (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
23	$59,489,000	Pending *	23	$59,757,000

Purpose: The cancer centers support activity provides funds for the development and support of centers which can generate new knowledge about cancer cause and prevention, detection and diagnosis, treatment, cancer biology, and rehabilitation and enhance the dissemination of this knowledge to those responsible for the health care in the surrounding communities. Core grants provide support for those elements of a cancer center that are required for the planning, development, evaluation, administration, and maintenance of an active and unified center. Exploratory projects provide support for planning new cancer centers or multidisciplinary programs, as well as, to expand, modify, or strengthen existing centers and programs.

Explanation: Cancer Research Centers, which serve as national research resources, promote effective interaction between basic and clinical scientists in the conduct of long-term multidisciplinary programs related to cancer. The dollars for research are provided by research grants and contracts and are reflected under the appropriate research and cancer control areas of this budget.

Accomplishments in 1977: Currently the NCI has recognized nineteen (19) Comprehensive Cancer Centers. In FY 1977, 63 core grants will be supported, as well as 7 exploratory projects.

Objectives for 1978: In FY 1978, core support will remain at the FY 1977 level with 13 exploratory projects being awarded.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Research manpower development (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
18	$33,510,000	Pending *	18	$31,647,000

Purpose: The Research Manpower Development Program supports clinical and fundamental training in areas such as; epidemiology, carcinogenesis, viral oncology, tumor biology, and immunology. The Clinical Cancer Education Program assists institutions, including medical and dental schools, in improving the quality and scope of their clinical cancer teaching activities directed toward undergraduate and graduate students, and practicing physicians and dentists.

Explanation: The grant mechanism is utilized to provide support (in the form of fellowships to the education programs) to individuals and institutions in performance of training and education programs related to cancer research.

Accomplishments in 1977: During FY 1977, 433 National Research Service Award fellowships to both individuals and institutions for training in the various research disciplines and 85 Clinical Cancer Education grants to medical and dental institutions will be awarded. Also, 129 Research Career Program awards will be made to both young developing investigators and established senior investigators.

Objectives for 1978: It is estimated that 407 National Research Service Awards (fellowships) will be awarded. Additionally, 77 Clinical Cancer Education grants and 125 Research Career Program grants will be funded. Only new post-doctoral individual fellowships awards will be started. No new institutional pre- or post-doctoral fellowships will be supported.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Construction (Public Health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
15	$22,873,000	Pending *	14	$12,895,000

Purpose: The major purpose of the construction program is to provide for the creation of new physical resources necessary for new and expanding cancer research programs, as well as the alteration and renovation of existing facilities for both basic and clinical research.

Explanation: Construction funds allow grants for the development of cancer research centers authorized under the National Cancer Act. Funds are also provided to contract for the renovation and updating of NCI facilities on the NIH campus, and at other Federal facilities, including the Frederick Cancer Research Center. Only after extensive review of the research program to be housed (including competence of the investigator, scientific merit and role in the National Cancer Program) can a construction project be approved and funded. The rate of Federal participation is up to 75% of eligible construction costs.

Accomplishments in 1977: Construction funds provided for fiscal year 1977 are being utilized to continue improvement of existing facilities necessary to support the efficient and rapid attainment of the goals of the National Cancer Program.

Objectives for 1978: Although contract construction will be carried out on the NIH campus and other Federal facilities, including the Frederick Cancer Research Center, the major component of the Institute's construction program will be NCI's participation in making available special containment facilities to prevent accidental harm to the environment or the community as a result of NIH's new major research efforts on recombinant DNA. Additionally, these funds will permit new construction, alteration and renovation of existing facilities and the completion of shell space in selected cancer centers.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

Program Purpose and Accomplishments

Activity: Cancer control (Public health Service Act, Title IV, Parts A and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
81	$60,101,000	Pending *	80	$60,835,000

Purpose: The primary goal of the Cancer Control Program is to establish and continue a national effort to assist in the most timely transfer of the latest proven and practical research knowledge or technological advances to the health providers and the general public of the United States. In order to achieve this, the Cancer Control Program coordinates its efforts and activities with State Health Departments, health care delivery institutions, other government agencies, and societies or associations involved in combating cancer.

Explanation: The program is defined in terms of three major areas of emphasis: (1) prevention; (2) detection, diagnosis and pretreatment evaluation; and (3) treatment, rehabilitation and continuing care. Cancer Control's principle objective is to relay significant findings or discoveries, and in so doing, minimize the incidence of cancer and prevent unnecessary death from the disease.

Accomplishments in 1977: Nine clinical oncology programs are being developed in community hospitals to implement and coordinate cancer control activities at the community level. Collaboration has begun with clinical cooperative groups to develop cancer control programs to increase the participation of community oncologists in cooperative treatment protocols. Six Radiologic Physics Centers for monitoring and providing quality control of the use of radiotherapy units were established to act as a resource in consultation and continuing education for medical physicists. More than 50 community hospitals are now participating in this quality control demonstration program.

Objectives for 1978: Some major projects to be pursued are: monitoring of at least 3,000 young women, born between 1943 and 1963 and exposed before birth to Diethylstilbestrol (DES). An association has been established between fetal exposure to DES and malignancies of the genital tract. An increased understanding by the general public of occupational and environmental carcinogens will continue to be promoted through interagency efforts with the Occupational Safety and Health Administration and the Center for Disease Control. Continuing emphasis will be placed on programs to assist community hospitals and local physicians to implement optimal treatment, rehabilitation, and continuing care patient management protocols using the most modern therapies and multidisciplinary teams through the Community-Based, Centers-Outreach and single Intervention program approach.

* Authorizing legislation expires September 30, 1977. Extension legislation is pending.

National Institute of Environmental Health Sciences

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DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
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MRS. PEGGY J. McKINNEY, BUDGET OFFICER, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH, BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now, we will hear the National Institute of Environmental Health Sciences. This presentation will be made by Dr. David P. Rall, the Director. We have your biographical sketch, which we will place in the record at this point.

[Dr. Rall's biographical sketch follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SERVICE

Name: David P. Rall, M.D., Ph. D.

Positions: Director, National Institute of Environmental Health Sciences, Assistant Surgeon General, Public Health Service.

Birthplace and date: Aurora, Ill., August 3, 1926.

Education: B.A., North Central College, 1946; M.S., Northwestern University, 1948; Ph. D., Northwestern University, 1951; and M.D., Northwestern University, 1951.

Experience

Director, National Institute of Environmental Health Sciences, 1971–present.
Associate Scientific Director for Experimental Therapeutics, National Cancer Institute, 1966–71.
Chief, Laboratory of Chemical Pharmacology, National Cancer Institute, 1963–69.
Head, Clinical Pharmacology and Experimental Therapeutics Service, General Medicine Branch, National Cancer Institute, 1958–63.
Scientist, Clinical Pharmacology and Experimental Therapeutics Service, General Medicine Branch, National Cancer Institute, 1955–58.
Scientist, Laboratory of Chemical Pharmacology, National Cancer Institute, 1953–55.
Intern, Second (Cornell) Medical Division, Bellevue Hospital, 1952–53.
Research Associate in Pharmacology, Northwestern University, 1950.
Assistant in Pharmacology, Northwestern University, 1949–50.
Baxter Fellow in Pharmacology, Northwestern University, 1947–49.

Associate memberships

American Association for the Advancement of Science.
Society for Experimental Biology and Medicine.
American Society for Pharmacology and Experimental Therapeutics.
American Association for Cancer Reearch.
American Society for Clinical Investigation.
Society of Toxicology.
Society for Occupational and Environmental Health.
American College of Preventive Medicine.

Special awards, citations, or publications.

Member, National Academy of Sciences/National Research Council Safe Drinking Water Committee, 1975 to present.

Member, Secretary's Review Panel on New Drug Regulation, 1975 to present.

Associate Editor, Journal of Toxicology and Environmental Health, 1974 to present.

Editorial Board, Archives of Environmental Health, 1973–76.

Chairman, DHEW Committee to Coordinate Toxicology and Related Programs, 1973 to present.

U.S. Coordinator, Environmental Health Program, United States-U.S.S.R. Health Exchange Agreement, 1972 to present.

U.S. Coordinator, Biological and Genetic Consequences Project, United States-U.S.S.R. Environmental Protection Agreement, 1972 to present.

Adjunct Professor, University of North Carolina, Chapel Hill, 1972 to present.

Chairman, OST–CEQ, Ad Hoc Committee on Environmental Health Research, 1971–72.

Associate Editor, Cancer Research, 1970–1974.

Chairman, HEW Departmental Committee on Drug Research and Regulations, 1970.

Editorial Board, Pharmacological Reviews, 1969–72.

Chairman, National Institute of General Medical Sciences Pharmacology-Toxicology Review Committee, 1967–69.

Member, Graduate Council, George Washington University, 1962–71.

Editorial Board, Proceedings of the Society for Experimental Biology and Medicine, 1962–65.

Lecturer in Physiology, Medical School, George Washington University, 1958–62.

Meritorious Service Medal; Distinguished Service Medal; Dr. Rall has authored and co-authored over 100 published papers relating to comparative pharmacology, cancer chemotherapy, blood-brain barrier, blood CSF barrier, pesticide toxicology, and drug research and regulation.

Mr. FLOOD. Do you have some people with you that you want us to meet?

Dr. RALL. I am delighted to introduce on my far left, Mrs. Peggy McKinney, our budget officer, and introduce to you on my immediate left, Mr. Paul Waugaman, who is our new executive officer, who you saw last time as the neurological disease executive officer.

Mr. FLOOD. All right, and we have your statement which we will insert in the record at this point, Doctor.

[Dr. Rall's complete statement follows:]

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, ON "NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES"

Mr. Chairman and members of the committee, It is a pleasure to appear before you again. This past year has been a good year and a bad year. It has been good in that NIEHS can now look forward to adequate physical facilities for research programs. Last year Congress appropriated the remaining funds needed for construction of our permanent buildings; these should be ready for our use in 1980.

Congress also provided NIEHS funds to start a national environmental mutagen screening program that will eventually test all compounds produced in commercial quantities. This program, now being initiated by NIEHS, consists of three different levels of testing systems. The first level, called tier 1, consists of several very simple testing systems composed of cells in culture plus mammalian activation systems that should be able to handle 1,000 compounds per year. Compounds will initially be screened for mutagenicity in tier 1, and the results obtained in tier 1, together with what is otherwise known about the compound, will dictate whether to continue the test of the compound in tier 2 and tier 3. Tier 2 consists of two different Drosophila systems, and tier 3 of four different whole-animal systems. By using the tier approach, NIEHS hopes to identify not only which compounds are mutagenic, but also which tests are most valid for determining mutagenicity.

NIEHS is also working closely with the National Cancer Institute (NCI) to obtain more information from their cancer bioassay program. For a number of

years, NCI has been testing several hundred chemicals for carcinogenicity in rodents. Up to now, the NCI program has properly examined only the carcinogenic effects of the chemicals tested and has not exploited potentially useful information on other subchronic toxic effects. Now, following last year's congressional mandate and funding for an NIEHS program in this area, our staff—together with NCI personnel—will study the use of new short-term tests for determining toxicity in order to establish priorities for testing additional chemicals in rodents. But more important, the two NIH Institutes will begin monitoring a wide range of effects on organs, physiology, neurology, and behavior.

NIEHS now has, thanks to the report of the second task force on research planning in environmental health science, a road map for future research in this area. The report of the task force—established at the direction of Congress to identify, review, and evaluate needs in the environmental health research area—contains specific recommendations to guide environmental health research. It places primary emphasis on preventive toxicology—prediction and prevention of environmentally related diseases before they become overt and beyond control.

Another major accomplishment during the past year was the passage of the Toxic Substances Control Act. This act not only provides authority to remove from commerce those agents that are toxic but, more important, it also provides tools to withhold from commerce those compounds we are not sure about due to insufficient data. Thus, it acts as a time-shortening device that will enable us to identify a compound as a hazard prior to its dispersal throughout the environment. The act also calls for strict control of the industrial chemicals polychlorinated biphenyls (PCB's).

In addition, the act has expanded the need for research manpower in environmental toxicology. Presently, industry, higher education, and government are experiencing difficulty in their ability to find and hire qualified individuals to perform or lead efforts in assessment of risk associated with exposure to environmental chemicals. In 1976, only one quarter of the positions listed in the Society of Toxicology Placement Bureau were filled, due to the dearth of appropriately trained individuals. Russell Train, in summing up his experience as EPA Administrator, has also mentioned the need for trained staff scientists in his agency. The NIEHS training program is the only focused Federal support mechanism by which universities and other nonprofit institutions are funded to train individuals for research careers in this area.

Mention of the PCB's reminds us that this has not been a good year for many people in the United States. NIEHS warned at a conference in 1971 that PCB's were a health hazard and must be controlled; yet, this year, we have seen the virtual demise of the Great Lakes' fishing industry—the closing of the Hudson River to fishing. Because of reports of PCB contamination of mothers' milk, we have seen a possible health question posed for nursing babies. We have also heard the anxiety expressed by residents of metropolitan Washington, D.C., who wonder about any adverse health effects from the asbestos in the dust from the crushed rock on their roads and driveways.

These are but a few examples of today's environmental health concerns, but they are indeed serious problems. Let me spend a few moments to discuss NIEHS' efforts to solve them.

I have discussed PCB's with you often; 1,400 million pounds of these heat-resistant, nonburnable industrial fluids have been manufactured to date, and over 1 billion pounds remain either in the environment or in use and are, therefore, likely to end up in the environment where they will persist for decades. We may be seeing not the end of the PCB problem, but the beginning.

Historically, human exposure has come from direct PCB contamination of fish, poultry, eggs, milk, and other foods as a result of an accident. Fortunately, these accidental leaks and exposures appear to have been controlled; and the primary route of human exposure currently is via freshwater fish which have bioaccumulated PCB's. The PCB's have entered streams and lakes via industrial effluents or sewage or landfill runoffs. Fish in these streams and lakes are able to concentrate these chemicals up to 300,000 times and store them in their bodies. It is presumed that this, now and in the future, will be the major source of human exposure.

PCB's are a mixture of closely related organochlorine compounds. Once in the body, some of these PCB's are slowly chemically altered, or metabolized, and excreted; but others resist metabolism and cannot be excreted and persist in the body for years. In the body, they are highly concentrated in the fatty tissues and

fluids. Human breast milk contains about 4 percent fat; and PCB's are concentrated in the milk fat. Nursing babies, therefore, receive a higher dose of PCB's per unit weight than the general population and are possibly at risk. PCB's have been shown to cause skin disorders, metabolic diseases, and—in some animal experiments—cancer. What risk is there for humans?

An NIEHS grantee—Dr. J. R. Allen at the University of Wisconsin—has fed rhesus monkeys low levels of PCB's in their total diet before, during, and after pregnancy and delivery. Their babies are small at birth, do not gain weight well, and have skin rashes; they are not healthy babies. The concentrations of PCB's the monkey offspring were exposed to are higher than those expected for human babies on mothers' milk. NIEHS is planning to launch a study of babies in North Carolina to determine PCB levels in mothers' milk and whether babies nursing on milk with high PCB levels do as well as those with low or nondetectable PCB levels. This study will take 18 months, but it will give us some answers to the questions about PCB's in mothers' milk; questions we simply cannot answer now.

I indicated that some PCB's cannot be metabolized, or chemically altered and excreted. NIEHS scientists have shown that these PCB's are actually excreted by the liver and bile into the intestine where they are promptly and almost completely reabsorbed. In essence, they are recycled. An NIEHS grantee, Dr. Philip S. Guzelian at the Medical College of Virginia, studying the workers exposed to the pesticide Kepone (which is a chemically similar persistent organochlorine compound), wondered if this cycle could be broken. That is, could a drug be given that would bind Kepone in the intestine, thus preventing its reabsorption and greatly accelerating its excretion and removal from the body. In an uncontrolled study with seven patients, Guzelian found that administration of a compound called chloestyramine increased the excretion of Kepone sevenfold; a controlled study is now confirming these results. Thus, by making use of basic knowledge about the metabolism and excretion of these agents, a potentially useful therapeutic regimen has been developed for humans suffering from exposure to Kepone. This offers hope that similar therapeutic treatment may be found for other members of this class of toxic persistent environmental pollutants, including DDT and its derivaties the PCB's and polybrominated biphenyls (PBB's).

The second problem I want to discuss with you relates to asbestos and to work underway at one of our university-based centers. Dr. Irving Selikoff's group at Mt. Sinai, responding to a request from concerned citizens, surveyed the area surrounding the Rockville, Md., crushed stone quarry. They found significant concentrations of asbestos around the quarry and at sites where the crushed rock was used. These concentrations were higher than those previously measured in other urban areas and communities, but much lower than typical occupational exposures. We promptly notified the appropriate regulatory authorities of Dr. Selikoff's findings.

What risk is there to those people exposed to dust from this crushed rock? We do not yet know, but these exposures may be equivalent to those causing "bystander" disease from asbestos. Within the next decade, we may or may not begin to see extra cases of either mesothelioma or lung cancer. What is needed now is a more thorough survey of asbestos concentration in those areas and, if the findings are confirmed as I am confident they will be, appropriate control action. This is not likely to be a problem confined to the Rockville quarry. The band of serpentine rock, from whence the asbestos comes, extends up and down the east coast. Other rock quarries north and south of Rockville may also contain unsuspected asbestos.

Problems such as those relating to PCB's and asbestos, and accomplishments over the past year, present us with an enormous challenge for the future. The Toxic Substances Control Act, for example, demands that those of us engaged in research provide rapid, inexpensive, and less manpower intensive means for determining which environmental agents are hazardous. It recognizes that screening large numbers of compounds is not possible using traditional whole animal tests, given their limitations of time, sensitivity, and cost, and stresses the essential role of rapid, simple test systems for implementing the program provided by the law.

To meet this challenge, Institute scientists are developing several rapid test systems for identifying chemical mutagens and, possibly, carcinogens. They are working on a spot test system using a DNA repair-deficient strain of the

Neurospora microorganism and on a system to detect mutations in mammalian sperm, which is based on staining under selective conditions.

Another area of challenge for us at NIEHS concerns neurological and behavioral toxicology. The effects of low chronic doses of environmental chemicals on neurological and mental functions are very subtle and largely undetectable at present. If, for example, a drug or chemical has caused a 15-percent decrease in the IQ of offspring, there currently would be no way of knowing. Yet, in many instances, neurological and behavioral changes may be produced by a chemical before significant somatic effects can be seen. In fact, we know that neurological and behavioral changes are among the early signs of toxicity of many, or even most, persistent chemicals, for example the heavy metals and chlorinated hydrocarbons. To respond to the challenge in this area, NIEHS is developing an intramural and extramural program aimed at developing objective methods for detecting early neurological and behavioral effects of environmental contaminants. If these methods can be devised, then neurological and behavioral changes would serve as an early warning system for other toxic effects; and they could uncover disease before irreversible damage is done.

Further challenges in the coming year will be to implement the marine and freshwater biomedical research support plan we have developed at the direction of Congress. The plan proposes core support for marine and freshwater biomedical laboratories. We intend to strengthen our technological surveillance program so that we can assess what is going on in the environment in order to obtain advance warning of potential problems in time to do something about them.

In all these activities, we have been and will continue to be mindful of the need for interagency coordination and cooperation with other agencies involved in environmental health concerns.

We will also continue to stress the importance of disseminating our research results as broadly as possible. In general, NIEHS deals with three publics—the regulators and the regulated, medical practitioners, and the general public—and it actively involves all three groups in its activities. One major NIEHS program that involves these three groups is the sponsorship of conferences on critical environmental health problems. These conferences are held in response to urgent or potential environmental health problems; and during the last year we sponsored meetings on such topics as environmental arsenic, health problems of energy technologies, environmental oxidants, and target organ toxicity. Because of the national importance of these conferences, press coverage is extensive and much of the information is published by the news media. NIEHS looks to the press to play a major role in informing the general public of potential environmental health problems and strategies for preventing human disease. Detailed conference proceedings are published in Environmental Health Perspectives, a professional journal sponsored by NIEHS, which is widely distributed to those in the environmental health field and to interested citizens.

Other ways NIEHS encourages wide communication of its research results are through publication of its scientists' work in a wide variety of professional journals (including those read by medical practitioners), through interagency liaison activities, and through frequent contacts with news media personnel on environmental health problems or potential problems. We also prepare and distribute pamphlets on our mission and research programs and respond to a number of public inquiries regarding particular environmental health concerns. In addition, during this past year, I have been taking part in the work of the NIH Task Force on Communication, which is attempting to develop improved means for disseminating research information. All these efforts will continue.

In conclusion, Mr. Chairman, the budget request for the National Institute of Environmental Health Sciences for 1978 is $58,100,000. I shall be pleased to answer any questions you may have.

NEW RESEARCH GRANTS

Mr. FLOOD. Now, we notice that your whole budget proposes an increase of 20 percent over fiscal year 1977. However, when we take a look at your allocation for new research grants, I see that you are proposing the same level as 1977. Why isn't that category going up at least 20 percent?

Dr. RALL. It is going up less than we would like it to. It will go up a small amount.

Mr. FLOOD. Why isn't it going up 20 percent like the rest of the program across-the-board, why?

Dr. RALL. The same problem with competing priorities. We are in the process, as you are aware——

Mr. FLOOD. Is that what you call realining priorities?

Dr. RALL. That is a good phrase.

Mr. FLOOD. It is not mine. It is a classical one around the Hill.

Dr. RALL. The other phrase is the midcourse correction.

Mr. FLOOD. Yes, we have used that before.

Dr. RALL. We are in the process of trying to staff up in a logical, rational way for our new research facility, and we have put a larger fraction of our new resources in the intramural research program.

Mr. FLOOD. Is the level you propose then in the budget for the new research grants; is that about the maximum that you could effectively spend to initiate these new activities?

Dr. RALL. We could effectively spend it.

Mr. FLOOD. Can you use more?

Dr. RALL. Yes.

Mr. FLOOD. How much? In what areas?

Dr. RALL. In the grants area, we would like to increase it so we can have more new research grants, perhaps $1 million there. We think it is very important, and I hope we can talk about this more, in the research training area.

RESEARCH TRAINING

In research training we think we could add an additional $3.5 million comfortably. We think this is absolutely the major area we ought to focus on now because of the requirements with the Toxic Substances Control Act, and Resource Recovery and Conservation Act, both of which will place a major burden on this Nation's toxicologists and pathologists.

Mr. FLOOD. Take a look at your budget for training programs.

Dr. RALL. Yes, indeed.

Mr. FLOOD. If you are talking about the training program, how do you explain the rationale behind the 33-percent reduction in the training programs? You have an overall increase of $9 million for your institution. Why are you giving training such a very low, low priority? We keep hearing all about these needs for manpower in environmental health. Here you have a 33-percent reduction.

Dr. RALL. We lost an argument with our colleagues downtown on that. We think it is terribly important. We had placed a much higher priority on institutional training.

Mr. FLOOD. Now you know, Doctor, that the committee provided additional funds in the supplemental appropriation to train more toxicologists, and veterinary pathologists. We made a big thing out of that. What percentage of your proposed 1978 training budget will be used to train that type of manpower?

Dr. RALL. All of it. They overlap completely.

Mr. FLOOD. How much are you going to spend in 1978 to continue this training program that we set up in the supplemental just passed?

How much will you use in 1978 to continue the program we started in the supplemental?

Dr. RALL. It is my understanding that as of now we will not be able to continue the new level as reflected by the fiscal year 1977 supplemental in 1978. The 1978 request before you is based on the 1977 level of $2.2 million for training. In order to sustain the higher 1977 level into 1978 we estimate a minimum 1978 requirement of an additional $2.1 million for training.

Mr. FLOOD. What other kinds of manpower are you going to train under this budget that you have?

Dr. RALL. These are the primary kinds, the toxicologists, the vetinary pathologists and the epidemiologists. These are the three we need the most.

TRAINING DEMANDS

Mr. FLOOD. Do you have any data which shows the total number of people that should be training in environmental health sciences in order to meet the current demand as well as the demand for the next 10 years?

Dr. RALL. We have some data. Let me review it with you briefly.

Mr. FLOOD. You may want to put that in the record.

Dr. RALL. I shall, but I will say also that the Society for Toxicology has a total of 800 members. That is the total pool we are talking about. They have a job placement program each year. Over the last 3 or 4 years they have only been able to fill one-third or less of the available jobs with trained toxicologists. There are at least 100 job opportunities for a very specialized kind of toxicologist, the inhalation toxicologist. Not one of those 100 jobs has been filled.

As you know, the Toxic Substances Control Act was passed in October. The analysis by Booz-Allen, Hamilton and Foster D. Snell suggests this will require on Day 1 somewhere between 160 and 760 toxicologists in industry to fulfill the mandates of that act. The Nation simply doesn't have those trained people.

Mr. FLOOD. For the record, can you show us the demands for 10 years?

Dr. RALL. Yes, we will try to project that. It is a very serious demand.

[The information follows:]

TRAINING IN ENVIRONMENTAL HEALTH SCIENCES

The most up-to-date and reliable source of data assessing current and projected future needs for training in the environmental health sciences has been published in the "Report of the Second Task Force for Research Planning in Environmental Health Sciences." I would, therefore, like to enter into the record from chapter 16, page 49 of that report, the summary of their findings and recommendations:

Recommendations

Because of our convictions based on evidence presented above, we recommend:

(*a*) That the number of predoctoral trainees in environmental health sciences be restored to the level of 1971–72 (approximately 300 annually) by 1979, with additional increases to 400 annually by 1982. It is suggested that some 50 percent of this increase be allocated to toxicology;

(*b*) That the number of postdoctoral trainees in environment health sciences be increased by 75 to 100 per year in each of the next 3 years. It is

suggested that 50 percent to 60 percent of this increase be allocated to the combined areas of toxicology and noninfectious disease epidemiology. It is assumed that postdoctoral trainees will come largely from other discipline (mostly biomedical and other natural sciences). In order to attract able people from other disciplines at late stages in their careers, it is recommended that the postdoctoral period of recruitment be extended from 5 years postdegree to 15 years postdegree and that stipend leevls be adjusted accordingly, up to a maximum of $25,000. This recommendation is consistent with provisions of the National Research Act of 1974 (Public Law 93-348).

While the task force has only projected through 1982 (5 years), it is clear that the authors could have conservatively estimated continued training needs for 400 predoctoral trainees annually and an additional (above fiscal year 1977 level) 75-100 postdoctoral trainees annually for each of the succeeding 3 years and remain level at 425 per year. The estimated total trainees needed over the next 10 years would be:

ANNUAL INCREASES FOR FISCAL YEAR 1977-87

Years	Predoctoral	Postdoctoral
1977 [1]	(65)	(101)
1977 [2]	133	169
1978	200	275
1979	300	350
1980	350	425
1981	350	425
1982	400	425
1983	400	425
1984	400	425
1985	400	425
1986	400	425
1987	400	425
Total	3,733	4,194

[1] 1977 appropriation.
[2] Includes supplemental to the 1977 appropriation.

TOXICOLOGY TRAINING

Again referring to the task force report recommendation cited previously "50% of this increase (predoctoral) to be allocated to toxicology" and for postdoctoral, "* * * that 50 percent to 60 percent be allocated to the combined areas of toxicology and noninfectious disease epidemiology."

Thus, using 50 percent of both predoctoral and postdoctoral projections for the years 1977-87, the indicated need for toxicology trainees totals 3,963 during the period with a rough average of 200 predoctoral and 200 postdoctoral trainees to be added annually.

Mr. FLOOD. It seems, Doctor, and we have touched upon this before and with the earlier hearings today with the cancer people, that the private sector has a need for competent environmental health scientists just as well as the Government has.

Now what efforts are you making to involve the private sector in supporting university-based training programs in toxicology, pharmacology and so on? What are you doing about it?

Dr. RALL. We have been talking extensively with the major chemical companies which represent the private sector.

Mr. FLOOD. You are trying to involve the private sector?

Dr. RALL. Yes. I tried to hold up to them the example of the Burroughs-Wellcome Co. which, when about 15 years ago there was a need for clinical pharmacologists, set up the Burroughs-Wellcome Scholars in Clinical Pharmacology. This provided a substantial impetus to getting bright, young physicians into this important field.

Mr. FLOOD. Now you have the demands of this new toxic substances control act on top of that.

Dr. RALL. We are going to try to convince our chemical industry friends to do the same type of thing.

NEW ENVIRONMENTAL HEALTH SCIENCES CENTER

Mr. FLOOD. In your budget you are requesting funds to initiate a new Environmental Health Science Center. Your justification states that this new center will conduct research relevant to high priority programs in your Institute. You had better elaborate a little on that statement. Give us some idea about what the center will do. There are seven centers.

Dr. RALL. May we go off the record?

[Discussion off the record.]

Mr. FLOOD. Why is it necessary at all to create another environmental health center? With all that overhead and all the expenses and everything, why not expand one or more of the existing seven centers?

Dr. RALL. The seven centers are by and large as large as they can be because of physical space limitations that they have. The need for another center is really in two ways.

Mr. FLOOD. Can't you enlarge or expand them physically? Is there a physical problem?

Dr. RALL. That requires construction.

Mr. FLOOD. But you are going to build a new one.

Dr. RALL. We intend to build intellectually rather than with bricks and mortar. The idea is to coalesce existing research groups in one of the universities with mutual interests in the environmental toxicology area and provide them stable support so that they can begin to do a much more efficient job. This area is so interdisciplinary that it requires physicians, chemists, atmospheric chemists, toxicologists. You need a broad group of people.

It is our view that it is more efficient to get a new center started at a new university. This also has a very good effect on the university. It makes them begin to think about these problems. Most physicians don't think that chemicals can cause disease. They still look at the problem of infectious disease, et cetera.

The idea of teaching physicians that chemicals are an important cause of disease is something which I think is very important and is not being done enough today.

Mr. FLOOD. Do you think that, that chemicals don't cause disease?

Dr. RALL. I think if you ask the next 10 physicians you talk to——

Mr. FLOOD. Is that what you think?

Dr. RALL. I am sure of it. This is not high in their list.

SEVEN EHS CENTERS

Mr. FLOOD. Since we are talking about the centers and we raise this question, why don't you, for the record, give us those seven centers, where they are located, the description of the mission for each one of the seven, what they have accomplished to date and the future endeavors for each one.

Dr. RALL. Yes, sir.

[The information follows:]

ENVIRONMENTAL HEALTH SCIENCES CENTERS

1. The Center titled Occupational and Environmental Health is located in the School of Public Health, Harvard University. The Center Director is Dr. James L. Whittenberger, Professor of Physiology. The Center research and training program is concerned primarily with epidemiologic and toxicologic studies on the biologic effects of physical and chemical factors in the environment, with particular emphasis on the health of man. Approaches to the problems utilize methodology and expertise of biochemistry, physiology, comparative toxicology and epidemiology. Human diseases of greatest interest are cancer, chronic chemically-induced lung diseases, and congenital defects. Environmental factors under study include (a) general air pollution, (b) occupational air pollution, with specific emphasis on asbestos, granite dust, firefighting chemicals, and other compounds of concern such as plastics and other chemicals, (c) cigarette smoking, which complicates all studies of lung diseases, (d) pesticides, with emphasis on mechanisms of toxicity and interactions with other foreign chemicals, and (e) radiation, particularly as related to pulmonary carcinogenesis and basic cellular effects of low doses in partial and whole body exposure.

Center scientists have been notably instrumental in developing, refining or perfecting methodology for sampling and analyzing air and other pollutants; methodology and techniques for field and epidemiologic studies on human workers and the general public at risk from exposure to a variety of environmental agents, including asbestos, granite dust, talc, sulfur oxides, automobile exhaust fumes, vinyl chloride, lead, rubber particles and x-rays; in elucidating mechanisms of carcinogenesis; in understanding the pathogenesis of particles in the lungs of granite, talc, asbestos and rubber workers; in clarifying the toxic mechanisms of organophosphate insecticides and of pesticide synergists; and in identifying factors related specifically to bladder cancer. Work of the Center staff has resulted in 40 scientific publications during the past year, adding significantly to knowledge and understanding of health problems with which the Center is concerned.

Because of the stability in staff and facilities assured by core support of this Center, it is expected that pursuit of the important health problems now underway will continue and that the staff will participate in gaining understanding and solving new environmental health problems as they arise in the areas of expertise represented by the staff, each member of which is an eminent scientist in his field.

2. The Center titled Center for the Study of the Human Environment is located in the College of Medicine, University of Cincinnati. The Center Director is Dr. Raymond R. Suskind, Professor and Chairman of the Department of Environmental Health. The scope of the research and training efforts ranges from mechanism oriented research to the study of populations at risk and components in the environment which constitute human health hazards. Major problem areas include: (a) the role of essential trace metals in human health and disease as influenced by environmental factors; (b) health problems from non-essential toxic metals; (c) carcinogenic and teratogenic aspects of environmental agents; (d) pulmonary problems of environmental origin; (e) cutaneous injury induced by environmental chemicals and/or non-ionizing radiation, and (f) techniques and analytical methods for determining air quality.

This Center has concerned itself in a major way with heavy metal toxicology. Notable contributions have been made in understanding the effects of dietary variations in zinc, copper and carbohydrate on factors associated with cardiovascular damage and disease and the biochemical mechanisms of these effects; the effects of lead in kidney function and disease, growth and development, and on behavioral abnormalities. Other studies deal with the mechanisms of cadmium toxicity, body defenses against cadmium toxicity (the role of metallothionein), the role of cadmium in drinking water on pulmonary and cardiovascular systems. More recently new studies have been mounted and important contributions are being made in areas related to automobile exhaust gases, the chemical and physical basis of the health effects of anthracite

and bituminous coal dusts, thermal degradation products of plastics, pulmonary effects of industrial compounds such as trichloroethylene, acrylates, and isocyanates; and the role of various commercial compounds in skin diseases and allergies. Studies are also in progress with the types of substances mentioned to assess their potentials as carcinogens, mutagens and teratogens. A total of 98 scientific papers was published by the Center staff during the past year.

Center staff will continue to probe the importance of heavy metals, coal and other substances indicated as potential health problems and to elucidate the basic mechanisms by which injury in the skin, lungs, cardiovascular system, and in various body organs is induced. In addition, as in the past, they will participate in the identification of environmental health problems not yet recognized, especially those reltaed to developing fossil fuel technologies (shale oil extraction, coal liquefaction and gasification) and other health problems that fall within the areas of expertise of staff members.

3. The Center titled Center for Environmental Management is located at Oregan State University. The Center Director is Dr. Virgil H. Freed, Professor and Head, Department of Agricultural Chemistry. The Center emphasizes research and training in environmental health aspects of microchemical pollutants. Major efforts are directed toward (a) identification and inventorying environmental pollutants, (b) studies of the dynamics and distribution of pollutants, and (c) the biological effects and modes of action and metabolism of chemicals found in the environment. Important contributions have been and are continuing to be made regarding biological effects of toxic metals and organic compounds, environmental chemodynamics and distribution of environmental chemicals in biological systems. Toxic metals of interest include cadmium, methylmercury compounds, selenium and arsenic. Organic compounds of interest include PCBs, halogenated aromatic compounds, brominated fatty acids, dioxin, a number of pesticides and natural toxins such as pyrrolizidine alkaloids and aflatoxins. A major strength of the Center is its work in chemico- and pharmacodynamics, which involves the application of mathematical modeling to chemical transport and behavior in the environment and in the mammalian body. This work is aimed at developing predictive capabilities in the movement and fate of toxic substances, both inside and outside the body. From such understanding it is expected that toxic consequences and pathological effects may be predicted. A total of 65 scientific papers was published by the Center staff during the past year.

Projected plans are that the Center staff will continue to probe the environmental health problems in which they are now involved and will participate in efforts to identify, understand and solve new environmentally related problems that might arise in their areas of expertise.

4. The largest Center titled Research in the Environmental Health Sciences is located in the New York University Medical Center of New York University. The Center Director is Dr. Norton Nelson. Research under way and proposed is broadly relevant to adverse health effects caused by environmental factors. The general objectives of the research are to define the nature and extent of such effects with the aim of instituting appropriate preventive or control procedures where required. Interests range from acute to chronic health effects, including, in the latter, cancer and degenerative diseases. The research encompasses laboratory studies on the biochemical mode of action of a wide range of environmental toxicants, exploratory studies aimed at improving the reliability and efficiency of predictive toxicological tests, improvement of diagnostic procedures for diseases possibly related to environmental factors, epidemiological investigations and field studies on the distribution of pollutants.

Scientists at this Center have made notable contributions in development and refinement of inhalation toxicology procedures, analytical instrumentation and design and conduct of epidemiological studies in lead toxicology. The potent carcinogen bis(chloromethyl)ether was first discovered at this Center and significant contributions toward understanding structure-activity relations and mechanisms of carcinogenesis have been made. Center scientists have contributed also to understanding of the physicochemical aspects of SO_2 toxicology and dynamics as well as to the mechanism of oxidant air pollutant

effects. The Center staff published 312 scientific papers during the past year on subjects ranging from cancer initiation and promotion by environmental agents to the ecology degeneration of the Hudson River and its basin.

It is anticipated that the Center staff will continue and expand ongoing work in all areas--toxicology, respiratory diseases, environmental pollution and toxicology, chemical carcinogenesis, radiation carcinogenesis, epidemiology and biostatistics. They plan also to participate in continuing efforts to identify new hazardous industrial and environmental compounds, to endeavor to develop understanding of disease mechanisms, and to contribute to national strategies to limit or eliminate the sources of environmental health problems.

5. The Center titled Center in Environmental Toxicology is located in the Biochemistry Department of Vanderbilt University School of Medicine. Its Director is Dr. Robert A. Neal. The research areas of interest include food additives and adulterants, inorganic substances, mycotoxins and adventitous chemicals in foods such as pesticide residues and substances from packaging materials. The emphasis is on a chemical and metabolic approach to toxicology with the thrust toward determining the effects of toxic substances on enzymes, transport and hormone systems, the mechanism of metabolism of these substances, and the mode of absorption and storage. Coordinated with the research program of the Center is a training function directed toward the graduate education of students in toxicology and research.

The staff of this Center has made important contributions to understanding the enzymes and mechanisms of metabolism of foreign compounds, particularly organophosphate insecticides. They have also contributed in an important way to identification of natural toxins in foodstuff (grains and potatoes), elucidation of the structures of such substances and the sites and modes of pathogenesis. While a number of naturally-occurring compounds have been identified, detriment in human diets has yet been demonstrated, although the studies clearly point to the importance of surveillance of human foodstuff and quality control. Over the past year, this group published 43 scientific papers on research in progress. It is anticipated that work will continue in the areas described and that the search for harmful adulterants of foodcrops for human consumption will be pursued. The Center staff will also participate in research on new hazardous substances as they are identified in accordance with their areas of expertise.

6. This Center, one which you have heard a great deal about in the past two or three years, titled Environmental Agents: Relation to Human Health Effects is located in the Mount Sinai School of Medicine of the City University of New York and the Center Director is Dr. Irving J. Selikoff, Professor of Medicine and Professor of Community Medicine. The scope of the research and training efforts is focused on problems of biological effects of environmental alterations in relation to human health and disease. The environmental agents include those known or suspected of disease potential; but many are neither known nor suspected. Therefore, an important part of the work of this Center has been and will continue to be to undertake studies for their identification. Emphasis will be on major human diseases, as environmental cancer and environmental lung disease. Priorities are and will be devoted to problems that affect very large numbers of people and the research program is, and will continue to be, very much concerned with mechanisms ranging from the cellular level to the conceptual level, as in the delineation of multiple factor effects in environmental disease. The Center targets five major program areas--multiple factor etiology as mentioned, environmental cancer, effects of longterm low-level exposure to environmental agents, including those associated with asbestos, and the biological effects of ultramicroscopic inorganic particles. This past year has seen this Center very active in the asbestos problems of Duluth, the polychlorinated biphenyls (PCB) problem, and most recently the Michigan study of polybrominated byphenyls (PBB) which have caused serious human health problems. Over 40 scientific publications resulted from the work of this Center and they will continue to pursue the work already mentioned as well as responding to new environmental health problems as they arise within the scope of the Center expertise.

7. The most recently established Center (1975) is titled Trace Contaminants as Environmental Health Hazards to Man. It is located in the School of Medicine at the University of Rochester (New York) and is directed by Dr. Thomas W. Clarkson, Professor of Radiation Biology and Professor of Pharmacology and Toxicology. The core grant supports a vast program of research on trace contaminants with special emphasis on heavy metals most

likely to effect human health. During the first year and a half of operation, the Center staff has published eighteen scientific papers. In the immediate future, the Center will concentrate on the toxic heavy metals (Cd, Hg, and Pb) in continuation of well-established projects at Rochester. Since multiple exposures (e.g., dietary methylmercury and selenium from pelagic fish) also occur, the interaction of heavy metals with other substances will be studied as well.

FOOD ADDITIVES

Mr. FLOOD. In the past we have talked here about the research program of MIT involving food additives and their toxicity. Can you give us a brief update on that research and then for the record, because of the program, give us the details of the accomplishments up there at MIT, how their research results are being utilized by the various regulatory agencies such as FDA, for example, and the others?

You can do that for the record, but just touch upon it for the moment.

Dr. RALL. I think the kind of exciting thing they have done is look at the so-called dose response between the dose of aflatoxin, this mold that grows on many products including peanuts, which causes liver cancer. They have elegant data on what a low dose of aflatoxin can do.

Some people from the International Association for Research on Cancer in Lyon, France, have looked at two groups of people who eat moldy food and have high aflatoxin exposure. They find the response in man is almost the same as in the rodent. To me this is very important.

We will expand upon that.

Mr. FLOOD. You can see how you can develop that for the record.

[The information follows:]

Program on Food-Borne Environmental Toxicants
at the Massachusetts Institute of Technology

The non-nutrient components of food can be divided into two classes according to their origin--the intentional additives estimated to include up to 1500 or more compounds and the accidental contaminants which may number as high as 10,000 substances.

This program of research concerns the chemistry of food-borne environmental toxicants, characterization of their toxicity, carcinogenicity and mutagenicity in several bioassay systems and experiments related to interactions with cell macromolecules critical to carcinogenicity and mutagenicity.

Progress during the past year includes:

(1) Studies to improve the accuracy and dependability of a common mutation assay for N-nitroso compounds as an aid in prediction of their biological activity. Insights into the mechanism of biological activation will simplify the level of prediction of this activity. The mutagenic activity of a large number of nitrosamines has been determined and reported.

(2) Development of methodology to allow for the study of mechanisms and pathways of activation and metabolism of the nitrosamines which have been implicated in human cancer.

(3) Studies have been carried out to determine the interactions between proteins and peroxidizing lipids which lead to browning, off-flavor, protein insolubilization and destruction of labile amino acid residue resulting in damage in nutritional value and acceptability of food. Such interactions may also be involved in aging and other physiological deterioration.

(4) Development of a reliable quantitative assay for mutagenic activity in diploid human lymphoblasts as a means of differentiating hazardous from non-hazardous materials with regard to human health.

(5) Studies on alfatoxin B_1, suspected of being an important factor in the etiology of human liver cancer in certain sections of the world indicate that approximately 90% of the *in vitro* binding which occurs to cellular macromolecules can be attributed to 2,3-dehydro-2(guaninyl)-3-hydroxyaflatoxin B_1. These findings may help to clarify its role in carcinogenesis.

PBB (POLYBROMINATED BIPHENYLS)

Mr. FLOOD. In this budget we are talking about, is there sufficient flexibility to permit you to support studies that may be needed now to answer these environmental health problems? In the past and in the very recent past how did you support studies like that? Remember the Michigan dairy herd, PBB?

Dr. RALL. The way we supported that study—and we might want to talk about that a little more. We were not successful, if you remember, in creating a new center. Therefore, we had the excess funds. We were able to use that money to support Dr. Selikoff in his survey of about 1,000 farmers exposed. This is a terribly important survey because this is the first time a team of scientists, physicians, who thought chemicals might cause cancer, looked at these farmers and they found significant pathology.

Mr. FLOOD. And you actually did have results?

Dr. RALL. Yes.

Mr. FLOOD. That is the one I think is the best example I can think of off the top of my head.

Mr. Natcher?

STAFFING AND RESOURCES

Mr. NATCHER. Doctor, as the chairman has indicated, your budget proposes an increase. That is correct, isn't it?

Dr. RALL. Yes, sir.

Mr. NATCHER. In the light of the magnitude of the environmental health problems, and I for one believe that you did a good job of outlining them in your statement, I am just wondering if the budget proposal before the committee is sufficient to allow you to develop the tools to quickly identify toxic agents and to determine how these toxic substances affect people. What would you say about that, Doctor?

Dr. RALL. I would say it is a very good start. I think there are areas where we could use some more support. We are staffing and instituting new programs in anticipation of moving into our new permanent research facility. We certainly could use some extra positions and research money in that area to begin to let us hire now the very top people who can then build their staff so that when we move into the new building in 3 years they will be ready to go.

We need a modest amount of money in the contract area because as the chairman noted, this can be used flexibly. When an urgent problem comes up we can move very rapidly with the use of research contract money to deal with it.

MARINE BIOMEDICAL RESEARCH CENTERS

Mr. NATCHER. In your further statement I notice you will be initiating certain Marine Environmental Research Centers, correct?

Dr. RALL. That is correct.

Mr. NATCHER. Will you explain to the committee what kind of work these Centers will perform?

Dr. RALL. We will be initiating support for the activities of existing marine laboratories.

Mr. NATCHER. Not new locations?

Dr. RALL. Not new locations necessarily.

Mr. NATCHER. Where are the Centers located that you will be using?

Dr. RALL. The best marine and freshwater biology laboratories throughout the United States will be selected competitively through the grants review process. Those supported will have a demonstrated interest in research with biomedical application. A few examples of the types of laboratories I am talking about includes Mount Desert Laboratory in Maine, Marine Biological Laboratory at Woods Hole, in Massachusetts, University of Florida Laboratory at St. Augustine, the University of Miami Center in Miami, the Mote Marine Laboratory in Sarasota, the University of Texas Center at Galveston, Scripps Institute at La Jolla in California and Friday Harbor in the State of Washington.

Mr. NATCHER. You would be using existing laboratories and facilities?

Dr. RALL. Yes; the reason I feel this is an important program is that I have visited many of these and they have inadequate funds to keep their program going and to keep their buildings and boats maintained. Without these laboratories significant research effort important to our program cannot be continued.

If we lose one of these centers because it goes bankrupt, the property will go commercial because they are all in prime tourist areas, and we will never get that center back again. We have already lost the Lerner Marine Laboratory in Bimini which had been funded by the American Museum of Natural History. The Museum cannot afford a $150,000 a year deficit. That is on the market for sale now.

PERSISTENCE OF CHEMICALS IN THE BODY

Mr. NATCHER. Doctor, further in your statement you state that certain chemicals once ingested remain in the body and are not excreted. Is this just one class of chemical that you are referring to or are there many different kinds that react this way?

Dr. RALL. There are many classes of chemicals that react that way. The typical ones are the organic chemicals that are combined with either chlorine or bromine. These are very popular for use as pesticides and a whole variety of other commercial uses.

TREATMENT—KEPONE

Mr. NATCHER. What kind of research are you conducting now from the standpoint of treating people who are exposed to chemicals along the line that you have just mentioned?

Dr. RALL. This is a very exciting new finding. Dr. Philip Guzelian in the Medical College of Virginia has been studying the factory workers from Life Sciences, Inc., where there was the very tragic Kepone exposure some years ago. He has shown that the Kepone is excreted via the bile into the intestinal tract and almost totally reabsorbed from the intestinal tract so there is no net excretion.

He has introduced a drug called cholestyramine and given it, almost an ounce a day, to the people. The drug keeps the Kepone in the intestine and prevents reabsorption and increases excretion of the

Kepone fivefold to sevenfold a day. It is hopeful if we can develop other agents like this, we can strip the body of some of these toxic chemicals.

ASBESTOS IN ROCK QUARRY

Mr. NATCHER. You mentioned that people living in the Rockville, Md., section who have been exposed to asbestos from a stone quarry located near Rockville have exposure equivalent to those causing bystander disease from asbestos. What do you mean by bystander disease? What do you have in mind there?

Dr. RALL. It has been known for a long time that a worker in an asbestos plant has an increased chance of having lung cancer, gastrointestinal tract cancers, pulmonary damage and a rare tumor called mesothelioma.

The workers families and the households downwind of the plant also show an increased incidence of these diseases. That is what we call bystander disease. This refers not to the person engaged in the occupation but to those near it by family or location.

Mr. NATCHER. Have the health authorities taken any action to correct this situation near Rockville?

Dr. RALL. I do not know, I am sorry. They have all the information. A paper is coming out in Science Magazine describing Dr. Selikoff's finding.

Mr. NATCHER. You don't know if there is any action?

Dr. RALL. They have been doing repeated sampling, but I don't know what the action is if they have taken any.

Mr. FLOOD. Mr. Obey?

TASK FORCE FOR RESEARCH PLANNING

Mr. OBEY. Dr. Rall, you mentioned the Task Force for Research Planning in Environmental Health. You mentioned the direction that environmental health research should take in the future. Could you very briefly highlight some of those recommendations with particular emphasis on those that offer the most immediate promise for improving man's health?

If you could also tell us how this budget request relates to your ability to carry out the recommendations.

Dr. RALL. The task force brought forth a major concept that most of the chronic diseases today are due in large part to environmental factors. We heard discussion that cancer is due to environmental factors in 60 to 90 percent of the cancers. There is evidence that cardiovascular disease, neurological disease, and birth defects are all due in substantial, but as yet undetermined, fraction to environmental factors.

A major recommendation of the task force is to look at those, see if we can eliminate them and cut down chronic disease. The task force also made an eloquent plea for more training as we have discussed earlier and they also pointed out that we need to study the toxicity of chemicals to the various major organs, kidney, liver, lungs, pancreas, et cetera. This is being done in a totally inadequate way today.

Further, perhaps the last recommendation I will highlight concerns the problem of environmental forecasting. How can we prevent a taconite mine opening up in some new Duluth and putting a new form of asbestos into a body of drinking water?

I think environmental forecasting is an idea whose time has come. We have all talked about it and now I think we should do something about it.

I will be happy to supply a brief summary of these important recommendations for the record.

[The information follows:]

MAJOR RECOMMENDATIONS OF THE SECOND TASK FORCE

The Second Task Force on Research Planning in Environmental Health Sciences recognized that development of some chronic diseases may now be traceable to environmental factors. For example, cigarette smoking is clearly associated with major increases in pulmonary and cardiovascular diseases, community and occupational air pollution are responsible for much chronic respiratory disease and undoubtedly aggravate heart disease, and epidemiologic research has indicated that a majority of human cancers are initiated or promoted by environmental factors. Accordingly, the task force recommended that emphasis be placed on the search for environmental factors in the etiology of major chronic diseases particularly cardiovascular and pulmonary disorders, cancer, neurological debilities, and structural and functional birth defects. They stressed that, to be effective, a concerted program to investigate these areas must involve coordinated research, including epidemiologists and laboratory scientists who seek knowledge on basic mechanisms of biological effects in animal studies.

Yet, the task force found that epidemiologists and toxicologists, in particular, are in short supply in the environmental health field. They emphasized that scientists trained in these disciplines are vital to successfully implement the needed programs. The task force, therefore, recommended that increased support be provided for research manpower training programs to provide institutional and individual support, as well as for support of curriculum development. The main goals of these programs would be to develop individuals who have in-depth training in one of the disciplines relevant to environmental health sciences and who have enough interdisciplinary training to bridge several fields essential to research in this area.

They expressed the view that epidemiologic studies, or studies of illness in human populations, are crucial to inferences regarding the effects of the environment on human health. But, although techniques required for these epidemiologic studies are vastly better than they have ever been (or were a decade ago), inadequate resources are invested in this potentially important research area. They, therefore, recommended that greater resources be devoted to chronic disease epidemiology.

The task force also recommended that increased emphasis be placed on research on mechanisms of action of toxic agents. This will facilitate both the understanding of disease production by chemicals and the development of better toxicologic test methods. They noted that studies of mechanisms of chemical carcinogenesis are resulting in the development of rapid bacterial and cell culture tests to identify potential carcinogens and that similar approaches for other chronic effects should be fruitful. These approaches, they believe, will offer the possibility of studying synergistic or antagonistic effects of various mixtures of two or more agents when each is at a concentration too low to produce an effect. These mechanism studies also offer the best means of improving the reliability and precision of dose-response extrapolations from experimental animals to man, especially when these involve long-term, low-level exposures.

To guide priorities for biologic research in the environmental health area, the task force recommended establishment of a mechanism for systematic environmental forecasting. Such forecasting could help identify technologies likely to develop or the possibility of important technologic changes. Once this forecast has been made, an analysis of the effect of a new or changing technology on environmental health could be undertaken, which should take into account the chain extending from the emission source to the receptor, man. It should also incorporate practical methods for ranking chemicals or classes of chemicals according to their apparent potential for impact on human health. The task force believes environmental forecasting would have broad application to decision making in the health and environment agencies and could provide early warnings of potential problems.

The task force found that one of the major impediments in the environmental health research area is the poor development of resources for the utilization of existing health data and for developing newer data. To overcome this obstacle, they recommended that additional funds be allocated to appropriate Federal agencies (particularly the National Center for Health Statistics, the Social Security Administration, and the NIEHS) to permit more in-depth analysis of data now being

collected and quick response to special requests from qualified investigators for use of the data, especially those investigators wanting to undertake epidemiologic studies of industrial workers--a notable high-risk group in our society. They also recommended establishment of a National Death Index at the earliest possible time and the convening of an interagency task force to determine under what circumstances, and with what safeguards, present individual records and other data collected by Federal agencies could, and should, be linked for epidemiologic purposes. They suggested that the interagency task force should consider the research uses of data that are part of a plan for a National Health Insurance Program. They emphasized that safeguards against the misuse of medical information must be maintained and, indeed, strengthened, but said that there is a point at which the cost of such mechanisms to society, in terms of hinderance to health research, outweighs the potential benefit to the individual. They further recommended establishment of a National Environmental Data Registry to collect and catalog information on contaminant concentrations in air, water, and food. Human health effects information would be a major component of the Registry, which could provide considerably better quality data for epidemiologic studies of environmental hazards than are currently available.

Finally, the task force recommended that more formal mechanisms be developed for DHEW advisory input into the regulatory development process on all environmental regulations that impact on health. They believed this mechanism should require that input be given at an earlier point than at the time of the final Federal interagency review. The task force recognized that to carry out this recommendation would require significant increases in the scientific staffing of the DHEW.

The task force stated that implementation of these research and training recommendations would strengthen DHEW's advisory capability for assisting Federal regulatory agencies. They also believed it would broaden the base of the academic community to serve as a source of scientific information upon which sound regulatory decisions could be made.

ASBESTOS IN WINE

Mr. OBEY. I have more basic questions which I will go back to later.

In connection with Duluth, I drink wine. I like it. I have been told that there is a study floating around that indicates that certain foreign wines, French wines, are filtered through asbestos. Is that a fact?

Dr. RALL. There is a study in the Presse Medical by Jean Bignon, Paul Sebastien, and coworkers. They have looked at 22 samples of French wine. In 9 of those they found significant amounts of asbestos varying from 2 million fibers per liter to 64 million fibers per liter.

Mr. OBEY. How does that compare to the concentration in water in Duluth?

Dr. RALL. That is in the same range as fibers found in Duluth water. These are chrysotile fibers. They appear to be somewhat larger than the fibers in Duluth and would be somewhat more hazardous. There have been sporadic reports in the past. Two Canadians, Cunningham and Pontefrack, showed sporadic asbestos contamination in samples of port and sherry. Italian vermouths seemed to have concentrations of 12 million fibers per liter and French Vermouths less.

It is my understanding that bourbon and Canadian Club are relatively clean. I wanted to have some good news for the committee as well.

Mr. OBEY. Given the fact that asbestos is regarded as being fairly dangerous, how do people find out which wines are heavily laced with asbestos and which ones are not?

Dr. RALL. There is absolutely no way of knowing right now.

Mr. OBEY. Well, I just happen to have in my hand a letter which I was going to be sending to you in the next couple of days. I wanted to ask you two things.

One, since as far as I know, no agency is systematically surveying imported or domestic wines for that problem, would it be appropriate for your operation to conduct that kind of survey and could you do it within your present budget?

Dr. RALL. I think we are eminently well set up to perform a preliminary survey. I think it would be difficult to do an adequate survey within our own budget.

Incidentally, as I am sure you are quite aware, we have no regulatory function, but if we could determine the extent of contamination, we could bring it to the attention of the appropriate regulatory agencies.

Mr. OBEY. I would think that would be quite important. I forgot what the consumption rate for wine is in America, but I know it has been rising very fast in the last 5 years. I would think that would be fairly important for an operation such as yours to conduct.

I will be sending you a letter on that and I would appreciate a response as quickly as possible.

Second, would you not think it would be appropriate, since I would think the consuming public would at least have the right to know which products provided the greatest dangers, would you not think it would be appropriate for our Government to require labeling of products which were filtered through asbestos filters and did contain asbestos fiber?

Dr. RALL. As an interim measure, yes, but I think that might perhaps beg the issue, that there are adequate ways of filtering without the danger of asbestos contamination. This does leave you with the elegant wine that is 3, 4, 6, or 7 years old.

Mr. OBEY. Mr. Chairman, I think the 10 minutes is up. I will get back to the other questions later.

Mr. FLOOD. Mr. Early?

TOXICOLOGY MANPOWER

Mr. EARLY. I want to address just one question with regard to the search for manpower in toxicology. What do you suggest we do?

Dr. RALL. Historically, toxicology has not been viewed as one of the more exciting sciences. The brightest young people have gone into molecular biology and other things. I think there are some bases for this. The old-fashioned toxicology was pretty dull. Toxicologists were called "rat killers" in the parlance of scientists. I think toxicology is changing and adopting techniques of molecular biology. The young people are increasingly socially conscious and I think they will turn to toxicology if we can provide them adequate training programs to make the transition into toxicology easier. That is why I have been asking for the increase in the training programs.

Mr. EARLY. What efforts did you make last year in the training of toxicologists?

Dr. RALL. We are very interested in the business of taking people trained in areas close to toxicology, out of their Ph. D. perhaps 10 years, and giving them 2-year didactic and practical courses to bring them up to speed in toxicology. This would perhaps give us a few hundred well-trained people within a year or two which would be very important.

That is one of the programs.

Mr. EARLY. In some of those fields do we have a surplus in personnel?

Dr. RALL. Not a surplus, but you could retrain over 50 or 100 without serious impact, because the fields are so large.

TOXIC SUBSTANCES CONTROL ACT

Mr. FLOOD. Doctor, how do your institutes' responsibilities change under the new Toxic Substances Control Act?

Dr. RALL. In terms of legal responsibilities I don't think there will be any change, but clearly the NIH Institutes and NIEHS, in particular, are the ones who provide the research that will make the Act function. Until the very rapid tests for mutagenesis, like the Ames test was developed, it just seems to me that the Act could never have been passed; it would have been too difficult a job. With more rapid, specific tests we can begin to look at the thousands of compounds we have without being incredibly expensive.

Mr. FLOOD. Can your Institute assume the same kind of role with EPA, the way the National Institute for Occupational Safety and Health have tied in with OSHA? NIOSH makes the scientific determination of what is safe, but OSHA goes into enforcement.

Dr. RALL. In many ways that is the role that NIH and NIEHS are playing now with EPA. We are concerned that the demands that EPA will put on us will strain our resources considerably, and we estimate something like 12 positions and $7 million or $8 million a year. Would you like that submitted for the record?

Mr. FLOOD. Yes, indeed, we would like to see that.

[The information follows:]

RESOURCES NEEDED BY NIEHS TO IMPLEMENT ADEQUATE RESPONSES TO THE TOXIC SUBSTANCES CONTROL ACT (TSCA)

Implicit in the Toxic Substances Control Act is the expectation that the Federal research agencies (primarily within the Department of Health, Education and Welfare) will provide the basic knowledge and technology to permit the conduct of faster, simpler, more accurate and less expensive toxicity testing. We assume full and timely funding and staffing of the NIEHS as projected in our Forward Plans and looking towards full occupancy of our new building by FY 1981. We expect to meet this expectation in a timely manner if the needs in our program plans are met. In addition to these projected research needs, a highly specialized staff will be needed to deal with TSCA problems. These are people that would not have been needed without TSCA and therefore represent additions starting as soon as EPA makes its first request to us.

	(Dollars in Thousands) 1977 Estimate	
	Positions	Amount
Staff Resources -- Collection and coordination of research data for timely and accurate response to TSCA demands	12	$225
Grants -- Strengthen ability of ongoing Environmental Health Sciences Centers to be responsive to TSCA	---	700
Develop understanding of toxic chemicals and develop and verify test methods	---	2,000
Research Contracts:		
Toxicity bioassay	---	1,100
Mutagenicity and *in vitro* screening	---	1,500
Ten conferences for collection and coordination of data from academic and other sources	---	200
Research training grants in environmental toxicity and health	---	2,100*
TOTAL	12	7,825

*$2,000 of this amount has been included in a supplemental to the 1977 Appropriation

TOXICOLOGY INFORMATION

Mr. FLOOD. We have had people say to us in the last several months especially, there is a need for a central source of information. You remember what gave birth to this, regarding toxic substances. I think you are the Chairman of the HEW Committee that Coordinates Toxicology with Related Programs; that is another hat you wear. Is your committee doing anything to develop a centralized information system on the toxic substances? What I have in mind is the Legionnaires' disease; when that Legionnaires' disease took place in Philadelphia, what role did your committee play in helping us solve that problem?

Dr. RALL. Our committee did not play any role at all in that one. The Director of CDC did not ask us to advise him.

Mr. FLOOD. We realize since they have determined that it is a bacterium that caused this disease, anyway, but at the time there seemed to be very little expertise available concerning the effects of toxic substances.

Dr. RALL. We have been supporting the toxicology information program at the Library of Medicine; our scientists, using that program in a novel way, were able to rapidly identify perhaps 10 candidate compounds that could cause the sort of toxicity, pulmonary toxicity, that was seen in the Legionnaires' disease. I am convinced with better support of the toxicology information program we can begin to use that for a rapid response in terms of new incidents where there appears to be a toxic chemical.

Mr. FLOOD. Is your toxicology committee developing a plan for responding to future incidents?

Dr. RALL. Yes.

Mr. FLOOD. Similar to the Legionnaires' disease?

Dr. RALL. Yes.

Mr. FLOOD. This same committee we are talking about, your committee, currently to coordinate toxicology and related programs, you only have the HEW people as members. Do you feel this committee should become right across-the-board a Government-wide committee with EPA and Energy Research and Development Agency as full members?

Right now, all these non-HEW members simply merely attend your meetings as observers and just sit there.

Dr. RALL. We call them observers, and we call our people members, and the only distinction is whether or not they can vote, but we have never had a vote in the committee. They participate very fully as observers.

Theoretically, yes, I am convinced there is a need for an interagency committee to do this. I would wonder whether perhaps the new Office of Science and Technology Policy and/or the Council on Environmental Quality might not be an appropriate locus for that, or the Federal Council for Science and Technology. There is a need for it. I think it probably should not be in one agency but should be above the agencies. That is my personal opinion, I might say.

INTERAGENCY TRANSFER OF FUNDS

Mr. FLOOD. Do any Federal agencies at all transfer any of their funds over to your shop, your institute, to support research, such as EPA asking for studies in any of the health-related programs?

Dr. RALL. Yes; EPA has transferred about $3 million to us.

Mr. FLOOD. How much are you going to get in 1977?

Dr. RALL. About the same.

Mr. FLOOD. How much in 1978?

Dr. RALL. About $3.1 million, to work on energy-related problems.

Mr. FLOOD. How will you use the money that is transferred? Is it going to be intramural research; are you going to support grants and contracts? How are you going to handle the money?

Dr. RALL. It is split about equally between intramural, grants, and contracts, not completely, but about equally.

RAPID TOXICITY TESTS

Mr. FLOOD. Last year, you talked to us about these rapid test methods, also bacteria and the human cells in culture at a stage where you might be able to use them for screening from 10,000 to 15,000 environmental chemicals. What is the status of your work now in this area?

Dr. RALL. We would build up to a level of about a thousand compounds a year. We have one contract now with a very rapid test that is giving us information on 10 compounds a month. We have a number of contract protocols being prepared now. By the end of this fiscal year, we expect we will be able to evaluate about 300 compounds per year in the bacterial tests.

Mr. FLOOD. How much are you going to spend in 1977, and 1978, to develop more reliable rapid test methods for the screening of chemicals?

Dr. RALL. That really moves then into the other parts of our budget, where a significant fraction of our various activities in reproductive and mutagenic toxicity is that new test development. I would say on the order of 20 percent of our budget is involved in that sort of a program, developing new tests, getting the information so that we can design these new tests.

Mr. FLOOD. Do your best for the record to show what you are going to spend in 1977 and 1978 for that.

[The information follows:]

Test development

1977 estimate	$5,000,000
1978 estimate	6,000,000

A significant portion of the total NIEHS program is concerned with improving test methodology; including basic research intended to understand chemical metabolism and metabolic processes, preliminary trials to evaluate test methodology, and limited trials to validate test results.

Mr. FLOOD. Is there interest in this, a very high level of interest in the whole scientific community to do this kind of work you are talking about? Are you getting a lot of applications, a lot of grant applications?

Dr. RALL. Not yet. But the number is steadily increasing. We have had a series of conferences on this concept, and they have been very successful, attended by academic scientists, industry, and the regulatory agencies.

MERCURY AND LEAD

Mr. FLOOD. In the past we have talked a great deal about your work on mercury and lead and the diverse effect on learning behavior. I

think you told us you were conducting a lot of preliminary experiments. How much are you going to spend in 1978 on this, and what kind of research are you going to conduct in 1978? We have had evidence time and again about the inner city children ingesting high levels of lead paint.

Dr. RALL. We will spend almost $4 million on lead research in 1977, and about $4.3 million in 1978. We have just recently appointed a head of our behavioral and neurological toxicity group in our intramural laboratories. He is staffing up and will be deeply involved in this process.

POLLUTANTS INDUCED LUNG DISEASE CONFERENCE

Mr. FLOOD. Again, last year, you sponsored a conference on pollutants-induced lung disease and its very possible amelioration by a vitamin therapy. You were very concerned about that. What happened to that conference; any recommendations or any new initiatives? You know we have all these scientists thinking vitamin A and vitamin E are going to wipe out emphysema and lung toxicity.

Dr. RALL. It wasn't a sort of conference that brought out recommendations. It was a research conference to sort of lay out what the new approaches were, and there is considerable interest in that and research is moving forward.

Mr. FLOOD. It certainly is.

Mr. Natcher?

Mr. NATCHER. No further questions.

Mr. FLOOD. Mr. Obey?

INGESTED ASBESTOS STUDY

Mr. OBEY. Yes, Mr. Chairman.

As the chairman indicated, several years ago we included money in this appropriation for large-scale study of asbestos. Can you tell us how that study is coming and when we can expect to have results?

Dr. RALL. As I indicated last year, we had trouble obtaining well characterized samples of asbestos. We now have most of those in hand. We have 9 animal groups to test, out of about 20 that we will eventually have. Those that are on test we expect an answer on a little over 2 years from now. We have a couple of more groups that should go on test as soon as the new sample of amocite is received; it is supposed to be this month. So this now is in full swing and moving very rapidly. I have a report which I will submit indicating that.

[The information follows:]

February 28, 1977

NIEHS STUDY OF

BIOLOGICAL EFFECTS OF INGESTED ASBESTOS

While there has been growing concern for the past two decades about the pathogenic effects of inhaled asbestos, relatively little attention was given to the biological effects of ingested asbestos. Early in 1973, it was recognized that fairly extensive pollution of Lake Superior waters with mine residues containing asbestiform fibers was resulting in contamination of the municipal water. In addition, other sources of asbestiform fibers find their way into material which man consumes; examples are natural contamination from serpentine rock, transmission of water through asbestos cement pipes, and use of asbestos filters for such products as beer and wine.

A conference on the Biological Effects of Orally Ingested Asbestos was organized and held in 1973 cosponsored by the National Institute of Environmental Health Sciences and the Environmental Protection Agency; the conference was held in Durham, North Carolina, November 8-20, 1973. The proceedings of this conference were published in Environmental Health Perspectives 9, December 1974.

The DHEW Committee to Coordinate Toxicology and Related Programs formed a subcommittee to review existing knowledge of the biological effects of ingested asbestos and recommend future research needs. This subcommittee had representation from the Food and Drug Administration, National Cancer Institute, National Institute of Environmental Health Sciences, as well as working observers from EPA and other agencies. It concluded that there was not sufficient data to determine biological effects of oral ingestion of asbestos, and it proposed that specific studies be undertaken. The subcommittee then prepared a working draft of a research protocol which was widely distributed for comments both within and without the government. An open meeting was held on February 18, 1976, in Bethesda, Maryland, to receive comments, suggestions, and criticisms on this draft protocol. Based on comments received at the open meeting as well as other comments provided, the Subcommittee revised its original working draft and prepared a final protocol which it again submitted to various agencies for comments. Subsequently, the National Institute of Environmental Health Sciences developed research contracts to study the effects of oral ingested asbestos in rats and hamsters. These studies are being conducted at Hazleton Research Laboratories, Vienna, Virginia, and the Illinois Research Institute of Technology Research Institute, Chicago, Illinois. Other research is being performed at the National Institute of Environmental Health Sciences and the U.S. Bureau of Mines. The EPA is also funding a portion of these studies. The NIEHS is being advised in the contract by an ad hoc committee composed of Dr. R. Shapiro, FDA; Dr. R. Tardiff, EPA; and Dr. M. Stanton, NCI.

Asbestos

The current protocol is to study two forms of chrysotile, one which represents a range of fibers less than 10 microns in length and a second which has a broader range of fiber lengths. In addition to the two chrysotile samples, two forms of amosite (again reflecting the broad range of fiber length as well as a second sample which is restricted to the shorter fiber length), tremolite and crocidolite will be evaluated. Great care is being given in the preparation and characterization of the asbestos material to insure that the samples are truly representative. All are to be extensively characterized as to chemical and physical properties. The characterization will be accomplished by the U.S. Bureau of Mines and IITRI Fine Particles Laboratory.

Animal Studies

All materials will be tested in rats, whereas the two chrysotile samples and broad range amosite will also be tested in hamsters. The hamster represents the "second species;" as such, it is being fed a material that represents a serpentine and an amphibole type of asbestos. Each material is to be fed continuously in the diet at a 1% level. The two short-range fiber sizes will be fed at something less than 1% to take into consideration the correlation of mass/fiber relationships.

All studies are to encompass the life span of the animal, which is defined as the age an animal begins eating solid food until its death. To determine newborn effects, a segment of the study incorporates exposure by gavage from birth to weaning, followed by consumption of asbestos in the diet till death.

A portion of the study seeks to determine if there is an interaction between asbestos and a chemical known to cause tumors of the gastrointestinal tract.

Progress (through August 1976)

1. The tremolite sample is being characterized as to physical and chemical properties.

2. The two chrysotile samples have been purchased and received; they are currently being characterized.

3. The amosite and crocidolite samples are being prepared by the Ontario Research Foundation under the supervision of the U.S. Bureau of Mines.

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4. Studies that determine the chemical as well as the dose of chemical to be used which measure the interactive effects of asbestos and a chemical known to produce intestinal tumors are in progress (9 and 11 months into a 12-month study in hamsters and rats respectively). Dimethylhydrazine and methylazoxymethanol are the candidate chemical carcinogens.

5. Studies are completed that determined the diet, which contains asbestos, could be pelleted without adversely affecting the fibers. Use of pelleted diets will significantly reduce the potential aerosol exposure of experimental animals and research personnel to the asbestos fibers. A source for the preparation of asbestos-containing feed has been selected.

6. The short range chrysotile, medium range chrysotile, neonatal gavage, and chemical carcinogen/chrysotile interactive feeding studies in rats will start in September.

Progress (August 24, 1977-February 1977)

1. Characterization of asbestos types: The short range chrysotile, intermediate range chrysotile, and tremolite samples have been characterized from a physical, chemical, and fiber distribution standpoint. The reports of these characterization efforts are in preparation.

2. Laboratory studies that determine the appropriate chemical to be used in assessing the interactive effects of asbestos and a chemical known to produce intestinal tumors are completed. The chemical selected is dimethylhydrazine. Doses to be used in rats are 7.5 mg/kg for males and 15 mg/kg for females. These doses produced an intestinal tumor incidence in 5/27 male and 5/24 female rats respectively. The hamster interactive study will also use dimethylhydrazine. The specific does will be decided when the final histopathologic evaluation of the tissues has been completed in March 1977.

3. The interactive study using dimethylhydrazine and intermediate range chrysotile in the rat has been started.

4. The lifetime study on the biological effects of short range chrysotile at 1% in the diet in the rat has been started.

5. The lifetime study on the biological effects of intermediate range chrysotile at 1% in the diet has been started.

6. The lifetime study on the biological effects of tremolite at 1% in the diet has been started.

7. It has not been possible to produce two samples of amosite which have a separate and distinct fiber size distribution. Although technically feasible to produce, it is not possible to produce the quantities required for these studies. As a result, a single amosite fiber is being prepared by Ontario Research Foundation under the auspices of the U.S. Bureau of Mines. This material is scheduled to be shipped to NIEHS in March 1977. The original amosite preparation was rejected because of metal contamination of the material during milling.

8. The chrysotile sample is scheduled to be prepared by Ontario Research Foundation in March 1977. It should be shipped to NIEHS in April 1977.

9. An article was published in an East German scientific journal which noted an increased tumor incidence in rats that received an oral dose of asbestos prepared from commercial filters. Consideration is being given toward initiating an additional experiment that assesses the biological effects in rats to ingestion of asbestos contained in filters that are used for a number of commercial food and beverage purposes. This experiment would expand upon the German work and provide a model that attempts to confirm this work.

10. The lifetime feeding study in hamsters with short range chrysotile fed in the diet at the 1% level is scheduled to start in March 1977.

11/12/75
NIEHS

TENTATIVE ORAL ASBESTOS ANIMAL TEST GROUPS

HAMSTER

	CHRYSOTILE INTERMEDIATE	CHRYSOTILE SHORT RANGE	AMOSITE	CROCIDOLITE	TREMOLITE
Asbestos diet	500	500	500	ND	ND
Asbestos diet plus chemical carcinogen[a]	350	ND	ND	ND	ND
Preweaning asbestos gavage plus asbestos diet	ND	ND	ND	ND	ND
Control diet[b]	500	250	250	ND	ND
Control diet plus chemical carcinogen[a]	250	ND	ND	ND	ND

TOTAL HAMSTERS: 3,100

[a]Numbers may be adjusted pending results of dose ranging studies to determine 15 ± 5% tumor incidence in controls.

[b]Control allocations are descriptive only; it is expected that experimental response will be evaluated against total controls (1000). Subsets of control will reflect temporal differences in commencing phases of study which is expected to be aggregates of 250-350.

ND - Not done.

TENTATIVE ORAL ASBESTOS ANIMAL TEST GROUPS

RAT

	CHRYSOTILE INTERMEDIATE	CHRYSOTILE SHORT RANGE	AMOSITE INTERMEDIATE	AMOSITE SHORT RANGE	CROCIDOLITE	TREMOLITE
Asbestos diet	500	500	500	500	500	500
Asbestos diet plus chemical carcinogen[a]	350	ND	350	ND	ND	ND
Preweaning asbestos gavage plus asbestos diet	200	ND	200	ND	ND	ND
Control diet[b]	175	175	175	175	175	175
Control diet plus chemical carcinogen[a]	250	ND	250	ND	ND	ND

DELETED[c]

TOTAL RATS: 5,650

[a]Numbers may be adjusted pending results of dose ranging studies to determine 15 ± 5% tumor incidence in controls.

[b]Control allocations are descriptive only; it is expected that experimental response will be evaluated against total controls (1000). Subsets of control will reflect temporal differences in commencing phases of study which is expected to be aggregates of 250-350.

ND - Not done.

[c]Deletion reflects availability of only one amosite.

Mr. OBEY. In this regard, is it correct that there was a German's study which related somewhat to the same area?

Dr. RALL. Yes, as we discussed before, previous studies on oral asbestos were small-scale and although they tended to be negative, they were not very convincing. Early this winter, Professor Gibel, from East Germany, published a paper in which he described an experiment in which he had ground up asbestos filters and fed them at quite high concentration to rats. About 30 percent of the rats died of malignant tumors whereas a low percentage of the control rats died. This is not, in our view, a very well performed experiment. We don't know enough details, but it certainly causes concern.

Mr. OBEY. I didn't understand. Did you say this was not a very well performed experiment?

Dr. RALL. It is not written up adequately to convince us that it is a well-performed experiment, but it certainly, I think, causes concern, and indicates the need for the sort of large-scale study that we are currently performing.

Mr. OBEY. This was a different study than you were referring to a moment ago when you were discussing wine filters?

Dr. RALL. Yes; this is an animal toxicity study.

ASBESTOS IN WINE

Mr. OBEY. Let me ask, again going back to wine, how much do we know about that? Is it confined? Do we have any way of telling whether it is confined to certain regions? Is it red wine, white wine, both?

Dr. RALL. At the moment, we don't know. The old method of filtering wine was to use silk, and this apparently was very effective but very expensive, and we are not even sure when the major wine producers in France switched over to the asbestos filter, but I think this is information we must get, and we can get it.

Mr. OBEY. Hasn't Dr. Selikoff developed some data which showed excess levels of cancer of numerous sites in the body, not just the lung?

Dr. RALL. Yes.

Mr. OBEY. How do you account for that? How does it get around and by?

Dr. RALL. I think it is increasingly likely that significant amounts of asbestos are absorbed through the gastrointestinal tract—the same author, Jean Bignon, who recently reported on asbestos and wine, is studying rats in which he feeds asbestos and then measures asbestos particles that come through the thoracic duct, which is the main drainage of the gastrointestinal tract, and he finds one-tenth of 1 percent, roughly, of the asbestos administered orally is absorbed and goes into the theoracic duct and into the general circulation. I think there is increasing evidence that asbestos particles get into the body by absorption where they can do their damage.

Mr. OBEY. So what you are after medically is a determination as to whether or not cells in other parts of the body react to asbestos the same way as lung cells, for instance?

Dr. RALL. That is right.

RESEARCH TRAINING

Mr. OBEY. Let me get on to some other questions.

The chairman indicated that we had added money to the supplemental for training centers, and how many centers did you say there would be?

Dr. RALL. Let me give you the answer a little different in terms of the number of people trained. I think that is the important one. This will enable us to train about 300 people a year. And that, I think, is the critical number. This year, without that supplemental, we would be training 166. In 1978 the budget before you provides training for only 115. The supplemental will let us add about 130 new trainees, and I think that it is critical that this additional effort be sustained.

Mr. OBEY. There are about 425 veterinary pathologists in the country. How many chemicals can a veterinary pathologist look at in 1 year?

Dr. RALL. Roughly three, and some would much prefer only to do two.

Mr. OBEY. How many of those pathologists are involved in actual treatment of animals or work unrelated to cancer research?

Dr. RALL. I was sort of thinking broadly of not just cancer in that a veterinary pathologist doing that sort of study would look at the animal for all the manifestations of toxicity he might see. In the typical toxicity study you know, you look for chronic liver, chronic lung disease, and so forth, and cancer is only one of a great variety of things you are looking for.

Mr. OBEY. In the interest of time, let me put three or four questions in the record at this point and save time.

SHORT-TERM TESTS

Mr. OBEY. And let me ask you something else. How many chemicals would you say are in general use in society right now?

Dr. RALL. The best estimates are about 10,000.

Mr. OBEY. And how many will you be covering with the short-term test?

Dr. RALL. In about 3 years we will be geared up to do 1,000 a year.

Mr. OBEY. 1,000 in 3 years.

Dr. RALL. And that will let us cover most of those that are introduced each year; in fact, more than cover those that are introduced each year.

Mr. OBEY. How many years will it be before we have even a short-term test for most chemicals we are now exposed to?

Dr. RALL. My thinking has changed a little bit since last year. Let me explain it. The Toxic Substances Control Act (TSCA) now requires that the manufacturer do this sort of testing; so I think it is very possible that in terms of new chemicals, we will be able to ignore those and rely on the manufacturer's tests and our facility can then be used to go back and look in the old chemicals for which there is much less requirement under TSCA for testing. If things work out the way I think they might, instead of using our resources for new chemicals, we can let the manufacturers do that and turn our re-

sources to the old chemicals and at the rate of 1,000 a year, we can certainly get through half of them in 5 years.

Mr. OBEY. Even assuming that we do this, you say we get half in 5 years; you are saying 10 or 15 years before we have a reasonably comprehensive field of tests? What is the principal inhibitor of expanding that number, the lack of trained personnel again?

Dr. RALL. Mostly, the fact that I am being a little conservative. We are dealing with tests now at the rate of 100 a year or 200 a year. We handle that beautifully. Move that up one order of magnitude to a thousand a year; I want to be a little more comfortable about how well that works. If it works the way I think it will, then I think it would be easy to make that 1,000, 2,000, or 3,000 a year, but I want to get a little more experience in this process before I make any promise.

Dr. FREDRICKSON. I am sorry, Mr. Obey. I was asking Dr. Rall if he was implying that all toxicity of those compounds would be covered. In fact, it is only their mutagenicity. That is an important difference.

Mr. OBEY. But my question still is, what limits, even after you know what you are doing and you are sure you know what you are doing, would it be a fair statement to make that the principal limiting factor on going any faster than you have just described is the number of trained personnel available?

Dr. RALL. Yes, I think so.

STAFFING

Mr. OBEY. Last year, you provided the committee with a table which showed your plans for staffing your intramural program. What was your projection for 1978?

Dr. RALL. We projected the addition of 100 positions.

Mr. OBEY. I apologize. The chairman may have asked a couple of these questions, but I was talking and I may have missed your answer.

Dr. RALL. We projected going from 331 to 430.

Mr. OBEY. What is your budget request?

Dr. RALL. No change from fiscal year 1977.

Mr. OBEY. So I assume your answer to that is the same as you gave to the chairman in a different question, that you lost an argument with some people downtown?

How many additional staff can you effectively use?

Dr. RALL. We can effectively use between 50 and 100.

EMPLOYMENT FREEZE

Mr. OBEY. I will ask you the same question I have asked the witnesses from NCI. Do you know how you are going to be affected by the job freeze?

Dr. RALL. We are very concerned about that. The Federal Diary Column in this morning's Washington Post suggested that the number of people we had onboard February 28 would be the base and attrition measured from that. That makes life very difficult for us and the Cancer Institute, who just were allocated the new positions about November 15. Those new positions are certainly not filled now. We have 29

names for the 60 positions, but the paperwork is nowhere near caught up with that, so we view that this could be very serious.

Mr. OBEY. You are saying even people you may have contracted with to come on, you are not going to be able to bring on?

Dr. RALL. If the paperwork has moved through the process, that is a formal commitment, but if we are talking to a scientist who typically wants to move in the summer, between academic years, we may not have completed the paperwork yet, but we may have a firm agreement that we want him and he wants us.

Mr. OBEY. But you may lose him?

Dr. RALL. Yes; we are worried.

Ms. WORMSER. Let me clarify. The instructions have not yet been released as to how this freeze is to be implemented, so in terms of the ability of the various members of the NIH to answer this, they just have no information.

Mr. OBEY. I have several other questions for the record, but it is pushing 5 o'clock, and I think I will save them for the record, Doctor. Thank you very much.

Mr. NATCHER (presiding). Mr. Early?

NEWS MEDIA

Mr. EARLY. Thank you.

Doctor, in your statement you suggest, on page 8, that you deal with three publics—the regulators and the regulated, medical practitioners, and the general public, and then you get to the communication of the news media.

What is your impression of the cooperation of the news media with you and the general public?

Dr. RALL. They have been very cooperative. I have very high regard for the science reporters in the Washington-New York area. I think they do an excellent job of reporting stories much more accurately than the average story I see in the newspaper.

Mr. EARLY. What is your feeling about the public's overreaction?

Dr. RALL. I am not a very good prognosticator of how the American public is going to react. There will be a little. Often what happens is somebody picks up a story like that, doesn't know much about it, but writes in very florid phrasing, and there is where you get the overreaction, and it may happen.

Mr. EARLY. Do we insist that domestic winemakers use a silk filter?

Dr. RALL. We have not been able to find out what the practice is in the California and New York State wines. We understand that they are using less and less asbestos, which suggests to me that they still are using some asbestos, but this is relatively new information. We simply haven't been able to find out, but we will as soon as we can.

ASBESTOS IN CONSTRUCTION

Mr. EARLY. We have, in the East, a tremendous problem with asbestos in construction. Have you addressed that at all?

Dr. RALL. I think it was Dr. Selikoff's measurements of asbestos in the air downwind of buildings that were being either constructed or torn down that showed how far the asbestos fibers could travel and

led to the regulations that restricted the use of asbestos in new construction, and decreased the risk significantly.

Mr. EARLY. So the regulation is there for new construction. But, are you satisfied with the steps taken for remodeling old construction? As I understand it, those regulations are being tremendously strengthened.

Dr. RALL. That is a regulatory gray area. When it is inside the building, EPA may not have jurisdiction. OSHA has jurisdiction as far as the building trades are concerned, and I think the building trades are quite cognizant now of the danger from asbestos.

Mr. EARLY. Aren't you involved in asbestos use?

Dr. RALL. Involvement in terms of getting information, but this is a case where I think we have the information and it is regulation that needs to take over now. We have excellent information about asbestos levels under those circumstances.

Mr. EARLY. Have the regulations kept up with your information?

Dr. RALL. Not in the area you are talking about, of older buildings. You know the example perhaps of the Yale Library, which was built with enormous amounts of asbestos sound-deadening material inside, and the asbestos fiber count in the library approached the occupational standards. That building has been totally renovated using very careful techniques worked out in part with Dr. Selikoff's group, whereby the workers were protected as they stripped off the asbestos and put something new on. I don't know what. And they now have essentially zero fiber counts.

It is a very expensive process and must be done with great care so the workers weren't exposed. There is an emerging problem of this same type in school buildings in New Jersey and probably elsewhere. In the fifties and sixties the sprayed asbestos ceiling was common in public schools. By now, this asbestos is beginning to flake off and again we have the problem that fiber levels in some New Jersey schools are at the same level as the occupational standard.

We are talking with Dr. Selikoff and hope we can work out a contract with him for a feasibility study to see if you can remove the asbestos from these school ceilings safely and replace it or seal it so the fiber counts will go down dramatically.

Mr. EARLY. Thank you, Mr. Chairman.

Mr. NATCHER. Thank you very much. The committee will adjourn until tomorrow morning.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record:]

$9 MILLION INCREASE

Mr. MICHEL. You have about a $9 million increase in your budget. Is there any particular area where that increase will be concentrated, or will it be spread more or less evenly throughout your Institute?

Answer. Of the $9 million increase, approximately 50 percent will be used to support increases in grants and contracts for noncompeting continuations in the research program areas. Of the increase, 23 percent will be allocated for continuation and some expansion of the intramural research program; and the remaining increase of approximately $2.5 million is about equally divided among competing research grants, new centers, and new research contract initiatives.

TOXIC SUBSTANCES CONTROL ACT

Mr. MICHEL. Regarding your responsibilities under the Toxic Substances Control Act, if a compound is withheld from commerce due to insufficient data as to

its potential hazardous effect, about how long does it take for you to conduct your evaluation and issue your findings?

Answer. It depends on the use of the compound—the extent to which people will be exposed. If a compound can also contact pregnant women, then teratolgy evaluation is required and this would require additional time. If in chronic use, the possibility of cancer exists and this would take at least 3 years to evaluate. If neither contact with pregnant women nor a cancer risk is involved, then acute toxicity tests would take about a year to do properly, if no preliminary data is available. If cancer and teratology tests need to be done, then up to 5 years would be required. To be completely correct, the act places the responsibility for this testing on the manufacturer; at the direction of EPA.

Mr. MICHEL. Do you have the authority under the act to withhold the compounds from commerce?

Answer. The Environmental Protection Agency is the only agency under the act to have authority to withhold new compounds from commerce. We can provide data to the EPA as to why a compound should be withheld from commerce.

Mr. MICHEL. Are you working with any other agencies in implementing the Toxic Substances Control Act?

Answer. We are primarily working with other PHS programs such as NCI, NLM, NIOSH, and FDA through two groups—the DHEW Committee to Coordinate Toxicology and Related Programs and the Public Health Service Coordinating Group. The coordinating group will be responsible for establishing and assuring the appropriate interface with EPA for implementation of the act; setting up appropriate inter and intraagency working groups for development of interagency agreements; and to designate working groups appropriate for developing the necessary subagreements and for carrying out appropriate coordination of the implementation of TSCA within the Public Health Service. This is quite important since the act could place a tremendous burden on the Public Health Service if not properly coordinated at the highest levels. At the working level our scientists have always and will continue to work closely with their colleagues in a number of Federal Agencies.

SHORTAGE OF TOXICOLOGISTS

Mr. MICHEL. Your statement refers to the shortage of qualified individuals to conduct the testing, et cetera, in the environmental toxicology field. Do you have any estimate as to what the shortage is nationwide in terms of total numbers?

Answer. Although, the precise figures for personnel demands in environmental toxicology are somewhat elusive due to the many variables which affect this demand, the estimates which I have given to Mr. Flood concerning the need for trained toxicologists represents the "Second Task Force for Research Planning in Environmental Health Sciences" assessment of needs for trained research toxicologists. On the basis of this analysis, the Institute feels that supporting 400–500 pre-and postdoctoral students annually (which would graduate 300 or so individuals each year) would not be out of line with potential demands. The current state of the art is such that experiments are individually designed to answer a specific question. This is slow, methodical research. But the payoff is an increase in knowledge about toxic mechanisms which may be useful in prediction of the potential hazard from untested chemicals. Therefore, in the long run this type of work is cost-effective.

Mr. MICHEL. Is this shortage being widely publicized in our school systems so that students are aware of the openings?

Answer. The NIEHS, as part of the NIH, makes known the availability of grants in areas of scientific need, through a coordinated mailing list based on the distribution of the "NIH Guide for Grants and Contracts." We also have extensive personal contact with university faculty and staff at institutions which train researchers in the sciences relating to toxicology. It is through these individuals that we also publicize our priorities. However, the need for trained toxicologists is not something that we usually need to tell them about.

The student population interested in toxicology is, however, in a bind. Support for graduate training has been declining in spite of the bright job prospects. Many of these prospective students must, therefore, decide between the opportunity for support for graduate school or postdoctoral training or to somehow support themselves for training in toxicology with hope of broad job opportunities at the end of their training.

Mr. MICHEL. What type and duration of education is usually required in this field?

Answer. For a Ph. D. in environmental toxicology, I could say that a didactic core of biological, chemical/physical and interactive sciences needs to be supplemented with both research training and research experience. A program of this type can take 4 to 5 years. Postdoctoral training is more specialized and assumes a background amenable to advanced research experience. However, since the environmental health sciences are amalgams of basic disciplines, I can envision a training program for "retreading" of scientists in one of the disciplines to bring them to a point where they can independently contribute new knowledge in environmental toxicology in 2 years.

KEPONE

Mr. MICHEL. Your statement refers to a controlled study in progress that may lead to improved therapeutic treatment for Kepone. How long will this study take?

Answer. The study is currently in its second year, and should be completed 2 years from now.

ENVIRONMENTAL RESEARCH INSTITUTIONS

Mr. MICHEL. Are there any particular institutions where much of the environmental research is being undertaken, or are the grants pretty well scattered?

Answer. A fairly high percentage of NIEHS grant-supported research is concentrated in a relatively small number of institutions with an interest in and commitment to environmental health research. For example, in fiscal year 1976, 15 institutions received approximately 64 percent of the total funds awarded for research. On the other hand, these same institutions accounted for only 35 percent of the number of grants awarded. This reflects the dollar impact of our environmental health sciences centers located at 7 of the 15 institutions.

INTRAMURAL AND EXTRAMURAL RESEARCH

Mr. MICHEL. How does your research break down between intramural and extramural, both in terms of dollar amount and types of research?

Answer. The 1978 budget provides $33.1 million for grants, $7.6 million for research contracts, $14.8 million for intramural research, and $2.6 million for direct operations and program management.

Intramural programs focus on areas not well covered extramurally, such as, inhalation toxicology, mutagenesis, noise, microwaves; and on problems where team-type research efforts are especially valuable, such as the mutagenesis screening efforts. Intramural research has also concentrated on problems where the national effort is diffuse and where one strong program can serve as a national focus such as marine pharmacology. Very little duplication of research occurs unless it is needed to support other areas, for example, drug metabolizing enzymes and mutagenesis screening.

The extramural program generally supports research and training in all aspects of environmental health sciences aimed at identifying, characterizing and ultimately limiting hazards in the environment.

PERMANENT FACILITY

Mr. CONTE. What is the status of construction for your new permanent buildings? When do you propose to move in?

Answer. A construction manager has been retained. Approximately 80 percent of the total construction program is now out for bids with all bids due in by mid-April. Contracts have been awarded for site preparation and utilities construction, and work on the site has begun.

NIEHS plans to occupy the permanent facility sometime between April and October of 1980.

MUTAGENESIS SCREENING PROGRAM

Mr. CONTE. How much money are you budgeting for your three-tier mutagenesis program? How long will it take you to test all commercial compounds at the rate of 1,000 per year? Could that be speeded up at all with additional funding?

Answer. For 1978 we have budgeted $1 million for the mutagenesis program; 1978 will be the second year and we will have the first two tiers functioning and will test 300 chemicals in the first tier. The full three tiers will be totally opera-

tional in 1980. By then there will be 1,000 compounds in tier I testing at an estimated cost of $4 million.

Since testing of new chemicals will be the manufacturer's responsibility under the Toxic Substances Control Act, our program will focus on the 10,000 compounds in general use; at the rate of 1,000 per year it will take at least 10 years.

With the magnitude of this program, programs at NCI and FDA, and the passage of the Toxic Substances Control Act the available expertise to conduct mutagenicity testing is going to be severely taxed in the near future. Additional scientists will have to be trained for research in genetic toxicology.

Toxicology Manpower Shortage

Mr. Conte. What would you estimate as the current shortfall of research manpower in environmental toxicology and related fields?

Answer. The placement bureau of the society of toxicology (SOT) has reported that between 1972 and 1976 qualified candidates for positions in toxicology were in very short supply. For example, in 1976 less than 20 percent of the positions for toxicologists advertised at the SOT placement bureau were filled. Last year, one professional placement service listed 100 positions for inhalation toxicologists and got no response to this listing. The great majority of training of toxicologists is supported by NIEHS. In fiscal year 1976, 136 pre- and postdoctoral trainees were supported by this Institute. The 1977 appropriation permits the funding for 85 trainees. Therefore, there is an obvious shortfall. Our best estimate of current and future needs for trained individuals is the "Report of the Second Task Force for Research Planning in Environmental Health Sciences." This report recommends that predoctoral training in environmental health sciences be raised to 300 per year by 1979 and 400 per year by 1982. About half of these individuals should be trained in toxicology. For postdoctorals the report states that the 1979 and 1982 levels should be 350 and 425 respectively. Again, the recommendation is that 50-60 percent of these positions be in toxicology.

1978 Cutback in Training

Mr. Conte. Your opening remarks state that the NIEHS training program is the only focused Federal support mechanism for the development of such manpower; and yet you are proposing major cutbacks in training funds. Do you want to explain that discrepancy?

Answer. The 1978 request is based on the continuation of the 1977 level of $2.2 million for training awards to individual trainees and the phaseout of institutional awards. Our request does not reflect the impact of the $2 million supplemental appropriation for 1977 recently approved by the committee.

Microbial Spot Test

Mr. Conte. Can you tell me how the spot test using a DNA repair-deficient strain of certain microorganisms works?

Answer. There are actually two types of spot tests which use the DNA repair-deficient bacteria; one measures gene mutations as in the "Ames test," the other measures DNA repair. Generally, a small amount of the chemical being evaluated is placed in a small droplet in the center of a Petri plate in which the bacteria are growing. The chemical diffuses out in a ring from the spot. The growth conditions are such that only the mutated bacteria will grow and form colonies which are clearly visible to the investigator. Often there will be no colonies in the center of the spot, indicating the killing by high concentrations of the chemical, and a ring of colonies surrounding.

Energy

Mr. Conte. What are you doing to look at the health effects of accelerated development of alternative energy sources—things like coal gasification, for example?

Answer. The energy-related research supported by NIEHS focuses on a number of toxicology subdisciplines essential to the understanding and assessment of the potential health hazards of environmental factors associated with energy technologies. These include: Indicators of toxicity; biochemical mechanisms of toxicity; mechanisms of incorporation, metabolism, disposition, and turnover; dose response relationships; extrapolation of laboratory models to man; muta-

genesis, developmental toxicity and carcinogenesis. These subdisciplines are used to study the potential health hazards related to energy production and conservation. The energy-related hazardous agents studied by NIEHS fall into the following categories: Gaseous air pollutants; suspended particulates; industrial by-products and intermediates; trace metals; and physical factors. The energy-related gaseous air pollutants being studied by NIEHS-supported investigators include nitrogen dioxide, ozone, sulfur oxide, and carbon monoxide.

Studies on suspended particulates are concerned with the pulmonary effects of coal dust and the role of components of the dust in the etiology and pathogenesis of pneumoconiosis. Other studies are concerned with the relationship between soot and associated benzo(a)pyrene and other carcinogens which could be important in the use of low-grade fossil fuels such as bituminous coal. A number of potentially hazardous trace metals which could be released to the environment through the operation of various energy technologies include mercury, lead, cadmium, chromium, copper, manganese, arsenic, and some other rare earth elements. Various physical factors of concern to NIEHS in connection with energy technologies include heat, noise, and electromagnetic fields.

Heavy Metals

Mr. Conte. What are you doing to investigate the effect of heavy metals on intelligence deficiencies? Does this relate at all to the lead based paint program?

Answer. The intramural behavioral toxicology program will be looking at the spectrum of behavioral and neurotoxicity tests for their reliability and validity for detecting low-level chronic effects of known and suspected neurotoxins. Special attention will be paid to heavy metals and interactions of metals with hydrocarbons, especially in the developing animal where the behavioral and neurological patterns are being laid down and thus represent systems most likely to be susceptible to toxic effects. Also, intramural studies are being conducted on both the prenatal and postnatal effects of lead in rodents. These studies have been followed out to 6 months of age, which is considered to be an adult animal, and the effects on learning are being studied.

Grantees are investigating the effects on the central nervous system and behavior in the adult and newborn mammals of mercury, lead, and cadmium, including motor performance, emotional stability, and biochemical indication of intoxication. In addition, various therapies to ameliorate these effects are being studied.

Average Grant and Percent Funded

Mr. Conte. What is your average grant amount? About what percentage of your applications are funded?

Answer. The average research grant amount for 1977 is estimated to be $88,679. We estimate that we will be able to fund approximately 55 percent of our approved research grant applications in 1977 and 60 percent in 1978.

Intramural Research Program

Mr. Conte. To what level do you ultimately intend to increase your intramural research program?

Answer. In order to be able to cover the major disciplines needed in environmental health sciences, we have projected a need for some 850 to 900 permanent slots for the intramural research program. We would not reach this size until 1981 at the earliest.

Continuation Funding

Mr. Conte. What level of funding is needed to maintain continuation funding for projects to which you have a moral commitment?

Answer. A level of $46,664,000 is needed to maintain continuation funding for approved grants and contracts; and ongoing intramural and support activities.

Synergistic Effects

Mr. Conte. Has any work been done with environmental agents which are harmless in themselves but which may be carcinogenic when combined?

Answer. The answer to the question is yes and it relates to some fundamental considerations of toxicological research: synergism, potentiation, competition, and antagonism. Toxicological studies must always take into consideration the

possibility of interactions of compounds. The varied activities of compounds and their biological effects depend upon basic tenets of dose-response relationships, stimulation or inhibition of metabolic enzyme competition for binding sites, protein binding, storage and excretion, among others.

One of the goals of research into the health effects of environmental agents is the identification of agents which may be harmful. There are numerous examples of substances in the environment which per se are thought to be either harmless or to cause infrequent health effects, but when combined with other substances or under unusual conditions (heat, cold, age, stress, and so forth) or as the result of generating metabolic derivatives within the cell, may indeed become a health hazard. For example the combination of smoking and exposure to asbestos, or exposure to certain trace metal chemical combinations increases the incidence of cancer. Nitrosamine is also thought to be noncarcinogenic per se, but derivatives produced by cell interactions seem to be potent carcinogens.

The great preponderance of agents in the environment to which man is exposed have not been tested for toxicity and priority, limitations in the state of the art, facilities and manpower dictate that known and suspected harmful agents be first studied. These studies have brought to light a number of agents previously thought to be harmless which act synergistically to cause harmful effects.

Marine Biomedical Research Centers

Mr. Conte. Can you tell me more about the creation of your marine biomedical research centers program? Where will it be located? What sorts of facilities will it have? What will the requested $600,000 actually be used for?

Answer. Since 1975, the Congress has been asking NIEHS to develop a program in the area of marine biomedicine. Part of this directive was to develop a program of support for those marine and freshwater laboratories whose research has biomedical applications. In 1978 we propose to begin core support funding for three or more of these centers. Awards will be made on a competitive basis following review of applications from existing laboratories. I have previously mentioned a few examples of the types of laboratories that I am talking about but until the review process is completed, it is not known which ones will be supported.

The marine biomedical centers program will parallel the Environmental Health Sciences Centers program in many ways. The funds will be used to provide salary support for the center leadership, key research staff, and visiting scientists, to operate and maintain equipment and special facilities such as research vessels, holding or breeding facilities, experimental organisms. The funds will also be used for preliminary support of research projects which, if feasible should be able to compete for continuing support from regular grant programs. These centers will have a unique opportunity to advance knowledge in the environmental health sciences because so many pollutants eventually get into rivers, lakes and oceans. The pollutants then show up as contaminants in drinking water or enter the food chain. We have already faced hazards from the insecticide Kepone in the James River, the industrial chemical polychlorinated biphenyl (PCB) in the Great Lakes and Hudson River, the phthalate esters in the Mississippi River, and mercury in the Great Lakes.

Smoking and Environmental Pollutants

Mr. Conte. What evidence has been found to demonstrate the detrimental effect of combinations of smoking and environmental pollutants?

Answer. Based on research at our Environmental Health Science Center at Mount Sinai School of Medicine, directed by Dr. Selikoff, it was concluded in studying the incidence of bronchogenic carcinoma in asbestos workers, that cigarette-smoking workers had 100 times the risk of lung cancer when compared to their nonsmoking fellow workers. Less strong but similar statements have been made by other scientists regarding the increased lung cancer risk in smoking uranium miners.

Professional Judgment Budget

Mr. Obey. Would you please review your entire budget to give your careful estimate of each area in which you need more adequate funding?

Answer. In my professional judgment, I feel that NIEHS could effectively use an additional $11.5 million. This would provide $1 million for funding of addi-

tional new research grants; an increase of $400,000 for the marine centers program, $3.1 million for training, which includes $2 million for continuation costs associated with the supplemental included by the House Appropriations Subcommittee for training in 1977, bringing the number of individuals in training during fiscal year 1978 to a level of approximately 360; and $3 million for research and development contracts to provide additional funding for the mutagenesis screening and toxicity bioassay programs, new research contracts, and more adequate funding for the existing research contracts. Further we could use $4 million and 99 positions for the intramural research, direct operations, and program management activities to further develop new programs in epidemiology, behavioral toxicology, and pulmonary toxicology; for expansion of existing programs in biophysics, toxicology, mutagenesis, pharmacology, chemistry, and biometry; and for more adequate staffing for the review and approval of grants and program management areas. This would provide staffing as outlined in last year's hearings before this committee on the planned growth of the institute. I would like to submit the following table reflecting this optimum level for the record.

[The information follows:]

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, 1978 OPTIMUM LEVEL

[In thousands of dollars]

	1978 estimate		1978 optimum level		Difference	
	Number	Amount	Number	Amount	Number	Amount
GRANTS						
Regular:						
Non-competing	135	$13,018	135	$13,018	0	0
Competing	122	9,186	135	10,186	+13	+$1,000
Subtotal	257	22,204	270	23,204	+13	+1,000
Special:						
Environmental health sciences centers	8	8,331	8	8,331	0	0
Marine biomedical research centers	3	600	5	1,000	+2	+400
RCDA's	22	500	22	500	0	0
Subtotal	33	9,431	35	9,831	+2	+400
Training programs	48	1,485	110	4,600	+62	[1] +3,115
Total	338	33,120	415	37,635	+77	+4,515
	Positions	Amount	Positions	Amount	Positions	Amount
DIRECT OPERATIONS						
Intramural laboratory and clinical research	283	14,826	365	18,426	+82	+3,600
R. & D. contracts		7,585		10,585		+3,000
Other direct	13	1,505	20	1,655	+7	+150
Program management	35	1,064	45	1,314	+10	+250
Subtotal	331	24,980	430	31,980	+99	+7,000
Total	331	58,100	430	69,615	+99	+11,515

[1] Includes $2,000,000 for continuation costs of 1977 supplemental for training.

PERMANENT FACILITY

Mr. OBEY. I understand that you have prepared for the Senate your plan for equipping and staffing your new facility. I would appreciate your submitting this for the record.

Answer.

[The information follows:]

Report to

Subcommittee on

Departments of Labor and Health, Education, and Welfare

Appropriations

on

UTILIZATION OF AND REQUIREMENTS FOR THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES PERMANENT FACILITY IN RESEARCH TRIANGLE PARK, NORTH CAROLINA

February 1977

87-155 O - 77 - 22

Introduction

During 1980, the National Institute of Environmental Health Sciences will occupy its 177,000 net square feet permanent research facility in Research Triangle Park, North Carolina.[1] This occupancy is an important milestone in a sixteen year effort that began when the Congress recognized environmental factors as significant threats to man's health and well-being. At the outset, Congress, the scientific community, those in Government, and others with knowledge about man's delicate interaction with his environment, appreciated the magnitude of the problem and the paucity of scientific information and understanding available regarding this relationship. Little was known about the mechanisms by which man, the most complex of biological systems, reacted to his general environment and more particularly to the specific agents in that environment. Generally, we lacked specific knowledge on what was in the environment and could make only educated guesses as to what the health effects of these agents we knew were. We had no reliable way of anticipating the adverse health effects of agents in our future and could do little more than speculate about the health effects of low dose chronic exposures. The year 1976 has brought us new knowledge and understanding and finds in place a number of Governmental and private sector efforts directed toward developing the basic information essential to our comprehension of this delicate relationship. However, progress has not stilled itself for research to catch up. In addition to the thousands of untested chemicals currently in use, an additional 1000-1500 new chemicals are introduced each year into the environment. We know more now, but there is so much more to know. Research and technology have made significant strides in identifying the agents in our environment and understanding the biological and chemical basis of their interaction with man. We have accumulated significant research data and better understanding regarding man's interaction with environmental agents and health effects of some of these agents. Now more than anytime before, we are able to make use of these findings to predict the health effects of chemicals as they are developed or enter the market place.

We are pleased with the progress made in environmental health in light of the resources that have been available. However, we are reminded of the questions that remain unanswered and the research to be done by episodes such as the Kepone exposure in Virginia, polychlorinated biphenyls (PCB's) in mother's milk, polybrominated biphenyls (PBBs) exposures in Michigan and the most recent leptophos exposure in the Southwest. In addition, the passage of the Toxic Substances Control Act places significant burdens on the Federal research community to develop new information and test methodologies for assessing the health effects of a wide range of chemicals and other substances. We are confident that the research potential made available by this new facility, when coupled with our existing research program and facilities, will allow us to fully develop the program necessary for addressing the important problems and issues in environmental health.

[1] Appendix I. provides diagramatic layouts of the facilities.

We share the Committee's concerns for adequate planning and resource identification and we agree that these are essential to the full and effective utilization of the facility and the development of a high quality and responsive research program. We have, throughout the design phase, been engaged in a planning effort that has involved significant numbers of Institute personnel. The planning has included program leaders, bench scientists, administrative personnel, and research support service groups. The information provided in this report is the direct result of that planning effort. It is neither absolute, nor final; but represents the best thinking and information available at this point on a planning spectrum that began several years ago and will continue until the facility is occupied. The information is based on a number of assumptions such as future utility costs, orderly growth and support in terms of dollars and staffing, and completion and beneficial occupancy of the new facility by FY 1980.

I. Personnel

A. Laboratories

The National Institute of Environmental Health Sciences, as the principle federal agency for biomedical research on the effects of chemical, physical and biological environmental agents on man's health and well being, is concerned with man as a total system and with all diseases suspected or known to have their etiology in exposure to these agents. The research approach must necessarily be broad, to parallel the scope of the problem, yet must be of sufficient depth and intensity to provide meaningful information. This information will aid in the diagnosis and prevention of environmentally-related diseases and will provide the basis upon which the Environmental Protection Agency and other regulatory agencies can prevent environmental exposures through controls and regulations.

In our planning, we have recognized the need for a multidisciplinary approach. We have identified, in general terms, those core research groups representing the various disciplines essential to the research effort. Because they must interact and support each other, we have further identified those programs which must be proximate to one another. In our planning, we recognize the need to establish a critical research mass within each of the disciplines in terms of numbers of staff and sub-specialties represented. We have attempted to define the minimum "critical mass" staffing level within each of the disciplines. Along with the concept of "critical mass," we believe that orderly program development is essential to a high quality research program. Excellence breeds excellence. First, we must hire program leaders who have demonstrated their scientific and leadership abilities and then adequately support them so they can recruit and retain other high calibre scientists. The support, if available at the outset, assures a more orderly process and effective research effort. It is also critical to the recruitment effort and our ability to retain senior staff for sufficient periods

to allow for the full development of their research potential. Throughout our planning, we have assumed continued support for the growth and development of the NIEHS programs. We have used for planning purposes, a staffing level of 1,000 permanent full-time employees by September 30, 1983. In addition, our plans call for between 180 and 200 temporary staff composed of visiting scientists, guest workers and temporary employees. The same estimates were provided to the House Subcommittee on the Departments of Labor and Health, Education, and Welfare of the House of Representative's Committee on Appropriations during last year's hearings.

Within the Intramural Research Program we have identified twenty-eight (28) distinct work groups including research support programs such as Arts and Graphics, Laboratory Animal Support, Glassware and Media, etc. Of that number, nineteen (19) are distinctly research oriented.[2] They are:

- Reproduction and Development
- Chronic Organ Toxicity
- Behavioral and Neurological Toxicity
- Genetic Risk Assessment
- Genetic Monitoring
- Genetic Testing
- Biomathematics & Risk Extrapolation
- Epidemiology
- Physical Factors - Noise, Microwaves and other Radiation
- Biophysical Mechanisms
- Marine Biomedicine
- Toxication-Detoxication
- Pharmacokinetics
- Pulmonary
- Inhalation Toxicology
- Chemistry
- Comparative Biology
- Comparative Pathology
- Bioengineering

Of those programs identified, the following are scheduled to occupy laboratories in the new facility:

- Behavioral & Neurological Toxicity
- Comparative Pathology
- Chemistry
- Chronic Organ Toxicity
- Reproduction and Development
- Physical Factors -- Noise, Microwaves and other Radiation
- Genetic Risk Assessment
- Genetic Monitoring
- Genetic Testing
- Pharmacokinetics
- Comparative Biology

2 A brief description of each program is included in Appendix II.

The following chart presents staffing projections and space utilization within the new facility for these functions:

	(Full-time permanent staff)					f.[3]	Sq.Ft. Required
	77	78	79	80	84		
Behavioral & Neurotoxicity	9	9	16	22	26	1/300	7800
Comparative Pathology (2/3 of group)	10	10	15	22	18	1/206	3700
Chemistry	13	13	16	22	30	1/300	9000
Chronic Organ Toxicity (1/2 of group)	9	9	15	21	23	1/239	5500
Reproduction & Development	19	19	25	35	45	1/250	11250
Physical Factors	7	7	11	12	17	1/235	4000
Genetic Risk Assessment	18	18	22	32	40	1/211	8450
Genetic Monitoring	7	7	9	14	40	1/211	8450
Genetic Testing	11	11	16	23	46	1/211	9700
Pharmacokinetics (3/4 of group)	7	7	9	12	19	1/237	4500
Comparative Biology	7	7	13	15	15	1/280	4200
TOTAL	117	117	167	230	319	f1/240	76550
AVAILABLE LABORATORY SPACE							77000

3 Ratio of full-time permanent staff to net square feet of space. The figure includes all laboratory equipment, furniture and fixed equipment such as constant temperature rooms and electron microscopy suites. The figure varies from program to program on the basis of requirements necessary to support the specific research.

The following chart represents proximity requirements necessary for scientific interaction and research program support.

SPACE LOCATION

Chart 3

Floors	Module C.	Module D.	Module E.
4	Reproduction and Development	Chemistry[4]	Chemistry Chronic Organ Toxicology Pharmacokinetics
3	Reproduction and Development Genetic Risk Assessment Genetics	Gene Expression	Microbial and Mammalian Genetics
2	Comparative Pathology[4] Pharmacokinetics	Genetics Behavioral Toxicology Electron Microscopy[4]	Somatic Cell Genetics Genetics
1	Comparative Biology Behavioral Toxicology	Glassware[4] Media[4]	Genetics Physical Factors[4]
Basement	Animal Facilities[4]	Animal Facilities[4]	Animal Facilities[4]

Note: Modules A & B are devoted, by design, to office space, conference facilities, cafeteria and computer center.

[4] Represents location requirements fixed in the facility design to house and physically support specialized equipment.

B. Specialized Facilities

Within the program facility, there are a number of specialized support areas. The largest of these is the animal holding and care facility in the basement of Modules C, D, and E. The area is segregated into high access, limited access and quarantine areas to accommodate the wide range of animal care requirements. It will be staffed by approximately 60-70 permanent full time staff and will be utilized by all those research groups having animal requirements. In addition to the various types of animal facilities, the area includes operating suites, necropsy rooms, autoclaves, cage washing facilities, etc. In total, the animal facility occupies 34,694 net square feet of space. Full utilization is anticipated by 1983.

Another large area is occupied by the Glassware and Media Preparation function. They collect centrally, process, and reissue the large volume and variety of glassware items utilized by the research laboratories. They also prepare standard and specialized culture media for microbiological purposes and in vitro studies. This area encompasses 9,670 net square feet of space and will house 25-30 permanent full-time staff. Full utilization is also expected by 1983.

The other specialized areas include the conference facility, airline ticket office, self-service supply store, chemical supply center, employee health unit, cafeteria, arts and graphics center, photography, animal feed and bedding supply center and the mail and messenger center. These areas occupy approximately 20,045 square feet of space and will house approximately 15-20 permanent full-time staff and 15-20 contract or other non-Federal employees. These facilities will be fully utilized at occupancy.

C. Offices

Within the A and B modules of the research facility there are 29,554 net square feet of office space.

The office space is to be utilized in the open office landscape mode with task lighting. Such an arrangement allows for: maximum utilization of the space; maximum flexibility for moving people which is important to a fluid program such as ours; and maximum energy efficiency. The "open plan" is currently under design so it is impossible to provide exact figures on the numbers of staff to be housed in the area or the composition of that staff. The computing, biomathematics and epidemiology programs, consisting of about 80 full time staff, will be housed on the 3rd floors of the A and B modules. This is due to the fixed design location of the computer facility and the need for these programs to be adjacent to it and interact amongst themselves and directly with the

laboratory research program. In addition to these groups, we anticipate approximately 50 full time staff associated with or who have a requirement to interact with the Director to be housed in this area. The balance of the administrative functions such as procurement, budget, personnel, supply management, travel and conference services, and general administrative management will be housed in any remaining space. We are now estimating a full time staffing of from 50-70 for these functions. Any of these functions which cannot be housed in the new facility will be housed in our existing facility on the basis of their need to interact with themselves, other administrative functions and the research program.

D. Support Facility

The support facility complex consists of a power plant, an incinerator plant, a telephone exchange, an electrical substation, a warehouse and a shops and engineering support facility. It is difficult to project utilization within that space with any degree of accuracy due to the nature of the functions housed there and the plan for many of these functions to be carried out under contract with private firms. Examples of the latter would be the grounds maintenance, security, and janitorial services. We are now estimating that between 60 and 80 contract staff will work out of these facilities. In addition, we estimate that 85-100 Government employees will also utilize these facilities. The support facilities were designed by the architects in response to the programs to be carried out and the magnitude of the program, facilities and grounds to be supported from these facilities.

II. Other Requirements

A. One Time Start Up Costs

1. Equipment

A wide variety of equipment will have to be acquired to conduct the research and adequately support the facilities and grounds. Some of these items will have to be acquired in FY 1979 and the remainder in FY 1980 depending upon procurement lead time and when the items are actually required. The following chart depicts the current estimates for equipment.

Equipment	79	80
Scientific Equipment	7,000,000	7,000,000
Computers and Computer Support Equipment	300,000	---
Animal Support Equipment Cages, Cage Racks, Feeders, Cart System	1,750,000	---
Warehouse Rack Systems, Storage Bins, Fork Lifts, Cart System	300,000	---
Shops Grounds Maintenance, Trades and Crafts, Vehicles	300,000	---
Waste Disposal Dumpsters, Trucks, Compactors	200,000	---
Glassware Cart System	25,000	---
Spare Parts Equipment, Mechanical Systems	100,000	200,000
Total Equipment	9,975,000	7,200,000

2. Furniture

A wide variety of furniture will have to be purchased including the work stations for use in the open office landscape plan.

Furniture	79	80
	$750,000	$100,000

3. Glassware Stock

In the research facility, provisions have been made for a glassware processing facility. To be operational, we must acquire an adequate stock of glassware to provide for simultaneous use and processing.

Glassware	79	80
	$200,000	----

4. Warehouse Stock

To meet the needs of a larger and more diverse staff, it will be necessary to increase the existing stock levels.

Warehouse stock	79	80
	$100,000	---

5. Moving Expenses

Costs will be incurred to pack transfer and unpack laboratories and offices moving from the existing facility into the new facility.

Moving Expenses	79	80
	$6,000*	$40,000

B. Continuing Costs

(In Thousands)

	79	80	81	82	83
1. Janitorial Services	$12	$225	$260	$280	$300
2. Security Services	43	180	210	240	260
3. Grounds Maintenance	125	150	175	200	230
4. Trades & Craft Shops	200	300	1,000	1,200	1,400
5. Mechanical Plant	200	350	400	440	470
6. Incineration and Waste Removal	40	50	60	70	80
7. Warehouse	85	100	130	150	170
8. Utilities	520	1,900	2,200	2,500	2,800
Total Continuing Costs	1,225	3,255	4,435	5,080	5,710

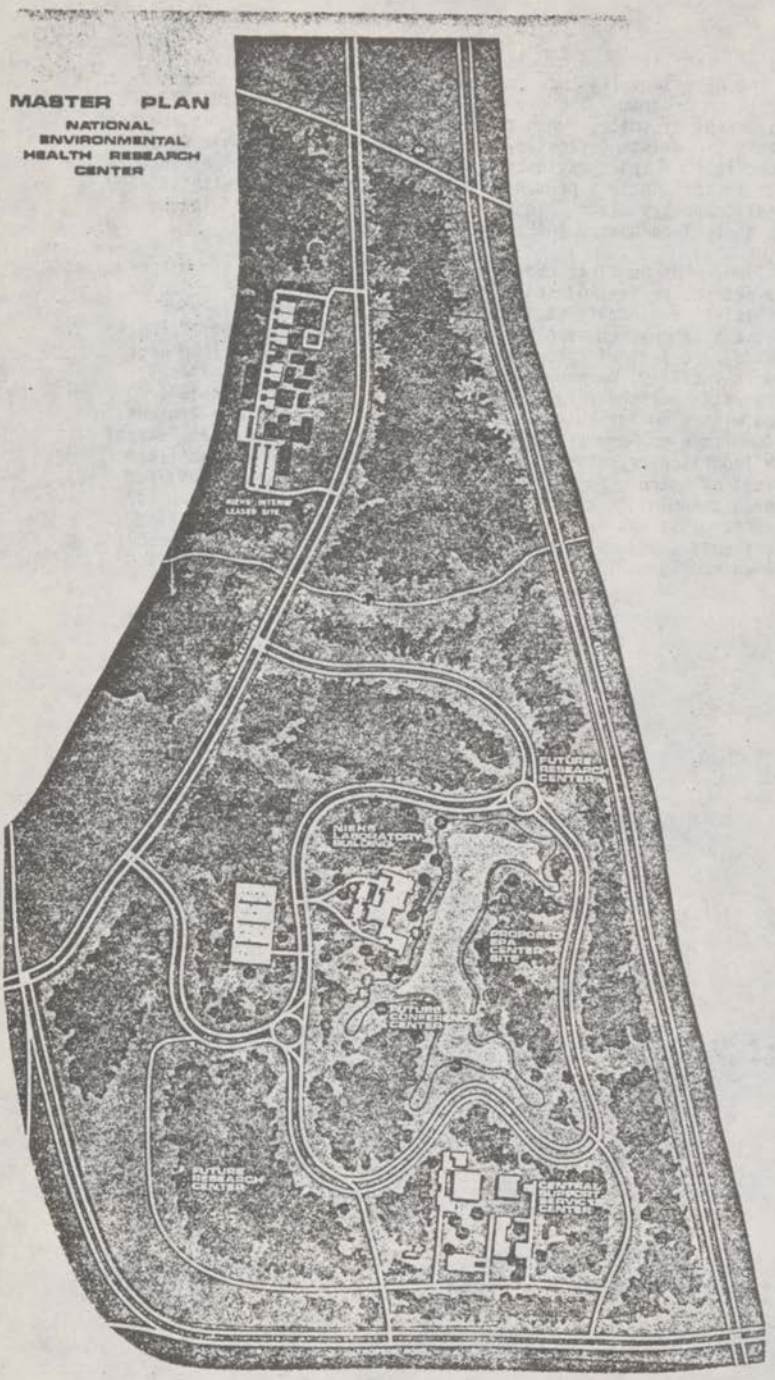
* Assumes opening of support facility prior to completion of program facility.

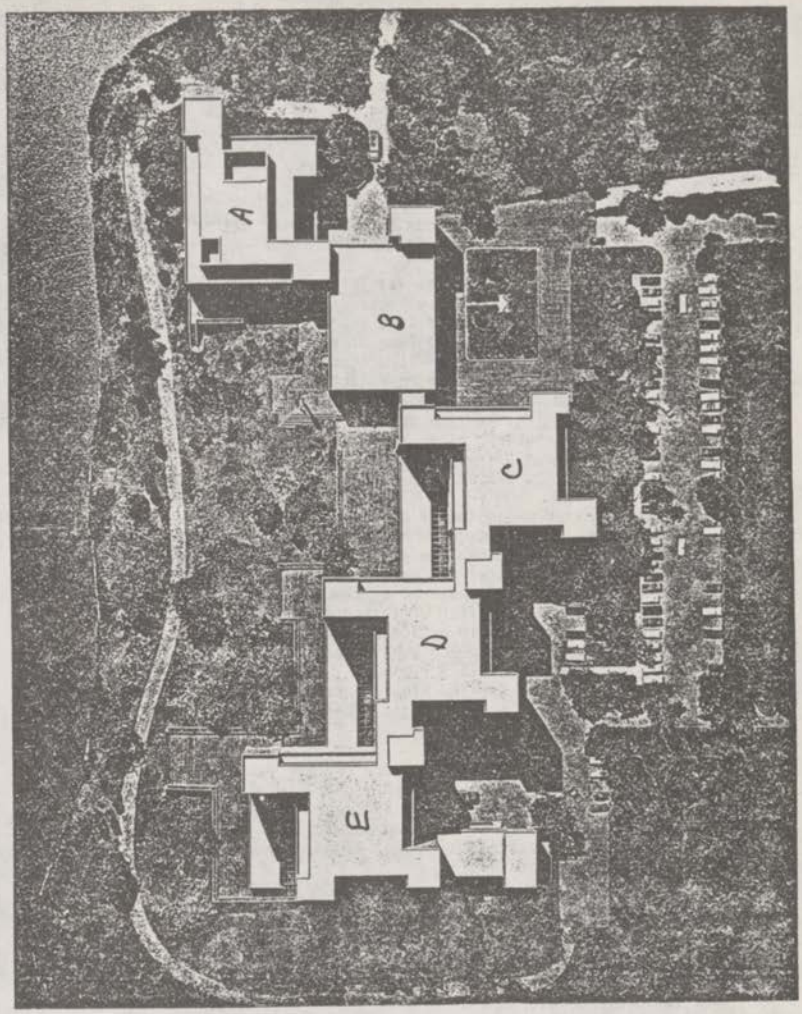
Summary

The new facility when coupled with our existing facility will provide the necessary latitude for orderly growth and development of the NIEHS research program. The new program facility will provide 177,000 net square feet of space. When coupled with the 115,100 net square feet of space in the existing facility, NIEHS will occupy just over 292,000 net square feet of space exclusive of the support facility. At occupancy in 1980, we anticipate a permanent full time staff of 700 with 180-200 additional temporary staff. This represents 70% of the anticipated staffing at full occupancy in FY 1983.

In 1980, when we first occupy the new facility, the ratio of permanent staff to net square feet of space will be 1/487 square feet including all facilities, equipment, etc., but excluding the support service facility, e.g. shops, power plant, warehouse. This figure will drop to 1/324 net square feet of space when fully staffed with 900 (1000 less 100 support facility) permanent full time positions in 1983. These occupancy rates compare very favorably with those reported in 1974 to the Subcommittee on Agriculture -- Environmental and Consumer Protection of the Committee on Appropriations.[5] For all occupied space at Federal research laboratories surveyed, the occupancy rate reported was 1/668 square feet of space. For HEW, the figure was 1/470 square feet; for the Veteran's Administration the figure was 1/509; for the Center for Disease Control it was 1/446 and for NIH (Bethesda) 1/270. The NIH figure reflects the density of their laboratory program and the problems they are currently having with space.

[5] Part 7 of Investigative Report on "Utilization of Federal Laboratories" published April 8, 1974.


MASTER PLAN
NATIONAL
ENVIRONMENTAL
HEALTH RESEARCH
CENTER
NIEHS LABORATORY BUILDING
FUTURE RESEARCH CENTER
FUTURE CLINICAL CENTER
FUTURE RESEARCH CENTER


A
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E

Appendix II.

National Institute of Environmental Health Sciences

Descriptions of Intramural Programs

1. Toxicology Branch

a) Reproduction & Development - Needs are for better methods and examination of later-appearing effects.

1) Presently: Two general areas--a) Teratology & reproduction - evaluation of teratological effects of selected chemicals by standardized protocols as well as evaluation of some newer test systems, especially in vitro (use of embryo culture); teratology information center-data from literature on chemicals tested; study of chemical effects on reproductive processes, e.g., effects of chemicals on fertility. b) Developmental physiology, biochemistry, pathology--enzyme pathways in selected tissues and patterns of development after birth, effects of environmental chemicals on these pathways; effects of chemicals on postnatal development, e.g., DES on male and female genital tract.

2) Proposed: Major expansion of programs in teratology and reproduction--both to develop better tests for environmental chemicals as well as look at mechanisms of effects; develop in vitro tests if possible. Developmental toxicology will look at biochemical and physiological functions altered by chemical exposures early in life, but manifest after birth and especially in early adulthood. Organ functions investigated would also relate to programs in Target Organ Toxicity and Behavioral Toxicology.

b) Target Organ Toxicity - A major kind of damage caused by environmental factors. Needs are for more sensitive function tests and for studies on chronic exposure effects.

1) Presently: Major emphasis on excretory and detoxifying systems--kidney, liver damage. Also effects on blood elements. Collaboration here with reproduction and development when there is a study of effects of environmental chemicals in placenta, developing organs. Some look at mechanism of organ damage and better tests for early organ damage.

2) Proposed: Careful study of presently-used organ function tests--attempts to develop more sensitive tests and tests able to assess more functions of an organ. Careful look at design of acute vs. chronic toxicity testing; what kind of function tests are different in acute vs. chronic testing? Studies of mechanism of toxic effect will stress development of broad principles so that toxicity of similar chemicals might be predicted. Study of other organ damages

too--organs not now usually studied for damage, e.g., intestine, pancreas, adrenals and sense organs like touch, smell and taste.

c) Behavioral Toxicology - Major needs: test validation, development of quantitative measures of behavior and its change by toxins. Also studies into the mechanism whereby environmental factors produce their behavioral and neurotoxic effects and the conditions which predispose individuals to these effects.

1) Presently: Initiating program with major emphasis on test validation for behavioral effects.

2) Proposed: Develop more sensitive tests for assessment of behavioral and neurological deficit in both animals and humans. Studies of mechanism of toxic effect with view toward development of principles so toxicity of similar chemicals might be predicted and/or methods of treatment might be developed. Study of conditions which predispose individuals to behavioral and neurotoxic effect (e.g., genetic background, sex, age, nutritional states and interactions with other chemicals) in order to identify the types of individuals at greatest risk from exposure to a given toxin.

2. Pharmacology Branch

a) Pharmacokinetics - Major needs: study time course of pollutant uptake, distribution, storage, and release from body tissues. This study is needed for all pollutants carrying risk to man, but especially for those which accumulate or persist in tissues. Such studies will allow rate limiting steps to be identified (e.g., liver metabolism of PCBs) and point to general principles and possible extrapolations from animals to man.

1) Presently: Core group focusing on PCB kinetics, and attempting to extrapolate from one animal species to another and to man.

2) Proposed: More data in many different species and with several other chemical types--will then be able to formulate models for predictions, e.g., given exposure, to be able to predict where chemicals will accumulate, for how long and what might be done to change clearance from body. Study of how chemical mixtures differ kinetically from single components.

b) Marine Biomedicine - Major needs: define models for predicting toxic substances in aquatic environments, e.g., can fish tumors be used to detect low concentrations of carcinogens in water? Can general principles be derived from study of pollutant accumulation in aquatic species, e.g., are there certain tissues where most pollutants accumulate; do some fish accumulate certain classes of pollutants only, or is this a function of diet, water temperature, etc.

1) Presently: Studies of accumulation of PCBs in marine species. Soon to begin: study of fish and seafood accumulation of aliphatic and aromatic hydrocarbons found in crude petroleum. Role of detoxifying systems in storage and removal of pollutants from storage sites in various aquatic species (with differing detoxication abilities).

2) Proposed: Study how mixtures of pollutants may change (increase) accumulation of toxic chemicals in fish (as compared with single pollutants). Begin studies on induction of tumors in fish by exposures to known pollutants (PCBs, benzopyrene, etc.). Correlate this with surveys of pollutant concentrations in harbors and incidence of fish tumors in these harbors. Possible use of certain marine species for models of mammalian toxicity induced by pollutants, e.g., neurotoxicity by chlorinated hydrocarbons in fish.

c) Pulmonary - Major needs: better tests for non-respiratory functions of lung and studies of effects of pollutants on these functions, e.g., metabolism of carcinogens, hormones; regulation of circulating concentrations of vasoactive compounds like prostaglandins. Better tests for low-level chronic effects of pollutants on both respiratory and non-respiratory functions.

1) Presently: Studies of pulmonary regulation of prostaglandins and use of certain enzymes in pulmonary lavage to detect lung damage by chemicals. Use of the isolated-perfused lung to study chemical effects on lung without confusion of biologic feedback and interaction with other systems and organs. Study of metabolism of carcinogens by lung as compared with other organs.

2) Proposed: Investigate other non-respiratory functions as possible indicators of chemical damage and early damage in reversible stages. More complete studies of carcinogen metabolism by lung in various species and man--seeking to understand the peculiar susceptibility of lung to certain chemical toxins and carcinogens. Especially needed: more pathologists and a leader of this very small group.

d) Toxication-Detoxication - Major needs: define balance between toxication-detoxication systems in various organs; how do these systems differ from one species to another and how this balance can be affected by pollutants, genetics, drugs, etc.

1) Presently: Characterization of a few key toxication and detoxication systems in a few tissues. Study effects of a few pollutants on these systems.

2) Proposed: More complete characterization of these systems in key tissues like lung, intestine, skin and excretory organs--especially kidney, liver--and at important barriers, e.g., blood

brain barrier, placenta. Need more and careful studies on these systems as regulated by heredity, and in primates and man. Almost all work is done in rodents. Especially need crash program in this area to make the rapid-screening methods work for testing for carcinogens and mutagens. Metabolic activation of chemicals in a manner similar to in vivo requires a thorough knowledge of how these systems work in vitro. Otherwise a whole series of misleading results will lead to premature rejection of a most promising development.

e) Molecular Pharmacology - Major needs: almost no chronic toxic injury is understood well enough to begin to 1) think about ways to treat it, 2) predict what other compounds will produce a similar effect, and 3) develop rational tests. Molecular studies seek to understand why and how a given chemical causes injury and thus is the most likely type of research to pay off big--by developing general principles making it possible to predict effect without having to test every chemical. Treatment, though not effective with most chronic diseases, can only be random and by luck until we understand the causes of injury.

1) Presently: A study of how a few chemicals which damage the lungs affect membranes, especially the ability of membranes to interact with hormones.

2) Proposed: A much broader look at basic mechanisms of chemical injury of barriers, e.g., membrane functions of several types in several tissues. Changes in membrane functions may signal early damage by chemicals. Extrapolation of results in animals to humans and primates, e.g., chemically damaged lung membranes in animals compared with human lung membranes from patients accidentally exposed to inhaled toxins, or from monkeys inhaling toxic vapors.

3. Mutagenesis Branch

a) Human Genetics (Genetic Monitoring) - Major needs: develop new test systems to monitor human population for changes in gene damage frequencies. More and better studies on human populations exposed to known or suspected mutagens (in collaboration with epidemiology group and population genetics group).

1) Presently: No program at present.

2) Proposed: Staff program with a core group to work primarily with epidemiology until the research program can begin to look at frequency of certain gene-linked functions, e.g., types of hemoglobin.

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b) Mammalian Genetics (Risk Evaluation) - Major needs: better methods to quantify mutagenic effects in various animal species and to distinguish mutagenic mechanism peculiar to mammals.

1) Presently: A few marker enzymes and functions are being looked at in a small number of mice strains.

2) Proposed: A much broader look at gene-linked functions in a wider variety of animals. Some concerns with mixtures rather than single chemicals and with combinations of radiation and chemicals and with chronic rather than just acute exposures.

c) Biochemical and Somatic Cell Genetics (Risk Evaluation-Testing) - Major needs: biochemical markers of genetic damage in germ and somatic cells. Biochemical systems especially sensitive to mutagens need to be identified and their role in the mutagenic event defined. In vitro systems need to be developed using mammalian cells capable of being exposed to mutagens and then tested for effects.

1) Presently: This is closely tied-in with program in mammalian genetics and is a key group in development of in vitro tests for mutagens.

2) Proposed: Major expansion into broader and more active in vitro screening program to uncover new genetic markers and develop better in vitro test systems for mutagenic damage.

d) Molecular Genetics (Testing) - The major needs here are to define weak links in gene regulated events, methods of repairing gene damage and factors altering this repair, mechanisms of gene damage and dose-response relationships of these effects.

1) Presently: No program.

2) Proposed: Initiate a research effort to define the problems outlined above. This effort is vital to understanding how to test for effects and design better systems for detecting effects.

e) Population Genetics (Monitoring) - Major needs: defining how different populations vary in frequency of genetic defects as well as susceptibility to genetic damage from chemicals, radiation, etc. Needs to be done in animals and man and comparisons between animals and man made.

1) Presently: Studies only in drosophila.

2) Proposed: Expand program to allow collaboration with the epidemiology group as well as study large populations of various animal species and more effectors and markers in single species.

f) Microbial Genetics (Testing) - Major needs: Define differences between genetic damage in microbial vs. mammalian systems. Develop microbial marker strains which accurately reflect genetic damage induced by chemicals in animals.

1) Presently: Some alterations of basic Ames mutagenesis testing system, and use of these to develop better in vitro testing systems.

2) Proposed: To expand testing to several hundred to a thousand chemicals a year by Ames or modified Ames tests; to look in depth at reasons for false positive and negative results of Ames tests, and to develop better in vitro assays.

4. Biometry Branch

a) Epidemiology - Major needs: Prospective studies of pollutant effects on health. Better methods for analyzing multifactorial systems. Better reporting systems and interdisciplinary studies on better-defined populations.

1) Presently: Limited effort restricted by staffing resources - PCB's and lead effects in children.

2) Proposed: A small core to look at a very few well-defined exposures to improve systems and develop models for dealing with more complex situations. From this small core the program would be expanded to include less defined multiple exposures in varying populations.

b) Biomathematics - Largely a collaborative effort--support programs in Branches needing significant mathematical backup, e.g., pharmacokinetics, behavioral toxicology, population genetics, aerotoxicology.

c) Computer Applications and Statistical Design - Help in designing experiments and analyzing data for all Branches--needed by almost all projects in Institute. Needs to grow in parallel with all research functions in Institute. Also will be used by service functions for information storage, retrieval, etc., e.g., by purchasing, warehouse, library, etc.

d) Risk Assessment - Major needs: develop theories and methods of testing these with respect to extrapolation from high to low doses for effects. Testing for thresholds and understanding how these may or may not be real.

1) Presently: Largely a study of high to low dose extrapolation with focus on carcinogenesis.

2) Proposed: Collaboration with mutagenesis programs, dose-response studies in pharmacology and toxicology; development of models and theories of differing kinds of dose-response relationships; especially important to new programs in epidemiology, population genetics, etc.

5. Biophysics

a) Noise - Major needs: determine most injurious types of noise, interactions of chemicals and noise, non-auditory effects of noise.

1) Presently: Effects of laboratory-defined noise on biochemical and physiological functions of cochlea and of hair cells. Interactions of noise and ototoxic drugs, mercury, on cochlear biochemical and physiological functions.

2) Proposed: Study different kinds of noise for effects--intermittent versus sustained, differing intensities, acute vs. chronic (repeated) exposures. Study non-auditory effects of noise; compare species.

b) Microwaves - Major needs: define physiological effects as distinct from heating. Define frequency-intensity parameters. Study effect of microwaves combined with other types of radiation or chemicals. Define dosimeter for reproducible exposures.

1) Presently: Small program concerned primarily with dosimetry.

2) Proposed: Concentrate on quantifying effects on neurological functions. Collaborate with behavioral toxicology group. Also more sophisticated studies on hematopoietic system and possible species differences here. Study combinations of microwaves and neurotoxic drugs and chemicals, e.g., pesticides, mercury.

c) UV, Ionizing Radiation - Major needs: define physiological effects especially when combined with other chemicals and pollutants, e.g., UV light plus pollutants causing effects on skin.

1) Presently: No program.

2) Proposed: Careful look at areas not being studied by other research groups or agencies--mixtures of pollutants plus UV or ionizing radiation.

d) Molecular Biophysics - Major needs: define toxic injury in terms of biophysical mechanisms, or use sophisticated biophysical techniques to study toxic injury. Biophysical approaches to toxicology are few in number and yet where applied have been most instructive, e.g., studies of toxication-detoxication system.

1) Presently: No program.

2) Proposed: Develop distinct and collaborative programs with molecular pharmacology and genetics groups to define and research those problems outlined above.

6. Research Resources

a) Inhalation toxicology - Major needs: determine the adverse effects of inhaled gases and particulate matter. A major portal of entry for many environmental chemicals is by inhalation. The deleterious effects produced by such chemicals may be directly on that with which they first come in contact, or the lung may act as a portal of entry for materials that are subsequently distributed to other areas of the body.

1) Presently: maintains a primary focus on effects directly produced on the lung, such as emphysema, asthmatic attacks, granuloma, as well as increased susceptibility to pulmonary infection.

2) Proposed: needs to expand to provide capability for other research programs in the Institute to study the adverse effects of chemicals which we normally inhale. In addition, there is a critical need for further development of specific methodologies that will assess the effects of chemicals on the lung. Work must be initiated that will determine the proper experimental design for assessing the chronic effects of environmental pollutants by inhalation.

b) Chemistry - Major needs: develop a concept which will allow one to predict those chemicals most likely to have adverse biological activity based on chemical composition and configuration; support the other intramural research by maintaining sophisticated analytical equipment that correctly identifies specific toxicants or their metabolites; synthesize chemicals of interest to intramural research efforts.

1) Presently: present effort is primarily to maintain competency in the area of analytical capabilities in gas chromatography, mass, infrared, and nuclear magnetic resonance (NMR) spectrometry. (Current expertise in Chemistry is principally restricted to halogenated organics.)

2) Proposed: develop greater depth in instrumentation as well as to expand efforts in other areas such as immunochemistry, physical chemistry, as well as heavy metal capabilities. Personnel needed to specifically research means by which chemicals are altered, either in the environmental or in the animal system, i.e., dechlorinated hydrolysis, etc.

c) Comparative Biology - Major needs: development of more sophisticated parameters as well as enlarging the scope of pathology capabilities in which to assess and characterize the spectrum of organ and tissue changes produced in experimental animals.

1) Presently: primary focus is at the stage of characterizing morphologic changes both at the cellular and subcellular level.

2) Proposed: increase the scope and size of the group. Increase size to support the toxicology evaluation of environmental chemicals, and develop capabilities in the area of electron microscopy and clinical pathology. Refine currently used procedures to assess toxicity by developing methods more sensitive and indicative of specific types of tissue and injury.

d) Bio-Engineering: Major needs - develop specialty instrumentation to assist scientists in the gathering and evaluation of their experimental data.

1) Presently: much of our search with animals requires the development of sophisticated instruments or apparatus. Since the need is dictated upon the experimental design of a specific study or series of studies, such instruments must be specifically designed. The pulmonary group, inhalation toxicology group, as well as the physical factors group are particularly dependent upon the development of this type of instrumentation.

2) Proposed: as these programs develop, there will be a need for people with the necessary technical, electronic, and mechanical background that can translate a biological problem to an instrument design that will monitor experiments leading to a solution of the problem.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Amounts Available for Obligation[1/]

	1977	1978
Appropriation.....	$49,141,000	$58,100,000

[1/] Excludes the following amounts for reimbursable activities carried out by this account: 1977- $129,000; 1978- $129,000

National Institute of Environmental Health Sciences

Budget Mechanisms

	1977 Appropriation			1978 Estimate		
	Number	FTE[1]	Amount	Number	FTE[1]	Amount
Grants						
Regular						
Noncompeting	95	---	$9,980,000	135	---	$13,018,000
Competing	40	---	2,605,000	53	---	3,606,000
New	68	---	5,315,000	69	---	5,480,000
Supplemental	(8)	---	102,000	(15)	---	100,000
Subtotal	203	---	18,002,000	257	---	22,204,000
Special						
Environmental health sciences centers	7	---	7,210,000	8	---	8,331,000
Marine biomedical research centers	---	---	---	3	---	600,000
Research career program	19	---	423,000	22	---	500,000
Subtotal	26	---	7,633,000	33	---	9,431,000
Total Grants	229	---	25,635,000	290	---	31,635,000
Training Program						
Individual awards						
Noncompeting	13	13	198,000	29	29	407,000
Competing	36	36	501,000	12	12	168,000
Subtotal	49	49	699,000	41	41	575,000
Institutionals awards						
Noncompeting	11	117	1,544,000	7	74	910,000
Competing	---	---	---	---	---	---
Subtotal	11	117	1,544,000	7	74	910,000
Total Training	60	166	2,243,000	48	115	1,485,000
Research and Development Contracts			6,200,000			7,585,000
Intramural Research			12,745,000			14,826,000
Direct Operations			1,287,000			1,505,000
Program Management			1,031,000			1,064,000
Total			49,141,000			58,100,000

[1] Full time equivalent.

DHEW - National Institutes of Health

CROSSWALK - 1977 COLUMN 1978 JUSTIFICATION

INSTITUTE: National Institute of Environmental Health Sciences
(Dollars in thousands)

Program	Mechanism										
	Research Grants										
	Regular Program		Specials		Training Programs		Research and Development Contracts	Intramural Research	Direct Operations	Program Management	TOTAL
	Non-Competing	Competing	Multi-disciplinary Centers	Other	Individual	Institutionals					
1. Environmental health sciences centers.....	---	---	$7,210	---	---	---	---	---	---	---	$7,210
2. Marine biomedical research centers.....	---	---	---	---	---	---	---	---	---	---	---
3. Environmental mutagenesis and reproductive toxicology...	$753	$1,200	---	$40	$58	---	$2,488	---	---	---	4,539
4. Etiology of environmental diseases and disorders.....	4,384	2,458	---	105	223	$325	1,136	---	---	---	8,631
5. Environmental pharmacology and toxicology.....	4,237	3,515	---	233	361	1,146	2,298	---	---	---	11,790
6. Environmental pathogenesis.....	606	849	---	45	57	73	278	---	---	---	1,908
7. Intramural research operations.....	---	---	---	---	---	---	---	$12,745	---	---	12,745
8. Direct operations.....	---	---	---	---	---	---	---	---	$1,287	---	1,287
9. Program management.....	---	---	---	---	---	---	---	---	---	$1,031	1,031
Total obligations....	9,980	8,022	7,210	423	699	1,544	6,200	12,745	1,287	1,031	49,141

DHEW - National Institutes of Health

CROSSWALK - 1978 COLUMN 1978 JUSTIFICATION

INSTITUTE: National Institute of Environmental Health Sciences

(Dollars in thousands)

Program	Mechanism										
	Research Grants										
	Regular Program		Specials		Training Programs		Research and Development Contracts	Intramural Research	Direct Operations	Program Management	TOTAL
	Non-Competing	Competing	Multi-disciplinary Centers	Other	Individual	Institutionals					
1. Environmental health sciences centers.....	---	---	$8,331	---	---	---	---	---	---	---	$8,331
2. Marine biomedical research centers.....	---	---	600	---	---	---	---	---	---	---	600
3. Environmental mutagenesis and reproductive toxicology....	$1,467	$1,575	---	$60	$60	---	$2,838	---	---	---	6,000
4. Etiology of environmental diseases and disorders.....	4,642	2,945	---	130	172	$213	1,358	---	---	---	9,460
5. Environmental pharmacology and toxicology.....	5,992	3,375	---	240	261	624	2,942	---	---	---	13,434
6. Environmental pathogenesis.....	917	1,291	---	70	82	73	447	---	---	---	2,880
7. Intramural research operations.....	---	---	---	---	---	---	---	$14,826	---	---	14,826
8. Direct operations.....	---	---	---	---	---	---	---	---	$1,505	---	1,505
9. Program management.....	---	---	---	---	---	---	---	---	---	$1,064	1,064
Total obligations.....	13,018	9,186	8,931	500	575	910	7,585	14,826	1,505	1,064	58,100

Summary of Changes

1977 Estimated Obligations	$49,141,000
1978 Estimated Obligations	58,100,000
Net change	+8,959,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Annualization of new positions in 1977	---	$670,000	---	+$330,000
2. Within-grade pay increases	---	40,000	---	+38,000
3. Wage board pay increases	---	240,000	---	+13,000
4. Federal employees compensation fund	---	8,000	---	+10,000
5. Utility increase	---	540,000	---	+100,000
6. Service and supply fund	---	200,000	---	+20,000
7. Payment for centrally furnished services	---	1,035,000	---	+111,000
(Standard level user charge)	---	(154,000)	---	(+20,000)
Subtotal	---	---	---	+622,000
B. Program:				
1. Research grants:				
a. Regular program:				
(1) Noncompeting continuations converted from competing status	---	9,980,000	---	+7,920,000
(2) Competing (new, renewals, and supplementals)	---	8,022,000	---	+9,186,000
b. Special programs:				
(1) Environmental health sciences centers	---	7,210,000	---	+1,121,000
(2) Marine biomedical research centers	---	---	---	+600,000
(3) Research career programs	---	423,000	---	+77,000
2. Training programs:				
a. Individual:				
(1) Noncompeting continuations converted from competing status	---	198,000	---	+375,000
(2) Competing awards	---	501,000	---	+168,000
3. Research and development contracts (new contracts and continuation of ongoing contracts)	---	6,200,000	---	+1,385,000
4. Intramural research (expansion and continuation of ongoing programs)	283	11,937,000	0	+1,617,000
5. Direct operations	13	1,060,000	0	+115,000
Subtotal	---	---	0	+22,564,000
Total increases	---	---	0	+23,186,000

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Built-in:				
1. One less day of pay in 1978.....	---	$6,024,000	0	-$22,000
B. Program:				
1. Research grants:				
a. Regular program:				
(1) Noncompeting completed or converted to competing status.....	---	$9,980,000	---	-4,882,000
(2) Competing completed or converted to noncompeting	---	8,022,000	---	-8,022,000
2. Training programs:				
a. Individual:				
(1) Noncompeting completed.....	---	198,000	---	-166,000
(2) Competing converted to noncompeting.....	---	501,000	---	-501,000
b. Institutional:				
(1) Noncompeting completed or terminated.....	---	1,544,000	---	-634,000
Subtotal.....	---	---	---	-14,205,000
Total decreases.....	---	---	---	-14,227,000
Total net change.....	---	---	0	+8,959,000

Obligations by Activity

Page Ref.	Program	1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
147	Environmental health sciences centers..	---	$7,210,000	---	$8,331,000	---	+$1,121,000
148	Marine biomedical research centers..	---	---	---	600,000	---	+600,000
149	Environmental mutagenesis and reproductive toxicology	---	4,539,000	---	6,000,000	---	+1,461,000
151	Etiology of environmental diseases and disorders.....	---	8,631,000	---	9,460,000	---	+829,000
153	Environmental pharmacology and toxicology.....	---	11,790,000	---	13,434,000	---	+1,644,000
155	Environmental pathogenesis.....	---	1,908,000	---	2,880,000	---	+972,000
156	Intramural research operations.....	283	12,745,000	283	14,826,000	0	+2,081,000
	(Standard level user charge).....		(129,000)		(146,000)		(+17,000)
159	Direct operations...	13	1,287,000	13	1,505,000	0	+218,000
	(Standard level user charge).....		(25,000)		(28,000)		(+3,000)
160	Program management..	35	1,031,000	35	1,064,000	0	+33,000
	Total obligations.	331	49,141,000	331	58,100,000	0	+8,959,000
	(Standard level user charge).....		(154,000)		(174,000)		(+20,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	331	331	0
Full-time equivalent of all other positions	125	125	0
Average number of all employees	431	450	+19
Personnel Compensation:			
Permanent positions	$5,569,000	$5,894,000	+$325,000
Positions other than permanent	1,170,000	1,172,000	+2,000
Other personnel compensation	150,000	160,000	+10,000
Subtotal, personnel compensation	6,889,000	7,226,000	+337,000
Personnel benefits	689,000	731,000	+42,000
Travel and transportation of persons	416,000	500,000	+84,000
Transportation of things	85,000	85,000	0
Rent, communications and utilities	1,255,000	1,430,000	+175,000
Printing and reproduction	125,000	150,000	+25,000
Other services	2,099,000	2,427,000	+328,000
Project contracts	6,200,000	7,585,000	+1,385,000
Payment for centrally furnished services	1,035,000	1,146,000	+111,000
Supplies and materials	1,970,000	2,700,000	+730,000
Equipment	500,000	1,000,000	+500,000
Grants, subsidies and contributions	27,878,000	33,120,000	+5,242,000
Total obligations by object	49,141,000	58,100,000	+8,959,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1977 House Report	
1. The Committee believes that it is very important to this country's future well-being that NIEHS launch a program of testing for mutagenicity all compounds produced in commercial quantities. (page 42)	1. The plans for the mutagenesis testing program have been completed. They include development of the research requirements for all phases of the testing as well as manpower needs for intramural support and contract management. Research protocols are being finalized for chemical management, data processing and handling, and the short-term mutagenicity tests. The Institute will develop new contract requirements, evaluate proposals, and make awards to initiate the program.
2. The Committee believes it is important that a broader testing program be begun and directs the NIEHS to embark on a collaborative program with the National Cancer Institute aimed at testing compounds in the NCI system for a wide range of physiological, neurological, and behavioral effects. (page 43)	2. NCI/NIEHS interaction on the toxicologic component of the Carcinogen Bioassay Program has begun. An Experimental Design Group composed of employees from NIEHS and NCI has been organized to develop protocols for toxicologic evaluations, evaluate results of acute and subchronic studies, and recommend doses, dosing procedures, and test species to be used in 2-year carcinogen bioassays. The NIEHS objective of the program is to determine the spectrum of dose related toxic effects associated with environmental chemicals. Much of the research will be done in conjunction with studies underway within the National Cancer Institute Bioassay Program, which seeks to evaluate chemicals for carcinogenic properties. A strong focus of the NIEHS effort in this program is aimed toward developing a sound understanding of the distribution of chemicals within the body as well as determining whether the effects caused by these chemicals are due to the chemical itself or other substances formed from these chemicals within the body. This type of data is vital to an understanding of why certain toxicities develop as well as provide a sound basis for designing lifetime studies that determine if a chemical is capable of causing chronic (including carcinogenic) effects.

Item	Action taken or to be taken
1977 Senate Report	
1. For a number of years, the Committee has expressed concern that inadequate attention was being paid to the potential health importance of our marine environment. The Institute has moved exceptionally slow on this important initiative and a broad national environmental marine plan has yet to be developed or submitted to the Committee. The Committee directs that this be done prior to the fiscal 1978 hearing. This report should be broad in scope and encompass plans and numbers of centers, resources necessary to carry out this mission and the goals and objectives of the program. (page 63)	1. The Institute has developed the requested report for a proposed program in marine and freshwater biomedical research support. The report will be submitted to the Committee in February 1977. The Institute is proposing in FY 1978 to undertake core funding of three marine biomedical laboratories whose programs offer the best opportunities for advancement of marine biomedical research.
2. The Committee realizes that there is a great deal of environmental health research being conducted throughout the Federal Government, and the NIEHS has the responsibility of coordinating this. It would therefore be helpful and informative to the Committee if a report listing where all areas of environmental research are conducted and the funding extent of this. (page 63)	2. This report will be submitted to the Committee in February 1977.
3. The Committee has allowed funds to complete the new NIEHS Center. It is important that proper plans be made in order to assure that this facility will be fully and efficiently utilized. With this in mind, the Committee would like the Institute to develop a report which would entail such anticipated needs as personnel, equipment, and special services or requirements to properly use this building. (page 64)	3. This report will be submitted to the Committee in February 1977.

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act Section 301--Research and Investigation, in general	Indefinite	
Title III, Part A--National Institute of Environmental Health Sciences	Indefinite	$56,615,000 2/
Title IV, Part I--National Research Service Awards	1/	1,485,000 3/

1/ Authorization expires September 30, 1977.

2/ Funding estimate only.

3/ Extension legislation is pending.

National Institute of Environmental Health Sciences

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	18,328,000	18,328,000	17,423,000
1971	19,843,000	20,620,000	21,620,000	20,620,000
1972	25,271,000	26,436,000	31,991,000	26,436,000
1973	29,017,000	30,956,000	32,000,000	30,956,000 1/
1974	25,263,000	28,879,000	28,879,000	28,397,000 2/
1975	28,684,000	32,594,000 3/	35,000,000	34,949,000
1976	31,113,000	35,915,000 4/	35,915,000 4/	37,660,000 5/
1977	46,141,000	49,141,000	49,141,000	49,141,000
1978	58,100,000			

1/ Appropriation after reduction as authorized by P.L. 93-192.

2/ Appropriation after reduction.

3/ Excludes Research and Development Contracts not considered by the House due to lack of authorization.

4/ Excludes fellowships and training grants -- not considered due to pending legislation ($1,745,000).

5/ Includes $1,745,000 authorized by Continuing Resolution for training.

National Institute of Environmental Health Sciences

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$20,016,000	$16,690,000	$20,016,000	$16,690,000
1969	17,668,000	17,110,000	17,668,000	16,992,000
1970	17,897,000	17,897,000	17,897,000	17,897,000
1971	19,517,000	20,187,000	21,187,000	20,187,000
1972	24,960,000	26,065,000	31,565,000	26,065,000
1973	28,652,000	30,532,000	31,576,000	30,532,000 1/
1974	25,383,000	28,999,000	28,999,000	28,517,000 2/
1975	28,804,000	32,714,000 3/	35,069,000	35,057,000
1976	31,233,000	36,035,000 4/	36,035,000 4/	37,780,000 5/
1977	46,141,000	49,141,000	49,141,000	49,141,000
1978	58,100,000			

1/ Appropriation after reduction as authorized by P.L. 93-192.

2/ Appropriation after reduction.

3/ Excludes Research and Development Contracts not considered by the House due to lack of authorization.

4/ Excludes fellowships and training grants -- not considered due to pending legislation ($1,745,000).

5/ Includes $1,745,000 authorized by Continuing Resolution for training.

The figures presented in this table have been adjusted to reflect the transfer of major functions. This presents a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

Justification

National Institute of Environmental Health Sciences

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Environmental health sciences centers	---	$7,210,000	---	$8,331,000	---	+$1,121,000
Marine biomedical research centers	---	---	---	600,000	---	+600,000
Environmental mutagenesis and reproductive toxicology	---	4,539,000	---	6,000,000	---	+1,461,000
Etiology of environmental diseases and disorders	---	8,631,000	---	9,460,000	---	+829,000
Environmental pharmacology and toxicology	---	11,790,000	---	13,434,000	---	+1,644,000
Environmental pathogenesis	---	1,908,000	---	2,880,000	---	+972,000
Intramural research	283	12,745,000	283	14,826,000	0	+2,081,000
Direct operations	13	1,287,000	13	1,505,000	0	+218,000
Program Management	35	1,031,000	35	1,064,000	0	+33,000
Total	331	49,141,000	331	58,100,000	0	+8,959,000

General Statement

The National Institute of Environmental Health Sciences seeks to increase our understanding of the extent to which environmental agents can adversely affect man's health either immediately or over time. This is based on two premises: (1) environmental agents can cause disability, disease, and death; and (2) results from biomedical research can be used to prevent or limit environmental diseases and disorders. The results of the Institute's research are promptly made available to agencies having responsibility for environmental monitoring, standard setting, and control. The Institute seeks to determine the human health hazard resulting from exposures to chemical, physical, and biological agents in the environment. Underlying mechanisms of effects are examined in order to determine the principles on which to base air, water, and other environmental standards by agencies with the regulatory responsibility in this area.

Among the beneficiaries of the basic knowledge developed by the Institute are professionals concerned with the environmental components of human disease - e.g. - physicians treating poisonings by environmental chemicals, and medical teams concerned with the etiology of new diseases peculiar to certain locales or puzzled by drug interactions with environmental components. Our data are also useful to other programs dealing with environmental components of cancer, teratology, mutagenesis or heart and lung diseases (e.g. - National Cancer Institute, National Institute of Child Health and Human Development, National Heart, Lung and Blood Institute). Close liaison is maintained between the Institute and academic and medical communities and other Governmental agencies concerned with the environment -- Environmental Protection Agency, Food and Drug Administration, National Institute for Occupational Safety and Health, and the Occupational Safety and Health Administration. Such contacts maintain mutual awareness of programs, avoid unnecessary duplication of efforts, and foster collaboration.

Extramural Research

Grant support of research and training in the environmental health sciences is an essential component of the national effort to identify, characterize and ultimately limit hazards in the environment. The grants program enables the Institute to enlist expertise nationwide in the attack on the complex and growing problems of environmental contamination and health hazard assessment and prediction.

Intramural Research

The intramural program gives priority to research areas in which there is an insufficient information base for adequate understanding of environmental hazards or for regulatory decisions. It investigates the actions, interactions, and mechanisms by which chemical, physical and biological agents damage the structure or function of biological systems at any level and, where possible, the effects found in experimental models are compared with effects in man. Because of the general insufficiency of data for such comparisons, however, a major effort is being made in comparative physiology and toxicology and in biometrics in order to develop capabilities for reliable extrapolation of data from physical and biological models to man.

The Institute's extramural and intramural programs are a blend of fundamental and applied research in areas identified as justifying broad scale investigation. For administrative purposes the research is circumscribed within seven programs: (1) Environmental Health Sciences Centers, (2) Marine Biomedical Research Centers, (3) Environmental Mutagenesis and Reproductive Toxicology, (4) Etiology of Environmental Diseases and Disorders, (5) Environmental Pharmacology and Toxicology, (6) Environmental Pathogenesis, and (7) Intramural Research. The programs serve as a prime and unique focus for national and international efforts to evaluate and ameliorate the negative impact of environmental factors on human health.

The narrative material which follows provides information about current and planned investigation for support or conduct of research through grants, contracts, and in the Institute's own laboratories. The Institute's activities are discussed here in terms of programs. They are planned and operated as part of a total national program with each component complementary to the others, and all directed toward understanding of hazards to health resulting from man's interaction with his environment.

Environmental Health Sciences Centers

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Environmental health sciences centers.....	7	$7,210,000	8	$8,331,000	+1	+$1,121,000

Introduction

The Environmental Health Sciences Centers foster applications of expertise across disciplinary lines to environmental health problems. They are characteristically made up of groups of scientists who collaborate to develop information about the causes and nature of environmental diseases. Because of the variety and complexity of environmental problems, several Centers with complementary spheres of interest are required to fulfill the national need. Accordingly seven Centers, each with special expertise in one or more of the major categorical programs of the Institute, are supported. Collectively, they provide outstanding capabilities in traditional basic and applied disciplines vital to the Institute program including, among others, chemistry, cell biology, genetics, physiology, biostatistics, pharmacology, toxicology, pathology, epidemiology, behavioral sciences, nutritional science, occupational medicine, and chemical and environmental engineering.

Program Plans for 1978

Important new data and insights are being developed regarding specific environmentally-related health problems, including chemical carcinogenesis; teratogenesis and other reproductive disorders; neural and behavioral anomalies, respiratory, circulatory, and kidney diseases; and fundamental aspects of toxicant metabolism and disruptive interactions at the molecular and cellular levels. Further advances are also being made in long-term population studies with emphasis on chemical epidemiology and on methodology for detecting early symptoms of fibrotic diseases of the lung, emphysema, and other disorders associated with exposure to environmental chemicals and dusts in the work or social environment. Epidemiological studies conducted during 1977 on randomly selected populations exposed to polybrominated biphenyls (PBB's) in Michigan have revealed that a substantial number of exposed individuals exhibit symptoms of neurological damage. These studies will be continued to affirm suspected involvement of PBB's in the disorders and to develop further understanding of the underlying mechanisms of PBB effects.

The requested funds will permit the funding of the seven currently active centers and one new center relevant to high priority program areas of the Institute.

Marine Biomedical Research Centers

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Marine Biomedical Research Centers	---	---	3	$600,000	+3	+$600,000

Introduction

Marine Biomedical Research Centers are core centers selected for their interests and capabilities in multidisciplinary research closely related to the mission and responsibilities for the National Institute of Environmental Health Sciences. Freshwater and marine environments are receptacles of many of the hazardous environmental agents encountered in terrestrial environments; thus, marine organisms properly selected, provide excellent models for study of functional cells, tissues, and organs of man and their injury by environmental agents. Further, marine species may act as sensitive indicators of pollution hazards. These centers, therefore, complement and provide an additional dimension of research now being conducted and supported by the Institute.

Program Plans for 1978

Three marine and freshwater biomedical centers are planned for 1978. Core support will be provided on the basis of merit and relevance of the proposed research to the NIEHS mission. Plans are also being made for support of visiting scientists at the centers, dual-training in marine and environmental health sciences where appropriate, and individual research projects. The latter will be subject to the usual NIH dual review and awarded on the basis of scientific merit. Specific programs will be developed in accord with the expertise of the staff of each center selected.

Environmental Mutagenesis and Reproductive Toxicology

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research grants:						
Regular:						
Noncompeting	12	$753,000	21	$1,467,000	+9	+714,000
Competing	17	1,200,000	22	1,575,000	+5	+375,000
Subtotal	29	1,953,000	43	3,042,000	+14	+1,089,000
Special	2	40,000	3	60,000	+1	+20,000
Subtotal, research grants	31	1,993,000	46	3,102,000	+15	+1,109,000
Training programs:						
Individual	4	58,000	4	60,000	0	+2,000
Institutional	---	---	---	---	---	---
Subtotal, training programs	4	58,000	4	60,000	0	+2,000
Research and development contracts	18	2,488,000	18	2,838,000	0	+350,000
TOTAL	53	4,539,000	68	6,000,000	+15	+1,461,000

Introduction

The mutagenesis and reproductive toxicology program deals with delineating known and potential roles of chemical agents found in air, water, food and occupational situations, in altering the genetic makeup of man, his reproductive capability, and in the development of the embryo or fetus. Induction of permanent changes in human genetic material is the most profound long-term potential danger associated with environmental agents. In addition to anatomical defects generally ascribed to mutations, it is clear that subtle deficits in mental capacity and susceptibility to degenerative and infectious diseases also result from genetic aberrations. A major obstacle in assessing mutagenic potential of chemical agents has been the lack of rapid inexpensive test systems with unequivocal quantitative relevance to man. This program is designed to fill this gap and to develop reliable techniques for extrapolation of results from laboratory test systems to man.

Program Plans for 1978

Advances are being made toward further understanding of the chemistry of molecular interactions between DNA and mutagenic agents. The studies are designed to provide an understanding of the genetic basis of changes in biochemistry and morphology and serve as a guide in devising test procedures to determine the frequency of mutations caused by different classes of environmental mutagens.

The Institute recognizes serious deficiencies in available mutagenesis testing procedures; and, in many cases, the relevance of existing methodology to man at realistic mutagen levels is questionable. It recognizes also the necessity to establish valid tests as a basis for further and more rapid progress in this area. Thus, new initiatives have been taken to interest the scientific community in applying the necessary effort and expertise to develop human mutagenicity test systems.

In reproductive toxicology, the agents of primary concern are organophosphate and chlorinated hydrocarbon insecticides, polychlorinated biphenyls (PCB's), chlorinated furans and dioxins, heavy metals, toxic fungal metabolites, vinyl chloride and other intermediates of important industrial processes. Another important area of concern is the relationship between gestational periods and the nature and degree of damage induced in the fetus of experimental animals by certain pesticides and fungal toxins. These studies are designed to shed further light upon both the maximum risk time during gestation and the relationship between time of exposure and the nature of deformities in the offspring.

The importance of this program in maintaining the genetic fidelity of mankind and in assuring the conception and delivery of healthy babies now and in the future cannot be overemphasized. Ongoing programs will be continued and new ones will be initiated during the coming year to enlist the skills of geneticists and scientists in related fields in the university community to complement and extend strong efforts currently underway in the Intramural program.

The mutagenicity screening program will be expanded in 1978. The House and Senate added additional funds to the 1977 Appropriation Bill for the initiation of this contract program. This program is currently being designed and will be set up in close collaboration with the National Cancer Institute in vitro testing effort. In addition, existing contracts will be utilized to improve methods and to test a limited number of chemicals of high interest. Within three years, the mutagenicity testing program would expect to test approximately 1,000 compounds annually.

Etiology of Environmental Diseases and Disorders

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research grants:						
Regular:						
Noncompeting	29	$4,384,000	39	$4,642,000	+10	+$258,000
Competing	31	2,458,000	39	2,945,000	+8	+487,000
Subtotal	60	6,842,000	78	7,587,000	+18	+745,000
Special	5	105,000	6	130,000	+1	+25,000
Subtotal, research grants	65	6,947,000	84	7,717,000	+19	+770,000
Training programs:						
Individual	15	223,000	12	172,000	-3	-51,000
Institutional	2	325,000	1	213,000	-1	-112,000
Subtotal, training programs	17	548,000	13	385,000	-4	-163,000
Research and development contracts	4	1,136,000	5	1,358,000	+1	+222,000
TOTAL	86	8,631,000	102	9,460,000	+16	+829,000

Introduction

The objective of the etiology program is to identify causal associations between human diseases and environmental chemicals and physical factors. It includes broad surveys of chemical agents now in use, or proposed for use, that adversely affect biological systems. Concomitantly, it seeks to identify specific malfunctions caused by these agents in body organs. This research provides a basis for clinical recognition of environmentally-related disorders in man, determination of their causes, and implementation of therapeutic and preventive measures. It will serve also as a basis for management of current technology and future industrial and energy development in such a way as to make them compatible with human health and well-being.

Program Plans for 1978

Thousands of new chemicals are synthesized each year. By use of newly developed techniques and models, some pesticides have been found to disrupt nerve function and to influence behavioral and learning patterns. The potential of certain of these compounds to modify man's behavior is exemplified by recent reports of brain and neural disorders caused by the pesticide Kepone. Further probing of the long-term effects of mercury and lead in the central nervous system has verified and extended our knowledge of the adverse effects on learning and behavior. The effects are seen in experimental animals which exhibit no visible lesions in the nervous system. Studies of this nature add a new dimension to problems of detection of cause-effect relations. They indicate the need to reassess our thinking in regard to meaningful dose-endpoint relations and appropriate environmental tolerance levels. Research already conducted in this area demonstrates the scope of problems that must be dealt with.

Nitrites used as food preservatives were shown to form nitroso derivatives, a class of compounds known to be potent carcinogens and at least mild mutagens. Work on air pollutants shows that ozone and nitrogen dioxide affect the lung lining. Sulfur dioxide from the air and sulfites used as food preservatives interact with some sulfur-containing compounds, forming thiolsulfonates which distribute and release sulfite throughout the body. Hydrazine, used in making a number of useful pharmaceuticals, produces lesions characteristic of diabetes in experimental animals. Dichloroethylene, vinyl chloride and other compounds used in the plastics industry were found to be liver toxins and carcinogens which present considerable hazards to workers and perhaps others in the general population. Further epidemiological studies on asbestosis revealed heretofore unrecognized dangers associated with asbestos inhalation. Cancer of the lungs and a rare cancer of the lung and abdominal linings, called mesothelioma, occur more frequently in insulation workers and others in building trades who are exposed to relatively small amounts of asbestos.

The importance of the agents and the scope of disorders indicated emphasize the necessity for continued efforts to establish associations between environmental agents and disease and physiological stresses. Despite the difficulties of testing all environmental agents and combinations of agents, some new principles are beginning to emerge which permit cautious generalizations with respect to etiological relations of classes of compounds. Work will continue on the hazards of specific agents in carcinogenesis, teratogenesis, lung and cardiovascular diseases, neurotoxicity and other less debilitating but costly disorders and degenerative processes.

Much of the ongoing research in this program area impacts directly upon the goals and intent of the recently enacted Toxic Substances Control Act. The Institute intends to maintain its present directions and commitments within its present mandate. In addition, it will increase its efforts, along with other responsible agencies, to be responsive to and facilitate implementation of the provisions of the Act, through both its extramural and intramural programs.

Environmental Pharmacology and Toxicology

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research grants:						
Regular:						
Noncompeting	46	$4,237,000	63	$5,992,000	+17	+$1,755,000
Competing	49	3,515,000	44	3,375,000	-5	-140,000
Subtotal	95	7,752,000	107	9,367,000	+12	+1,615,000
Special	10	233,000	10	240,000	0	+7,000
Subtotal, research grants	105	7,985,000	117	9,607,000	+12	+1,622,000
Training programs:						
Individual	26	361,000	19	261,000	-7	-100,000
Institutional	8	1,146,000	5	624,000	-3	-522,000
Subtotal, training programs	34	1,507,000	24	885,000	-10	-622,000
Research and development contracts	16	2,298,000	14	2,942,000	-2	+644,000
TOTAL	155	11,790,000	155	13,434,000	0	+1,644,000

Introduction

The pharmacology-toxicology program is designed to develop understanding of the principles and mechanisms of toxicity of environmental agents. The research ranges from mechanistic studies of factors that alter the toxicity of chemical agents to studies on absorption, metabolism, and transport within the body. The nature and sites of defense systems and molecular targets associated with visible functional disorders are also being investigated. The goal is to provide a rational basis for maintaining, through environmental management, reasonable safety margins between environmental and body burdens of toxic agents in order to safeguard human health.

Program Plans for 1978

Studies will be continued and expanded on enzymes that modify foreign agents and on the mechanisms by which such agents are metabolized, accumulated, and excreted. Past work has shown that many organic compounds are susceptible to transformation by light, UV (ultraviolet) and other factors in the environment and by the action of various enzymes in the body. While nontoxic substances are generally formed, more toxic compounds are sometimes generated. Continuing studies show that aromatic petroleum products, common as air pollutants in urban areas, give rise to carcinogenic agents. Several pesticides, particularly some organophosphates, and certain carcinogens are activated by enzymes within the body. Other pesticides such as aldrin and dieldrin are converted to more toxic derivatives upon exposure to sunlight.

Understanding of the movement and sites of action of such substances is vital in establishing the hazard of the compounds to human health. New projects will continue to focus on transformations of compounds in order to understand the nature of proximal toxicants and their subsequent effects on cellular and tissue targets. In many cases, interactions between combinations of compounds

result in dangerous enhancement of toxicity even at levels at which the individual agents are normally considered to present no risk to man. Such interactions will be identified and assessed for their long-term risk of birth defects, genetic change and general toxicity.

Research contracts which investigate the effects of ingested asbestos over a life-time exposure in experimental animals will continue. The recent East German report where feeding asbestos filter material to rats produced cancer, underscores the importance of these NIEHS contracts. Results of these studies should allow for the evaluation of the public health consequences of asbestos in foods and liquids in a thorough manner. These contracts are in response to the Congressional directive that NIEHS initiate a long-term study on the effects of ingested asbestos.

The House and Senate added additional funds to the 1977 Appropriation Bill for the initiation of a new program in toxicity bioassay. NCI/NIEHS interaction on the toxicologic components of the Carcinogen Bioassay Program has begun. An Experimental Design Group composed of employees from NIEHS and NCI has been organized to develop protocols for toxicologic evaluations, evaluate results of acute and subchronic studies, and recommend doses, dosing procedures, and test species to be used in 2-year carcinogen bioassays. The NIEHS objective of the program is to determine the spectrum of dose related toxic effects associated with environmental chemicals. Much of the research will be done in conjunction with studies underway within the National Cancer Institute Bioassay Program, which seeks to evaluate chemicals for carcinogenic properties. A strong focus of the NIEHS effort in this program is aimed toward developing a sound understanding of the distribution of chemicals within the body as well as determining whether the effects caused by these chemicals are due to the chemical itself or other substances formed from these chemicals within the body. This type of data is vital to an understanding of why certain toxicities develop as well as provide a sound basis for designing lifetime studies that determine if a chemical is capable of causing chronic (including carcinogenic) effects.

As a specific example, NIEHS scientists are to provide an extensive toxicologic evaluation on polybrominated biphenyls. These chemicals, like many other substances found in our environment (i.e., polychlorinated biphenyls) are mixtures of a number of specific chemicals. One needs to know which chemicals cause biological effects so that extensive research will focus on them rather than the other materials that may be present but are of little biological significance.

Environmental Pathogenesis

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research grants:						
Regular:						
Noncompeting	8	$606,000	12	$917,000	+4	+$311,000
Competing	11	849,000	17	1,291,000	+6	+442,000
Subtotal	19	1,455,000	29	2,208,000	+10	+753,000
Special	2	45,000	3	70,000	+1	+25,000
Subtotal, research grants	21	1,500,000	32	2,278,000	+11	+778,000
Training programs:						
Individual	4	57,000	6	82,000	+2	+25,000
Institutional	1	73,000	1	73,000	0	0
Subtotal, training programs	5	130,000	7	155,000	+2	+25,000
Research and development contracts	4	278,000	5	447,000	+1	+169,000
TOTAL	30	1,908,000	44	2,880,000	+14	+972,000

Introduction

The pathogenesis program focuses upon the details and time sequence of molecular and cellular events that culminate in recognizable diseases following exposure to toxic agents. Diseases of the pulmonary, cardiovascular, hepatic, renal, reproductive, digestive and the central and peripheral nervous systems, as well as degenerative disorders of complex and long-term etiology have been documented and related to one or more environmental agents. The program is also intended to clarify the interactions through which environmental agents play a secondary or ancillary role in the progress of degenerative disorders. Knowledge of initial or very early molecular and cellular lesions and understanding of their role in pathological endpoints offers the best hope, apart from prevention of toxic exposures, for detecting and countering the development of diseases before damage in target organs becomes irreversible.

Program Plans for 1978

Studies are currently being conducted on many environmentally-related diseases. Among these are phototoxicity and light-induced cancer, degenerative diseases associated with aging, kidney disorders induced by metals and their compounds, fibrotic diseases of the lung, including asbestosis and berylliosis, a number of forms of cancer, and neurological diseases.

Many other fundamental studies are currently underway to determine effects of environmental chemicals and dusts on cilia and lung macrophages in the respiratory tract and the consequences of inactivation of these cells in terms of development of chronic bronchitis, emphysema, fibrosis and other lung disorders.

Although considerable progress has been made, much remains to be done to develop a clear understanding of all ramifications of environmental agents in acute and chronic disease development. New and ongoing projects will continue to focus on these problems.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Research Program.....	283	$12,745,000	283	$14,826,000	0	+$2,081,000

Introduction

This activity supports the intramural research program and the provision of centralized administrative and clerical services. The intramural research program is directed toward development of a reliable data base for use in establishing standards and devising remedial methods in a variety of populations at risk from exposure to environmental and occupational chemicals and physical factors. The Institute is fostering research on a wide range of environmental problems which, on the whole, present the greatest potential hazard to the present population and future generations. These include airborne toxicants, metal toxicants, pesticides, mutagenic compounds, physical factors, and non-categorical hazardous compounds.

Program Plans for 1978

The mutagenesis program at NIEHS will continue to be the focus of mutagenesis research in the Government and will function centrally to collaborate these activities between all parts of the Government and with non-governmental groups, including international activities. A basic goal of all research conducted intramurally is to develop better test systems for screening chemicals and other environmental factors that can produce genetic damage. Studies of the mechanisms by which such damage is produced or repaired will provide new methodology for detecting effects, extrapolating from simple tests to the situation in animals and man, and in devising best interventions to minimize genetic damage in populations which must continue to be exposed to genetically-damaging environments.

New test systems, especially using mammalian tissues combined with detector organisms like Salmonella, yeast, etc, will be studied in depth with emphasis on validating several of these with a variety of chemicals having been previously tested and of known varieties of mutagenic or carcinogenic capacity. The results of all of this will be the construction of a tiered testing strategy wherein chemicals showing mutagenesis in simple systems are tested in increasingly complex systems approaching what is likely in man. In this way, false positives can be identified before long-term, expensive tests are used and the most reliable and quickest of the simple tests can be identified and can serve to screen many of the chemicals needing testing.

Thus, the 1978 efforts in mutagenesis will be: (1) to initiate a several-tiered testing program geared to testing several hundred chemicals per year for mutagenesis/carcinogenesis activity; (2) a validation of several of the proposed tests at several levels of complexity in this tier system; (3) the initiation of a new program on molecular genetics wherein the emphasis will be on mechanisms of damage and repair of damage of genetic material, permitting the development of better tests for genetic damage; tests capable of detecting unusual types of genetic damage (not now detected even with the newer tests); tests for detecting people with defective repair systems for genetic damage; and (4) application of tests for detecting aberrant hemoglobins of plasma enzymes in people accidentally exposed to chemicals which might be mutagenic to see if these blood markers can serve as an index of exposure to dangerous chemicals.

Research efforts in the area of pharmacokinetics will be increased. Studies of routes and rates at which chemicals are absorbed, distributed, metabolized and excreted can be used to predict where chemicals will localize in tissues and for how long. Such studies are especially useful in designing tests for dangerous exposure and in devising therapy for people poisoned or overexposed to dangerous chemicals. These approaches have been used extensively and successfully in recent episodes exposing man to kepone and polybrominated biphenyls (PBB's) and more capability in this program area is needed.

The new programs in behavioral and neurotoxicity will be further developed. Initial studies seek to validate a variety of test systems using environmental chemicals. We hope to be able to select from a variety of behavioral tests those that can best serve as early indicators of toxicity for chemicals like kepone which have been shown to be neurotoxic in man at very high doses. In addition, studies on the mechanism of neurotoxic and behavioral effects of chemicals will be made with the goal of devising better tests for such toxicity. The behavioral effects of microwaves and selected chemicals will be tested and studied in several species to better understand species variability in effects.

A new focus in pulmonary toxicity is planned. The major interests are to devise better tests for detecting early pulmonary damage by chemicals -- concentrating on non-respiratory functions of lung as test parameters. This group will work closely with the aerotoxicology group whose major programs are in testing of mixtures of airborne pollutants for effects and devising systems for delivering complex pollutant mixtures to animals.

The new program in epidemiology will be expanded and strengthened. Studies in North Carolina on the possible effects in newborn infants of polychlorinated biphenyls (PCB's) in mother's milk will be initiated. Also being considered are studies on lead levels in children and the incidence of high blood pressure in these children. With both of these pollutants (lead and PCB's), there are suggestions that effects may exist, but studies in well-defined, exposed populations coupled with adequate biochemical testing of exposed people in adequate numbers are not available.

Several programs in developmental and reproductive toxicology will be strengthened. New test methods using embryo culture and other techniques are being devised for assessing teratogenic effects of chemicals. The Environmental Teratology Information Service is refining its data base and is in a preliminary stage of user evaluation. When fully developed, this service will provide to interested parties from government, industry, and academia information about what chemicals have been tested and how they have been tested. Information is added from both published and unpublished sources. Animal models for reproductive effects of chemicals (e.g. sterility, transplacental toxicity and cancer) are being sought along lines used in developing our mouse model for diethystilbestrol (DES) effects in male and female offspring of DES-treated mothers.

The marine biomedical research program will be expanded by adding a number of additional research programs. The major goals are to identify the processes by which toxic pollutants accumulate in edible aquatic organisms and to use certain aquatic species as markers for chemicals which are carcinogenic in man. This program will be closely coordinated with the extramural program in marine biomedical research.

The programs in biophysics and physical factors will be expanded, and a new program will be initiated in molecular biophysics. These programs will collaborate extensively with others at NIEHS, for example, in studies on the behavioral and neurological effects of noise and microwaves, the molecular basis of light-induced skin diseases and the interactions of light and chemicals on skin.

The intramural program provides a mechanism for on-going research to deal with specific research needs vital to the national interest, for focusing and coordinating national efforts in important research areas, and for fulfilling of the Institute responsibilities in research where sufficient effort and interest are not available elsewhere in the scientific community. In most instances projects and research development within the intramural program serve as catalysts to the scientific community, especially in interdisciplinary areas.

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Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations.....	13	$1,287,000	13	$1,505,000	0	+$218,000

Introduction

This activity provides scientific and administrative management for grant supported research and manpower programs of the NIEHS (Extramural Program); payment to the DHEW General Expense Fund; Program Evaluation; and centrally furnished services. The extramural program is responsible for the surveillance of ongoing grants supported programs; coordination of scientific merit and relevance review of competing applications; liaison with applicants, grantees, advisory bodies, other departments of the NIH, PHS, and other interested organizations; and compilation and reporting of scientific and fiscal information relevant to the programs.

Program Plans for 1978

During 1978, extramural program staff will expand programming efforts in emerging problem areas, with special emphasis on marine and freshwater biomedical activities. The staff will monitor approximately 350 active grants and awards, an increase of 20% over 1977.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.....	35	$1,031,000	35	$1,064,000	0	+$33,000

Introduction

Program Management encompasses the Office of the Director which provides the overall management for and direction of the varied Institute programs and activities. Included are the functional staff areas of program planning and evaluation, program coordination, public information, legislative analysis, interagency coordination, and health hazard assessment. In addition, the program provides supervision of centralized administrative services such as budget, personnel, procurement, supply management and office services.

Program Plans for 1978

The Office of the Director will continue to provide the resources necessary for managing and directing Institute programs. It will continue to accumulate pertinent information on research needs, evaluate this information and select those critical research problems in need of new or expanded investigation. Interagency liaison and coordination will continue through formal relationships such as those related to the Energy Related Research Program, the Toxic Substances Control Act and the DHEW Committee to Coordinate Toxicology and Related Programs. The Director is Chairman of this latter committee. In addition, informal relationships will be continued and expanded. The information program, designed to better inform the research community, interested groups and the public, regarding environmental health and the NIEHS programs, will be intensified and expanded. International cooperation and coordination will be expanded this year. The Director has recently assumed responsibility for the environmental health programs under the auspices of the U.S. - Egypt Joint Working Group on Medical Cooperation. He continues to serve as the American coordinator for the Environmental Health portion of the U.S. - U.S.S.R. Health Agreement and as Project Chairman of the work group on Biology and Genetic Effects of Pollutants under the U.S. - U.S.S.R. Environmental Agreement. The Institute will continue its relationship with the World Health Organization as a cooperating Research Center in Environmental Health.

The technology assessment effort, which interfaces closely with other agencies and departments, as well as the industrial community, is directed toward identifying those chemicals or compounds that will be in the future market place. With this information, we can attempt to predict potential toxic effects on the basis of existing knowledge and alert research programs to the needs for further research when existing knowledge is inadequate.

The Institute will continue to sponsor or co-sponsor topical conferences related to environmental health. Participation by national and international experts serves to define problems, focus on research needs and stimulate research efforts. Eight conferences were supported in 1975, twelve in 1976 and 10 in 1977. The proceedings of such meetings are usually published in scientific journals including the Institute's journal, Environmental Health Perspectives.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Health Sciences Centers
(Public Health Service Act, Title III, Part A)

1977			1978	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$7,210,000	Indefinite	---	$8,331,000

Purpose: The University-based Centers were created to integrate the efforts of scientists in several traditional disciplines and foster application of expertise across disciplinary lines to environmental health problems.

Explanation: Because of the variety and complexity of environmental problems, several Centers with complementary spheres of interest are required to fulfill the national need. Accordingly, seven Centers, each with special expertise in one or more of the major categorical programs of the Institute were supported in FY 1976. Collectively, they provide outstanding capabilities in traditional basic and applied disciplines vital to the Institute program. The Centers are characteristically made up of groups of scientists who collaborate to develop fundamental and practical information about the causes and nature of environmental diseases in order to guide corrective and therapeutic programs. Their areas of expertise include, among others, chemistry, cell biology, genetics, physiology, biostatistics, pharmacology, toxicology, pathology, epidemiology, behavioral sciences, nutritional science, occupational medicine, and chemical and environmental engineering.

Accomplishments in 1977: Each of the Centers has made important contributions to the objectives of the Institute. Their studies deal with a wide variety of hazardous agents in the environment which are the immediate focal points of public concern and with specific diseases and disorders of environmental origin. Advances have been made in the identification and characterization of the sources, modes of entry, sites and basis of cell and tissue damage, and persistence of known and potential noxious agents. These include vinyl chloride, bis(chloromethyl)ether, carbamoyl chloride, and asbestos. Important new data and insights have been developed regarding specific environmentally-related health problems, including chemical carcinogenesis; teratogenesis, and other reproductive disorders; neural and behavioral anomalies; respiratory, circulatory, and kidney diseases; and fundamental aspects of toxicant metabolism and disruptive interactions at the molecular and cellular levels. Further advances have been made in long-term population studies with emphasis on chemical epidemiology and on methodology for detecting early symptoms of fibrotic diseases of the lung, emphysema, and other disorders associated with occupational or accidental exposure to environmental chemicals and dusts. Particular emphasis has been directed in some Centers toward potential health problems that may arise from new and intensified activities in technologies related to energy production and conservation. One new Center with outstanding expertise and research capabilities in chemistry and hazards of mercurials and other heavy metals was added late in FY 1975.

Objectives for 1978: The budget request provides for funds to continue support of the 7 Centers funded in 1977, 3 of which are competitive renewals, and the initiation of 1 new center relevant to high priority program areas of the Institute.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Marine Biomedical Research Centers
(Public Health Service Act, Title III, Part A)

1977			1978	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	---	Indefinite	---	$600,000

Purpose: The purpose of Marine Biomedical Research Centers is to establish a stable environment within selected, medically-oriented laboratories for marine and freshwater biomedical research and training as they pertain to environmental health and other categorical programs of the National Institutes of Health.

Explanation: Marine and other aquatic organisms, properly selected and evaluated, may act as sensitive indicators of pollution levels in areas from which water and food for human consumption are taken. Further, some aquatic species provide excellent models for study of human systems, ranging from the simplest to the most complex, and for certain human diseases. The many classical contributions made to science through studies of marine organisms testify to their potential value in further studies in disciplines important to environmental health sciences.

Accomplishments in 1977: Not applicable -- program to be initiated in 1978

Objectives for 1978: Three marine and freshwater Biomedical Research Centers are planned for 1978. Core support for each Center will be provided on the basis of merit and relevance of the proposed research to the NIEHS mission. Plans are also being made for support of visiting scientists at the Centers, dual-training in marine and environmental health sciences where appropriate, and for individual research projects. The latter will be subject to the usual NIH dual review and awarded on the basis of scientific merit. Specific programs will be developed in accord with the expertise of the staff of each Center selected.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Mutagenesis and Reproductive Toxicology
(Public Health Service Act, Title III, Part A, Title IV, Part I)

1977		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$4,539,000	Indefinite	---	$6,000,000

Purpose: This program aims at clarifying the nature and structure-activity relations of chemical agents capable of altering the genetic makeup of man, his reproductive capability, and development of the embryo or fetus. Critical is the need to develop mutagenicity test systems with unequivocal quantitative relevance to man.

Explanation: A major effort in this program is being made in the Institute's laboratories. This is supplemented to a considerable degree, however, through individual, program and center grants. The studies will provide an understanding of the molecular basis for visible changes in biochemistry and morphology due to mutagenic and teratogenic agents. Efforts are also being made to assess existing mutagenesis test procedures for relevance to man and to develop new procedures. This is a high priority aspect of the program. Serious deficiences in present test systems must be bridged to facilitate progress toward assessment of man-made environmental chemicals, as well as natural products for mutagenic potential in man.

Accomplishments in 1977: Progress is being made toward further understanding of the chemistry of molecular interactions between DNA and mutagenic agents such as cyclamates, saccharine, azides, nitroso compounds, nitrites and polychlorinated biphenyls (PCB's). Studies in reproductive toxicology range from efforts to establish etiological relationships between toxicants and specific disorders to those designed to elucidate the molecular and cellular basis of teratogenesis and hormone changes. The agents of primary concern are widespread compounds such as chlorinated hydrocarbon and organophosphate insecticides, fungal metabolites, dioxins, mercurials, lead, cadmium and other heavy metals, and a number of pharmaceuticals and industrial intermediates, including vinyl chloride.

Further light has been shed on the gestational period during which the fetus is at maximum risk upon exposure of the mother to toxicants such as heavy metals, parathion, and certain mycotoxins. Progress has been made in the development of better teratology and fetal test systems in experimental animals. These methods include techniques for culture of fertilized eggs and fetuses from several species. The embryo or portions of it can be exposed to precise amounts of test compounds for exact periods of time at any desired stage of development. This and similar techniques will be extremely valuable in future efforts to identify critical cells in specific types of birth defects and in predicting the action of new and existing compounds with liabilities as teratogens. Such capability should notably enhance the effectiveness of preventive medicine in this area. A new program in mutagenicity screening, initiated as a result of Congressional action on the 1977 appropriation, will embark on testing all compounds produced in commercial quantities for mutagenicity. Within 3 years, the Institute would expect to test approximately 1000 compounds annually.

Objectives for 1978: The budget request provides for continuation and expansion of research on environmental compounds as they influence man's genetic makeup his reproductive capability, and the healthy development of future generations.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Etiology of Environmental Diseases and Disorders
(Public Health Service Act, Title III, Part A, Title IV, Part I)

1977			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$8,631,000	Indefinite	---	$9,460,000

Purpose: The central objective of the etiology program is to establish causal associations between human diseases and noxious chemical and physical factors in the environment. This involves description and characterization of pathological lesions and endpoints in specific target organs and interdependent physiological systems.

Explanation: This program is carried out both by the intramural staff and through grants and contracts. Thousands of new chemicals are synthesized each year. Many of these are brought into production, adding to the thousands already in use in industry, to make home and personal care products, food and fuel additives, pesticide and pharmaceutical preparations, and a host of others. Despite increased efforts by manufacturers and government agencies to test new and existing compounds, the biological effects of many of these substances alone and in combinations are still unknown. The research is designed to provide a sound basis for clinical recognition of environmentally-related disorders of man and their causes and for implementation of therapeutic and preventive measures. In a broader sense, its aim is to provide a foundation for wise management of current technology and future industrial development in order to make them compatible with human health and well-being.

Accomplishments in 1977: Evidence has been obtained that several widely used pesticides disrupt nerve function and may influence behavioral and learning patterns, induce cancer and interfere in reproduction. Further probing of the long-term effects of lead and mercury on the central and peripheral nervous systems has revealed adverse effects on learning and behavior even before visible damage to the nervous system is evident. The carcinogenic activities of industrial dust such as asbestos, have been investigated further and new evidence of synergism between particulates and cigarette smoking has been obtained. An important new class of carcinogens, carbamoyl chlorides, has been uncovered, and work is now in progress on their mechanisms of action. New toxins have been detected in fungi often associated with grains and other food staples. The different toxins cause a variety of syndromes ranging from carcinoma and edema of the lungs to photosensitization and neurological and kidney damage. Advances have been made in understanding the influence of heat stress, light, noise, microwaves and laser radiation on physiological systems. New insights have been developed into disorders of the lungs and cardiovascular systems induced by ozone, oxides of nitrogen and sulfur, and by industrial dusts from coal, plastics, asbestos, textiles and others. Epidemiological studies have provided evidence that cancer, fibrotic diseases, emphysema and bronchitis are often greatly enhanced by cigarette smoking and inhalation of lung irritants characteristic of urban atmospheres.

Objectives for 1978: The budget request provides for continuation and expansion of research on chemical, physical and biological agents in the environment that may act, singly or in combination, as progenitors of human disease.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Pharmacology and Toxicology
(Public Health Service Act, Title III, Part A, Title IV, Part I)

1977		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$11,790,000	Indefinite	---	$13,434,000

Purpose: The pharmacology-toxicology program is designed to develop understanding of the principles and mechanisms involved in the toxicity of environmental agents. Its further aim is to characterize the nature and sites of molecular, cellular and tissue interactions with toxicants and to relate these to functional disorders.

Explanation: These studies are carried out both within the Institute's laboratories and through individual grants and contracts and program and center grants. Work in several laboratories focuses on the nature and basic mechanisms of chemical transformations of environmental agents in the environment and in the body. A major segment of the program deals with inherent defense systems such as binding, exclusion, storage, metabolic and clearance systems. Substantial effort is devoted also to clarification of interactions between specific enzymes and metabolic targets responsible for gross manifestations of toxicity. The goal is to provide a rational basis for maintaining, through environmental management, reasonable safety margins between environmental and body burdens of toxic agents in order to safeguard human health now and in future generations.

Accomplishments in 1977: The nature of those body enzymes that alter foreign compounds and their roles in transformation of toxic chemicals, in body clearance, and in activation of carcinogenic agents have been clarified in large part, and the groundwork has been laid for more rapid progress in understanding pathogenesis mechanisms. The processes of deposition, absorption and transfer of a number of hazardous agents have been elucidated. These processes determine the load of foreign substances with which the body must cope. Storage, toxication-detoxication and excretion, which are gross indicators of how the body copes with foreign agents, have been clarified in many cases. Studies on the processes of enzyme induction, repression, and qualitative and quantitative aspects of metabolism have contributed substantially to understanding of toxicity endpoints and differences in response to specific agents due to age, sex, species, nutrition, current and antecedent diseases, and enzymatic, immunologic and genetic factors. Research contracts which investigate the effects of ingested asbestos over a life-time exposure in experimental animals will continue. These contracts were awarded in response to the Congressional directive that the Institute initiate a long-term study on the effects of ingested asbestos. A research contract awarded in 1976 to develop biological information on the chlorinated hydrocarbon pesticide Kepone and to attempt to develop therapeutic measures of effects of Kepone will continue. This research project will continue but will be primarily supported by a grant. In addition to being implicated as a cause of serious illness in factory employees, Kepone may prove to be a cancer-producing agent in exposed employees, relatives and persons living near the factory. A new toxicity bioassay program, initiated as a result of Congressional action on the 1977 appropriation, will determine the spectrum of dose-related toxic effects associated with environmental chemicals. Much of the research will be done in conjunction with studies underway at the National Cancer Institute Bioassay Program, which seeks to evaluate chemicals for carcinogenic properties.

Objectives for 1978: The budget request provides for continuation and expansion of pharmacological and toxicological studies of environmental agents as they enter the body, are distributed, and as they disrupt the normal functions and structures of the body.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Environmental Pathogenesis
(Public Health Service Act, Title III, Part A, Title IV, Part I)

1977		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$1,908,000	Indefinite	---	$2,880,000

Purpose: The pathogenesis program deals with the details and time sequence of molecular and cellular events that culminate in recognizable diseases and other endpoints upon exposure of individuals to toxic agents.

Explanation: This work is carried out both in intramural laboratories and through grants and contracts. Diseases of the pulmonary and cardiovascular systems, the liver, kidneys, reproductive system, and degenerative disorders of long-term and complex etiology have been well documented and related to environmental factors. The program is designed to develop knowledge of initial or very early molecular and cellular lesions that will facilitate implementation and improve the effectiveness of prophylactic or therapeutic measures.

Accomplishments in 1977: Further insight has been provided into the lesions caused by lead and mercury in the peripheral and central nervous systems. Damage to the sheath in nerve fibers and damage to structures constituting the blood-brain barrier provide understanding of brain damage which is common in lead-poisoned children, and of persistent changes in learning and behavioral patterns of such children. The basis of lung fibrosis from exposure to agents such as coal dust and asbestos has been clarified in large part through studies of immunology. The relationship between cancer and other diseases of the lung and industrial dusts and irritant gases have been considerably illuminated through basic studies of inhibition of lung defense mechanisms by such dusts and gases.

Recent pharmacological studies on carcinogens have led to better correlations between structures of numerous compounds and carcinogenesis. It is now apparent that environmental agents such as benzpyrene and chlorinated hydrocarbon pesticides are activated through metabolism. Studies of structure-activity relations of the metabolites show good correlation with cancer induction whereas little correlation could be established with the parent compounds. This now simplifies the study of carcinogenesis because the molecular interactions of the primary carcinogen can be followed. Analogous studies on metabolites of other compounds that produce other types of pathological lesions have also been enhanced by understanding of the primary toxicant. Examples include carcinogenesis by nitroso compounds derived in the stomach from nitrites and hepatotoxicity resulting from the action of oxygenated derivatives of chlorinated alkanes and alkenes such as vinyl cloride, ethylene dichloride and carbon tetrachloride.

Objectives for 1978: The budget request provides for continued research on the initial or very early molecular and cellular lesions that lead to human environmental diseases or the complication of pre-existing health problems.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Intramural Research (Public Health Service Act, Title III, Part A)

1977		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
283	$12,745,000	Indefinite	283	$14,826,000

Purpose: The purpose of the intramural research program is to investigate at a fundamental level the long-term overt and subtle effects of chemical and physical environmental factors without limitations regarding the origins and sources of such factors or of limits based on disease or organ orientation; e.g. cancer vs. heart. The program complements and coordinates with all activity in this national need -- regardless whether funded by this institute or not, so as to focus needed and scarce resources on most urgent and solvable problems and to cover gap areas.

Explanation: The intramural research program consists of four laboratories (Environmental Mutagenesis, Environmental Toxicology, Environmental Biophysics, and Pharmacology) and three branches (Environmental Biology and Chemistry, Biometry and Research Services); the last three have additional responsibilities for research support.

Accomplishments in 1977: Considerable effort has been devoted to studies on the toxicity of a few selected classes of chemicals: (1) chlorinated hydrocarbons such as polychlorinated biphenyls (PCB's), dibenzofurans and dioxins, and kepone; (2) aromatic polycyclic hydrocarbons such as benzypyrene; and (3) heavy metals such as mercury, lead, and arsenic.

Pharmacokinetics and toxication-detoxication studies seek to understand and determine what pollutants do once they enter the body and how the body deals with these in effective or adverse ways. The use of pharmacokinetic approaches to establish the similarities of effects and dangers of PCB's and polybrominated biphenyls (PBB's), and to delineate possible approaches to treating people poisoned with such compounds as kepone are two examples of the many payoffs of this program.

Mutagenesis research has developed some new tests to the point where applications to screening programs in man may be possible; e.g., in populations exposed to mutagens, the incidence of abnormal hemoglobins or unusual forms of blood enzymes may increase. Ways to detect such increases in large populations have not been developed. Additional tests to be used in a several-tiered screening system for mutagenic activity of hundreds of chemicals are being validated. These additional tests will supplement the Ames mutagenesis test and help to increase reliability and extrapolation to man of these simple in vitro assays.

In reproductive toxicology, the Environmental Teratology Information Center was begun and, together with the use of in vitro embryo cultures to study fetotoxic and teratogenic effects of chemicals, gives promise of quicker, simpler exchanges and tests for teratogenic toxicity of chemicals. The mouse model of DES transplacental carcinogenicity in males and females was further validated and these results were communicated to other groups working with humans exposed to DES in utero (up to 20 years ago). With information from our mouse model it is hoped to identify early lesions of DES in reproductive tracts of adolescent boys and girls from mothers given DES.

Various models of dose-response curves in carcinogenesis have been constructed and analyzed to show that, under the conditions of many such carcinogenesis tests, the extrapolation of results from high dose to low dose cannot be made using anything except a linear dose-response relationship even though huge numbers of animals are used. This has implications for "mega-mouse" type experiments on carcinogenesis seeking to establish thresholds of effects. Such research is part of a growing program in Biometry seeking to improve the basis for extrapolating toxicity results from high to low dose and from animals to man.

Objectives for 1978: The budget request will permit the development of new programs in epidemiology, behavioral toxicology, pulmonary toxicology, as well as the expansion of existing programs.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Direct Operations
(Public Health Service Act, Title III, Part A)

1977			1978	
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
13	$1,287,000	Indefinite	13	$1,505,000

Purpose: This activity supports the review and approval of grants (Extramural Program) and the payment to the DHEW General Expense Fund, Program Evaluation, and centrally furnished services.

Explanation: This activity provides scientific and administrative management for grant supported research and manpower programs of the NIEHS (Extramural Program); payment to the DHEW General Expense Fund; Program Evaluation; and centrally furnished services.

The extramural program is responsible for surveillance of on-going grant supported programs; coordination of the scientific merit and relevance review of competing applications; liaison with applicants, grantees, advisory bodies, other components of the NIH, PHS, and other interested organizations; and compilation and reporting of scientific and fiscal information relevant to the program.

Accomplishments in 1977: The extramural program staff expanded liaison efforts with the applicant and grant community, developed operating guidelines for program and Center grants, and maintained surveillance over approximately 290 active grants and awards.

Objectives for 1978: Staff will continue to strengthen liaison activities with grantees; will expand programming efforts, particularly in the area of marine and freshwater biomedical research; and will monitor approximately 350 active grants and awards, an increase of 20% over 1977.

NATIONAL INSTITUTES OF HEALTH

National Institute of Environmental Health Sciences

Program Purposes and Accomplishments

Activity: Program Management
(Public Health Service Act, Title III, Part A)

1977		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
35	$1,031,000	Indefinite	35	$1,064,000

Purpose: This activity provides for the overall administration, coordination, and direction of the varied programs and activities of the Institute.

Explanation: Program Management encompasses the Office of the Director which provides for the overall management for and direction of the varied Institute programs and activities. Included are the functional staff areas of program planning and evaluation, program coordination, public information, legislative analysis, interagency coordination, and health hazard assessment. In addition, the program provides supervision of centralized administrative services such as budget, personnel, procurement, supply management and office services.

Accomplishments in 1977: During 1977, the Office of the Director has devoted a significant portion of its resources to the selection of the research questions which most needed investigation and to the planning and direction of the total programs of the Institute. In addition, the Director has served as the American Coordinator for the Environmental Health portion of the U.S.-U.S.S.R. Health Agreement and as Project Chairman of the work group on Biology and Genetic Effects of Pollutants under the U.S.-U.S.S.R. Environmental Agreement. The Director has also assumed responsibility for the environmental health programs under the auspices of the U.S. Egypt Joint Working Group on Medical Cooperation. The Director has served as Chairman of the DHEW Committee to Coordinate Toxicology and Related Programs. The Institute has continued its relationship with the World Health Organization as a cooperating Research Center in Environmental Health. Interagency liaison and coordination has continued through formal relationships such as those related to the Energy Related Research Program and the Toxic Substances Control Act.

Objectives for 1978: Program Management will continue to devote most of its resources to the selection and assignment of priorities to research questions and to the planning, direction, and administration of the Institute's programs.

TUESDAY, MARCH 8, 1977.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

WITNESSES

DR. ROBERT I. LEVY, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ROBERT L. RINGLER, DEPUTY DIRECTOR, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
EVELYN L. ATTIX, EXECUTIVE OFFICER, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
JOHN H. REEDER, FINANCIAL MANAGEMENT OFFICER, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
H. RICHARD MILLER, ASSISTANT DIRECTOR FOR BUDGET, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. The subcommittee will come to order.

Now we have the National Heart, Lung, and Blood Institute.

The presentation will be made by Dr. Robert I. Levy, the Director. I see, Dr. Levy, we have your biographical sketch which we will place in the record at this point.

[The biographical sketch follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—NATIONAL INSTITUTES OF HEALTH

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Name: Robert I. Levy, M.D.

Position: Director, National Heart, Lung, and Blood Institute.

Birthplace and date: Bronx, N.Y.—May 3, 1937.

Education: June 1953—Graduated from Bronx High School of Science; 1957—B.A., Cornell University—highest honors and distinction in Zoology; 1961—M.D., Yale University—cum laude.

Experience: 1963 to present—National Heart, Lung, and Blood Institute, NIH, Bethesda, Md. 1975 to present—Director. 1973–75—Director, Division of Heart and Vascular Diseases. 1970–74—Chief, Lipid Metabolism Branch, DHVD. 1969–73—Chief, Clinical Service, Molecular Disease Branch. 1966 to present—Head, Section on Lipoprotein Metabolism and Intervention, Molecular Disease Branch. 1966–68—Attending physician, Georgetown University Medical Division, District of Columbia General Hospital, Washington, D.C. 1965 to present—Attending Physician, Molecular Disease Branch. 1965–66—Chief Resident, National Heart Institute. 1963–66—Clinical Associate, Section on Molecular Diseases. 1962–63—Assistant resident in Medicine, Yale—New Haven Medical Center. 1961–62—Intern in Medicine, Yale—New Haven Medical Center, New Haven.

Association memberships: American Society for Clinical Investigation; American Institute of Nutrition; American Federation for Clinical Research; American Heart Association Council on Arteriosclerosis; New York Academy of Sciences; American Society for Clinical Nutrition; American College of Cardiology; American Society for Clinical Pharmacology and Therapeutics.

Special awards citations, or publications: Kees Prize Research Thesis, Yale University, 1961; Alpha Epsilon Delta (premedical); Alpha Omega Alpha; Phi

Beta Kappa; Phi Kappa Phi; Sigma Xi; Arthur Flemming Award, 1975; DHEW Superior Service Award, 1975; Author or co-author of approximately 160 publications; editorial board, Journal of Lipid Research, and Circulation, and Dialogs in Nutrition; Humanitarian Award, Associated Health Foundation, 1976.

Mr. FLOOD. You have some people with you that you would like us to know, I am sure.

Dr. LEVY. Yes. My financial management officer, Mr. John Reeder; my executive officer, Mrs. Evelyn Attix; my deputy director, Dr. Robert Ringler, and the Director, NIH, Dr. Donald Fredrickson.

Mr. FLOOD. We have your statement which we will place in the record.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health
Statement by the Director
National Heart, Lung, and Blood Institute

Mr. Chairman and Members of the Committee:

It is a pleasure and a welcome opportunity for me to appear before you once again. This year, we are particularly mindful of the many new mandates facing the Institute in response to the 1976 legislation which changed our name to the National Heart, Lung, and Blood Institute and extended our authority to research into the use of blood and blood products and management of blood resources.

The challenge of these new responsibilities is great. Last year an estimated 10.2 million units of blood were collected in the United States. The cost of blood diseases and blood resources plus the yearly economic costs of the other diseases NHLBI is responsible for is over $62 billion.

More alarming than the staggering economic costs are the number of lost lives attributed to these diseases. For more than 50 years, heart and blood vessel diseases have been the major cause of death in this country. They account for over 50% of all deaths annually, nearly three times the number of deaths from cancer, the next highest cause. Virtually all Americans are to some degree afflicted with atherosclerosis, over 27 million suffer from hypertension and four million from coronary heart disease alone. Lung diseases are the sixth leading cause of death in the United States and account for more than 130,000 deaths annually. Blood disorders are intimately related to cardiovascular and pulmonary disease. The impact of clotting and bleeding disorders is considerable. Thrombosis may cause pulmonary embolism, a disorder responsible for 300,000 hospitalizations and 10,000 deaths annually. Hereditary blood diseases constitute another national health problem. For example, approximately 50,000 Americans, primarily black, have sickle cell anemia, and 25 thousand Americans suffer with hemophilia.

The ultimate goal of our Program is disease prevention, a long-term objective,

but the only true cost-effective effort. Treatment is aimed at restoring quality of life and productive living. We are proud of our recent progress as measured by the latest statistics dealing with mortality from cardiovascular diseases. From 1970 to 1976 deaths due to cardiovascular disease have declined by more than 15%, more than twice the decline from non-cardiovascular disease. In 1975, the number of deaths from major cardiovascular diseases dropped below one million for the first time since 1967 despite an ever-increasing and aging population. The death rate in our country has dropped below 9/1,000 for the first time in our history; it is clear that declining cardiovascular mortality is the major responsible factor.

Program Strategy

The program strategy employed by the National Heart, Lung, and Blood Institute consists of an ordered sequence from: acquisition of new knowledge, through fundamental, applied and clinical research; testing and validation of promising hypotheses via clinical trials; and application of new and existing knowledge by education and demonstration programs. Progress was and continues to be made in each area of this strategy.

I would like to summarize some of the accomplishments made in the cardiovascular, pulmonary and blood areas over the past year and highlight some of our newer manpower development programs and education activities.

Heart and Blood Vessel Diseases

Atherosclerosis, a slow progressive blood vessel disease which may start in childhood and produce no symptoms for 20-50 years or longer contributes to an estimated 84% of deaths from heart and blood vessel disease. The primary goal of the NHLBI research program is to prevent or postpone atherosclerosis and thereby reduce its morbidity and mortality. Fundamental research is concentrating on explaining the etiological and pathophysiological effects of high blood pressure, high cholesterol, diabetes and smoking, the four major risk factors for this disease. Three major clinical trials, the Multiple Risk Factor Intervention Trial,

the Lipid Research Clinics Coronary Primary Prevention Trial, and the Hypertension Detection and Follow-up Program represent a concentrated effort by NHLBI to test the efficacy of risk factor-lowering on cardiovascular disease.

Exciting progress is being made in the development of non-invasive instrumentation for the detection, characterization and quantification of atherosclerotic lesions and plaque in major arteries. Coordinated efforts by NIH scientists and physicians have resulted in a new technique, called radionuclide cine-angiography, for viewing the heart by computer-based movies. This technique for the first time enables actual non-invasive visualization of the walls of the beating heart during exercise and allows detection of abnormal cardiac muscle function, as well as precise measurements of the work of the heart. Most importantly, this unique and sensitive procedure coupled with echocardiography (the use of ultrasound) offers less risk to the patient and often the same or more information to the internist or surgeon than the present more costly conventional mode of diagnosis, cardiac catherization.

Hypertension, a major contributory factor to the more than 1,500,000 heart attacks and strokes each year, has been a major focus of our prevention, education, and control programs. Recent statistics indicate that the awareness of the American public to the dangers of hypertension have increased greatly. Total patient visits for high blood pressure have increased by 50% since the National High Blood Pressure Program began in 1972. Long-term compliance and adherence to treatment regimens is now the challenge. The NHLBI-supported Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure published guidelines in the January 17th issue of the Journal of the American Medical Assoication representing a consensus on therapeutic and diagnostic measures for hypertension. The report states that although the recommendations represent a cost-beneficial, practical approach to diagnosis and treatment, the quality of care has not been compromised.

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Another of the tangible benefits of the National High Blood Pressure Education Program has been an increased awareness of the benefits of hypertension control in the work setting, an appropriate place to reach a large segment of the unscreened population.

NHLBI is also developing a specific program in response to last year's congressional mandate to measure the effectiveness of statewide coordination of high blood pressure control. The Institute, working with State Health Departments, has proposed a pilot project to achieve and measure the impact of a large scale coordination of available resources into an efficient well organized control effort. The Institute has also established a Task Force on Hypertension to advise on the status, needs, and opportunities for biomedical research on high blood pressure.

The Institute recently launched a major effort to assess opportunities and needs for research in childhood heart diseases, in particular, congenital and acquired heart disease and the prospect of determining precursors of heart and vascular disease in the adult. Seven of every 1000 infants born alive suffer from congenital heart disease. Many researchers are now emphasizing that adult hypertension may have its origin in adolescence or infancy. However, relatively little has been done to identify the forerunners of high blood pressure. To remedy this, the Institute has initiated a program for the epidemiological investigation of the determinants of high blood pressure in the young. Diabetes, another disease which may start during childhood clearly is an independent risk factor for coronary heart disease, sudden death, congestive heart failure, stroke and peripheral vascular disease in adult life. In the past year, NHLBI solicited proposals to study the relationship of cardiovascular disease to diabetes. Because of enormous investigator interest, a second program focusing on diabetic cardiomyopathy will be initiated this year.

Lung Diseases

The Institute's program in lung diseases evolved and matured by originating new types of efforts aimed at filling particular research needs and capitalizing on opportunities to translate research results into health care applications. Most illustrative of the success of this approach is the program on structure and function in which a more sophisticated perspective on the lung has evolved. It is no longer viewed as a "bellows" but as a complex organ comprising many kinds of cells with an elaborate network of connective tissue performing various non-ventilatory functions.

Infantile respiratory distress syndrome (IRDS) is currently the principal pulmonary disease and the major cause of perinatal mortality. It accounts for approximately 12,000 neonatal deaths and 800,000 hospital days per year. Intensive multidisciplinary studies during the past 5-7 years have enhanced our knowledge of lung maturation, and this knowledge has been applied and coordinated rapidly with clinical findings; however, many important problems are still unresolved.

Prevention of IRDS remains a highly desirable goal and it may be possible by proper use of pharmacological interventions. The most promising drugs at present are corticosteroids, which in animal studies have proved effective in maturing fetal lungs when administered to the mother shortly before parturition. Data from one controlled clinical trial suggest that corticosteroids may be similarly effective in the human neonate. A clinical trial has recently been initiated in the United States to evaluate the effectiveness of corticosteroids in decreasing the incidence of IRDS. This study will also identify short or long-term adverse effects that may be associated with this treatment.

Chronic bronchitis and emphysema are the major contributors to the progressively debilitating, generally irreversible condition known as chronic obstructive lung disease or COLD. Asthma, cystic fibrosis and bronchiolitis may also be involved. A particularly difficult aspect of the problem is that chronic bronchitis and emphysema

develop so insidiously that many victims are unaware of their condition until irreversible lung damage has occurred. For this reason, great emphasis has been placed on research into the early detection of structural, physiological and biochemical abnormalities which precede the development of more symptomatic, relatively irreversible disease.

Due to the relative irreversibility of COLD, current therapeutic approaches are largely palliative and symptomatic. Cessation of smoking and avoidance of pollutants and other irritants will reduce cough and sputum production, and may slow the rate of progression of disease. Other types of treatment include the use of bronchodilators, corticosteroids, mucolytics, antibiotics and cnest physiotherapy. A controlled clinical trial has been initiated to evaluate the effectiveness of long-term intermittent positive pressure breathing (IPPB) treatment used an as adjunct to the overall care of ambulatory COLD patients. The cost of IPPB treatment in the United States is tens of millions of dollars per year.

Blood Diseases

Research approaches to blood diseases address a range of problems involving the formed elements (red blood cells, white blood cells, and platelets) and the whole complex of plasma proteins essential for control of clotting. No longer is hematology a single discipline concerned mainly with blood cells. Today the study of the blood groups, the numerous genetic variances of hemoglobin and red cell enzymes, the hemostasis mechanism, and the many other applications of the science of blood banking have become subspecialties in their own right. NHLBI's new mandate calls for the coordination of blood research in the various institutes. Our blood program seeks to improve the diagnosis, prevention, and treatment of blood diseases and related disorders; to assure the efficient and safe use of an adequate supply of high quality blood and blood products; and to promote the application of tissue and organ transplantation through a better understanding of transplantation biology.

The term hemophilia is applied to several different hereditary bleeding disorders caused by a deficiency of protein coagulating factor activity. The hemophiliacs under treatment have a median age of 11 years. The average cost of blood products alone is estimated to be approximately $2400 per year. Current treatment of hemophilia centers on blood transfusion in response to hemmorhage. Our basic research effort is aimed at isolating Factor VIII and investigating its role in the coagulation scheme and on platelet function. Recent evidence indicates that Factor VIII is present in hemophilic patients but is abnormal. Significant advances have been made in purification and characterization of the Factor VIII molecule. This progress should lead to better methods of treatment of hemophilia.

Blood substitutes (perfluorochemicals) once fully developed have tremendous potential value in that they would supplement and conserve the natural blood supply. Animal transfusion studies using blood substitutes have been highly encouraging. Primates have been maintained for several hours with up to 80% of their blood replaced with synthetic-type substitutes. Small animals have been completely transfused with substitutes. The animals recover and continue to live normal lives while replacing the blood substitute with their own blood.

Although sickle cell anemia and related severe hemoglobinopathies have been recognized for many years and numerous clinical and laboratory manifestations have been described, the clinical course of sickle cell disease is poorly documented. The ability to establish predictable interrelationships among signs, symptoms and laboratory test results is complicated by the complexity of the interaction of basic disease processes with other health-related events. Accurate delineation of the natural history and clinical course of sickle cell disease is necessary to an understanding of cause and effect factors related to variations in this disease. The Institute is planning a study of the natural history of sickle cell disease.

Cooley's anemia is an inherited hemolytic anemia in which patients are unable to synthesize normal amounts of hemoglobin. Blood transfusion remains the mainstay of

therapy; however, continual transfusion results in an iron burden, which in turn leads to significant morbidity and mortality. The Institute is supporting studies with iron-binding compounds to investigate whether such drugs will reduce the iron burden.

Clinical Trials

Clinical trials are an effective means and, often the only means, of resolving some particularly pressing scientific problems. Through careful accumulation and critical analysis of data, clinical trials lead to more rational and effective medical practice with less reliance on simple empiricism. One should not lose sight of the fact, however, that clinical trials commit an Institute to outlays in terms of budget and staff that far exceed those needed for the administration of other research projects. Several of our current trials are aimed at prevention or delay in onset of cardiovascular disease. Other trials are evaluating treatments to improve the quality and length of life. For example, the Coronary Artery Surgery Trial was initiated because over 50-60 thousand coronary bypass operations are now performed each year at a cost of one-half to over one billion dollars per year. While these patients apparently enjoy an improved quality of life, there is no convincing evidence demonstrating increased survival.

The Institute feels that clinical trials leading to prevention and treatment validation are so important that in FY 1976, over $50 million, or over one-eighth of the Institute's total budget, was spent on clinical trials. Though the outlays are large, the Institute feels it must continue to sponsor such trials. For example, a new trial of antiarrhythmic drugs to prevent sudden death in high risk patients is being planned at the present time because preliminary data from foreign studies show considerable promise. The savings in life and dollars would be great if we could control heart arrhythmias and prevent sudden death.

Training

As the Institute's mandate's continue to increase, its programs evolve in greater depth and scope. Newly trained scientists must be available to utilize the latest and more complex diagnostic techniques and sophisticated research approaches as well as to replace their older colleagues as they retire or move out of research and teaching. The general prospect for the next few years is a rising demand for new entrants into heart, lung, and blood disease research, especially in the new pulmonary and blood programs which have resulted from the 1972 National Heart, Blood Vessel, Lung, and Blood Act and its renewal.

The research training and manpower programs are developed and pursued by the Institute in relationship to the new and unique missions defined by legislation. The Minority Hypertension Research Development Summer Program was developed in response to the identified need for minority investigators in problems related to hypertension. This program, initiated in FY 1977, provides summer research experience for minority school faculty and graduate students, and will communicate knowledge of opportunities and required research skills to minority individuals within their own institutional settings. The Young Investigator Research Grant Program was introduced in the pulmonary area in 1974. As a result of the program's initial success, the program was expanded in 1976 to include the heart and vascular, and blood areas. The purposes of this program are to encourage research in fundamental as well as clinical disciplines, and to provide young investigators with modest support for a project of their own design. The success and value of the program have attracted considerable interest, and the program is serving as a model for similar programs now being developed by other Institutes at NIH.

Prevention, Education and Control

In response to mandates requiring greater concern for the translation and dissemination of research results, the National Heart, Lung, and Blood Institute has

identified fruitful areas for NHLBI activity, defined the resources necessary for carrying out these activities, and assisted the community in the development and implementation of prevention and health education programs. Proceedings of four NHLBI supported conferences have served as the impetus for the initiation of research in the health behavior area, in particular the reduction of heart attack and stroke, the relationship of emotional stress to the pathophysiology of sudden cardiac death and the methods of producing dietary behavioral changes. The Institute also has initiated a Task Force on Prevention, Education and Control for Pulmonary Diseases, whose report to be released this year, outlines the issues of primary concern in the area of chronic lung diseases. A task force in the area of prevention, education, and control of heart and vascular diseases will make its recommendations at the end of the calendar year. A blood task force has just begun deliberations. The recommendation from these task forces will be translated into education and demonstration programs.

In addition to the National High Blood Pressure Education Program and our three National Research and Demonstration Centers, several specific targeted programs are aimed at hastening the transfer of knowledge. A program has been initiated to develop and evaluate methodologies to motivate practicing physicians without specialty training in pulmonary medicine to seek and use continuing education resources in the field of pulmonary medicine. An allied goal is to evaluate procedures for assessing the impact of continuing education on the quality of care of patients with pulmonary diseases.

Tutorial programs initiated by the Comprehensive Sickle Cell Centers for students with sickle cell anemia have resulted in a decrease in school absenteeism, increased scholastic achievements, a decrease in the psychological pressures of adaptation, and overall increase in self esteem. Vocational rehabilitation of patients with sickle cell anemia is provided through individual career counselling. In addition

to help in making career selections, this service also assists in developing skills in older patients and increases their ability to become self-supporting. As a result of the evaluation of emergency room care for sickle cell patients at a large city hospital, a protocol for emergency room care which not only deals with treatment but also highlights clinical symptomatology and the considerations for a differential diagnosis has been developed. Increased awareness of the house staff, nurses, etc., has contributed to a marked improvement in management of patients with sickle cell anemia in the emergency room.

Coordination

The Institute, as part of its responsibilities to provide leadership for the National Program, continues to coordinate those aspects of all federal health programs and activities that relate to heart, lung, and blood diseases. The Interagency Technical Committee, established by the 1972 Act, has developed interaction and coordination throughout government in high blood pressure education, pediatric pulmonary diseases, sickle cell disease education, nutrition composition studies and cardiovascular biomedical engineering.

In conclusion, Mr. Chairman, we have provided a few recent highlights of our programs, both scientific and administrative aimed towards the prevention of heart, blood vessel, lung and blood diseases. We have chosen these examples to show the continuum of our efforts from fundamental knowledge acquisition to dissemination of clinical information. The budget request for the National Heart, Lung, and Blood Institute for 1978 is $403,642,000. I shall be pleased to answer any questions and supply additional information desired for the record.

GRANT AND CONTRACT FUNDING

Mr. FLOOD. On the 1978 budget you have an increase here of $7 million, but in spite of that increase of $7 million you show a reduction in the dollar level for new and competing research awards. Why is that?

Dr. LEVY. It is related to many things. It is primarily related to the fact that we have an increase in our noncompeting research grants relating to the awards that we have made in previous years. As for dollars for new research grants for fiscal year 1978 we estimate that there will be available somewhere between $17 and $20 million for new regular research grants.

Some of the dollars here are earmarked for a competitive renewal of comprehensive sickle centers. These figures compare with about $27 million available for the new research grants in fiscal 1977 and some $36 million spent for new research grants in fiscal 1976. As far as competing renewal grants we project $21 million will be available in fiscal year 1978 as compared to $27 million in fiscal year 1977.

Mr. FLOOD. With respect to the research and development contract program you only will be able to fund about 90 percent of these commitments in that particular program. What is going to be the impact of a 10-percent reduction in the level of effort and the program which will be most affected by such a cut?

Dr. LEVY. We are concerned about this, Mr. Chairman. Traditionally we fund our contract commitments at 100 percent. As you know, over 70 percent of our contract commitments are for the multicenter clinical trials that we have discussed here before. We obviously are going to have to cut corners or delay the onset of several clinical trials, several of which are mentioned in my opening statement.

Another option is to reprogram money from the grant line to pay this contract commitment. Of course, that would result in our paying less than 10 percent of approved new and computing renewal research grants.

Mr. FLOOD. That is the reason I asked you.

Dr. LEVY. We have distributed this money this way with a $10 million deficit in our contract program to attempt to meet at least part of the dollar needs for new research grants receiving excellent priority scores.

DECLINE IN DEATH RATE

Mr. FLOOD. Also, in your budget justification there you list some statistics. They show a decline in the death rate from stroke, hypertension, rheumatic heart disease. What is the source of all the information? What is the source of all those statistics?

Dr. LEVY. The statistics are all from the National Center for Health Statistics. We are very pleased with the results. The results show that we are winning the fight in terms of prevention of cardiovascular disease.

Mr. FLOOD. It was the source we were concerned about. Now on the age and sex adjusted basis, do these statistics we are talking about show a greater improvement in certain population groups while other groups remain at pretty much the same level for several years?

Dr. LEVY. Well, there are several things that can be said.

First of all, what the results show without age adjustment is that for the first time in the last decade there has been an absolute fall in heart disease deaths. The decline is becoming steeper. If we compare the years 1974 to 1976, there are 50,000 less heart attack and stroke deaths in 1976 than 1974. That is a reduction in deaths more than if we wiped out all automobile accident deaths.

In terms of who this is occurring in, it is both in males and females. The death rate is decreasing more in patients in the younger age group and more in patients with acute disease rather than chronic heart disease.

Mr. FLOOD. You have a greater survival rate for under 40 but no improvement at all over 65.

Dr. LEVY. No; there is an improvement in over 65. The improvement is not as dramatic, however, as in the group from age 40 to 65. But there is an improvement in all age bands and both sexes, Mr. Chairman.

FACTORS IN DECLINE OF HEART DISEASE

Mr. FLOOD. We read recently for the first time since 1967 death from all forms of cardiovascular disease, all forms, had dropped below the 1 million mark. Well, that is very significant. To what do you attribute that very significant decrease and can you relate any specific research advances and programs in your Heart Institute for this?

Dr. LEVY. Mr. Chairman, it is difficult to pinpoint one aspect when you have a population laboratory as diverse as the United States. But we can point to several specific things.

Mr. FLOOD. One thing, of course, that we have been concerned about that we have heard so much about is the matter of early detection and better treatment. We have the emergency medical system, the delivery of the heart attack victims to the hospitals much faster and in much better condition.

Dr. LEVY. Yes, and there are other major factors as well relating to disease prevention such as the initiation of the national high blood pressure education program in 1972 and the public's increased awareness of the dangers of cigarette smoking. The middle-aged male is smoking 25 percent less now than he was a decade ago. The coronary care units are having a decided effect on the acute heart attack mortality. People are more aware of the signs and symptoms of cardiovascular disease.

We also have evidence that the American public is changing its nutrition habits and that the amount of cholesterol and fat consumed in the diet is decreasing.

All of these factors are contributing to the rate of decline. It is intriguing that the sharpness of the decline, 22 percent in stroke and 16 percent in heart attack, follows chronologically the national high blood pressure education program's beginning.

Mr. FLOOD. Do you have a study of the research plus a comparison of the research versus health care to look at that?

Dr. LEVY. Clearly it is a combination of new research insights, new ways of treatment, diagnosis and prevention plus getting the information out to the practicing physician and the public as well as the public's beginning to take notice of these hints on how to prevent and

control disease that are making the difference. It would be impossible to emphasize any one item. They have all been important.

Mr. FLOOD. Can there be further reductions in death due to this?

Dr. LEVY. Looking at what has occurred over the last few years I would say that the promise for the future is very great, especially if we have the wherewithal to continue the research and to get the research results regarding improved diagnosis and treatment to the practicing physician and the new information on how and why to maintain good health habits to the public.

LOSSES ATTRIBUTABLE TO HEART DISEASE

Mr. FLOOD. Also, in your statement you mentioned that the economic losses attributed to diseases that your Institute is responsible for total $62 billion. That is a very intriguing number, $62 billion. Can you tell us briefly how did you calculate a number like that? You can just tell us briefly and by all means for the record insert the details of just how you made that kind of a calculation. You must have had a number of assumptions and for the record show us the assumptions.

Dr. LEVY. Actually we did not do that. Dorothy Rice, the current Director of the National Center for Health Statistics, did that. We merely took her paper that was based on 1972 figures and extrapolated to the present. What I would emphasize in that cost figure is that two-thirds of the cardiovascular cost is not for high technology or cost of care. Two-thirds of the cardiovascular cost described in Dorothy Rice's recent report is for lost wages and lost productivity due to premature death. That is why we are so excited with the decrease in heart disease death rates.

I would be pleased to develop the information on the cost of cardiovascular, lung, and blood diseases further for the record.

[The information follows:]

COST OF CARDIOVASCULAR, LUNG, AND BLOOD DISORDERS

The initial source of the economic impact information comes from a manuscript entitled "The Economic Cost of Illness Revisited," by the Office of Research and Statistics, Social Security Administration, compiled by Barbara S. Cooper and Dorothy P. Rice. That data presented economic costs as of 1972. The figures presented here have been conservatively extrapolated to 1976. The comparable mortality and other health statistics have all been obtained from the National Center for Health Statistics.

Economic costs of heart, lung, and blood diseases are dollar costs to society in terms of: 1. Health expenditures for hospital services, physicians' services, drugs, nursing home care, and similar expenditures attributed to these diseases. Utilization and cost data are obtained from national surveys of hospital discharges, physician visits, drug prescriptions, et cetera, and from costs reported by medicare and health insurance agencies. Data are primarily from the National Center for Health Statistics, medicare, Aetna, the National Disease and Therapeutic Index, and the National Prescription Audit. 2. Morbidity costs, that is, lost earnings incurred when illness from these diseases results in absence from employment or usual activities (for example housewife). Lost work days from these diseases are multiplied by mean annual earnings. Data are primarily from the National Center for Health Statistics, the Bureau of the Census, and the Bureau of Labor Statistics. 3. Mortality costs are calculated by multiplying the number of deaths from these diseases by the present value of lifetime earnings. Estimates of the present value of lifetime earnings take into account: Earnings, labor force participation, life expectancy, and a discount rate.

CLINICAL TRIALS

Mr. FLOOD. What percentage of your budget would be invested in the clinical trials? What specific trials are you supporting right now?

Dr. LEVY. Over $50 million, over one-eighth of our budget is invested in multicenter clinical trials. Some of these trials are designed to show that we can either prevent or delay heart or lung disease.

Others are designed to see if we can improve the quality of life. I have talked about several of the trials before. Perhaps today I might highlight the results of a trial, a trial that will be presented tomorrow at the American College of Cardiology meetings in Las Vegas.

It is estimated that 50,000 to 70,000 coronary artery bypass procedures are being performed a year now at a cost of between $500 million and $1 billion. The procedure clearly relieves chest pain, but whether it increases the length of life, and in what patients it should be done, and when, is still not clear.

We have a large coronary artery surgery trial that has just been begun. The smaller trial whose results will be presented tomorrow was begun over 4 years ago in the myocardial research units.

Mr. FLOOD. Is there a backing away from this surgery?

Dr. LEVY. As a result of the trial there probably will be. The trial randomized a group of patients with unstable angina, impending heart attacks. Half of them were randomized to strict medical treatment and the other half to surgical treatment, coronary artery bypass surgery. The trial results reveal that there was no benefit, no prevention of heart attack, no decrease in death among those patients who had emergency coronary artery bypass surgery.

The investigators concluded that the emergency treatment of patients with impending heart attacks by coronary artery surgery is not usually indicated. Clearly that result to be presented tomorrow will have a major effect on our health care delivery system.

Mr. FLOOD. Mr. Michel?

Mr. MICHEL. Thank you, Mr. Chairman.

RESEARCH GRANT FUNDING

Doctor, in the area covered by your Institute, what percentage of the research grant applications received during the past year have actually been funded?

Dr. LEVY. In 1976 we were able to fund about 60 percent of our competing research grants. In 1977, this year, we estimate that we will be able to fund 45 percent. In 1978 we may be able to fund 30 percent of competing research grants at this budget level.

Mr. MICHEL. What percentage of the grant applications approved by the study groups have actually been funded?

Dr. LEVY. I am sorry, the figures I was giving you represent those that were approved by the study sections. Of those submitted, the numbers would be proportionately less. I could provide that for the record. The numbers I provided you with were for the percentage of approved grants that we have been able to fund. This has gone from 60 percent in fiscal year 1976 to 45 percent in fiscal year 1977 to less than 30 percent in fiscal year 1978.

[The information follows:]

GRANTS OF FUNDABLE PRIORITY VERSUS GRANT APPLICATIONS RECEIVED, NHLBI

	Fundable percentage of applications received	
	Number of grants	Dollars
1976 actual	43	30
1977 estimated	26	28
1978 estimated	10	10

Mr. MICHEL. What is the average length of grants?

Dr. LEVY. About 3.2 years.

Mr. MICHEL. What percentage of total grant applications represent new requests?

Dr. LEVY. Of those that are competing in this Institute, we pay about two-thirds new, one-third competing renewals. Thus, when we include noncompeting continuations, about 20 percent, or close to 20 percent, of the grants we pay each year are new grants. That is a little higher than the NIH average and has been so for the last several years.

TRAINING GRANT PROGRAM

Mr. MICHEL. Now you have a training program for which you are projecting the expenditure of $20 million. Is there really a shortage of trained scientists?

Dr. LEVY. Yes, Mr. Michel, there is indeed a shortage. This Institute represents the heart, lung, and blood communities. In the blood area, we have a new mandate in the area of blood banking. It is the unanimous opinion of the advisory committee to the blood division composed of experts in the field that there is a shortage of trained research-oriented blood banking personnel. In lung it is clear there are not enough pulmonary doctors in the universities to take the jobs available.

In the heart field we are most concerned, that although our research training trends show the total number of Institute trainees are about stable over the past 6 years, the number of trainees in heart research has decreased by almost 50 percent in the last 4 years.

Mr. MICHEL. What do you attribute that to?

Dr. LEVY. The availability of funds and the unstable nature of the training programs which have been ever changing over the last few years. We are concerned about this.

Mr. MICHEL. Do we have to assume that these training programs also produce research along the way or are they strictly training?

Dr. LEVY. These training programs are to train researchers, that is they nurture our next decade's producers of research results. It is clear, however, that in training many of these young men and women end up producing new and important information.

EMERGENCY MEDICAL CARE

Mr. MICHEL. In that citation of the reduction in cardiovascular cases, is any of that attributed to what progress we have made in emergency medical care and treatment?

Dr. LEVY. Clearly a portion of that can be attributed to emergency medical treatment, programs like that in Seattle, programs in Miami, the public's awareness of cardiopulmonary resuscitation and what it can do, is saving lives.

The most striking advances, however, are not in patients with chronic heart disease, but they are in patients whose first sign of heart disease may be their last. Probably only a fraction of our cardiovascular reduction in mortality can be attributed to the emergency procedures. In the future, we would like to get to the patient before there is a need for emergency procedures.

CLINICAL TRIALS

Mr. MICHEL. You have 3 clinical trials underway to test the ways of lowering the risk factors for cardiovascular disease. Are there any preliminary results on those yet?

Dr. LEVY. All of these trials are blinded which means that the investigators, as well as most of those in the Institute, are not privy to the results of the trial. They are all in followup. The hypertension detection and followup program is the furtherest along. It has gone through 3 of its projected patient followup 5 years. The multirisk factor intervention trial and the lipid research clinics primary prevention trial are going into their second followup year.

All the studies are on target. The data and safety monitoring committees that watch the studies course for signs of toxicity and end point lowering have not sent us any distress messages but as far as how we are doing since the results are blinded we do not know. We do have some open evidence that tells us that in the hypertension detection and followup program we are achieving sustained reductions in blood pressure in the treated groups. We can see that in this community-oriented program we can achieve a significant blood pressure reduction and maintain it for over 3 years.

Mr. MICHEL. The full length of the trials, will they be 5 years?

Dr. LEVY. Each trial is different. Followup for the hypertension detection and followup program is for 5 years. In the multirisk factors intervention trial 6 years of followup are planned and in the lipid research clinics' coronary primary prevention trial 7 years are projected.

Mr. MICHEL. All three of them have gone to 3 years?

Dr. LEVY. The hypertension detection and followup program is through 3 years and the other two are into their second year.

CORONARY PLAQUES

Mr. MICHEL. Has any progress been made in developing ways of reducing or eliminating plaque?

Dr. LEVY. Very exciting progress has been made in animals, in nonhuman primates. Last year I told the committee that we could demonstrate that regression and reversal of atherosclerosis could occur. Now it has been shown enough times in the nonhuman primates that the question is no longer whether regression, that is, reversal of atherosclerosis can occur, but rather what factors produce reversal. For example studies show that if the nonhuman primate's cholesterol is lowered to 300 mg percent, reversal will not occur. If it is lowered to 200 mg percent, however, the atherosclerotic plaque will regress.

There are other studies of this sort now that are very encouraging to all of us in that the nonhuman primate—the monkey—is as close as we can get to man without studying humans.

Mr. MICHEL. I had a legislative assistant who just underwent a tour out at Georgetown. His cholesterol count was 456 when they took him in which obviously was very bad.

Dr. LEVY. One of our problems today in man is in being able to watch coronary plaques change. We are developing noninvasive techniques, like ultrasound (sonar) and high-energy image intensity X-rays to enable us to visualize large blood vessels and see whether changing diet or using drugs will cause the atherosclerotic plague to go away.

HYPERTENSION RESEARCH

Mr. MICHEL. How much are you spending on hypertension research?

Dr. LEVY. Approximately $52 million now on hypertension research, but that covers the gamut from basic research to the clinical trials to our high blood pressure education program.

Mr. MICHEL. Is that an increase over last year?

Dr. LEVY. Yes, sir.

THERAPEUTIC AND DIAGNOSTIC MEASURES FOR HYPERTENSION

Mr. MICHEL. Your statement indicates that the Joint National Committee on Detection, Evaluation, and Treatment recently published guidelines in the AMA Journal representing a concensus on the therapeutic and diagnostic measures for hypertension. Could you summarize for us the gist of these guidelines and then provide something more expansive for the record?

Dr. LEVY. I would be pleased to. Perhaps the key point which is in the first page of the guidelines is that though this is a cost-effective and practical guide it does not compromise patient care. The report describes the cut points that physicians should use for detection; what levels they should go ahead and treat immediately and at what levels they should merely watch the patients, what levels should they just advise the patient to have a checkup. They recommend the blood tests that should be done to evaluate the patient. They advise on the steps in treatment using mild drugs and then stronger drugs depending on how difficult it is to control blood pressure.

Perhaps the most exciting thing about this is that it is the first time that we have been able to achieve concensus in the cardiovascular community among the large numbers of different primary and secondary care groups who meet and see patients with high blood pressure.

[The information follows:]

HYPERTENSION GUIDELINES

Prior to blood pressure measurement, the patient should be asked whether he has been or is currently under treatment for high blood pressure. Anyone under treatment should be encouraged to continue. The blood pressure should be taken with the subject seated and resting comfortably with his arm suitably bared. Both systolic and diastolic pressures should be recorded, with the diastolic pressure being equated to the disappearance of sound. Each subject should be informed of the numerical value of his blood pressure in writing and why further evaluation or only periodic measurement is needed.

All adults with diastolic blood pressures of 120 mm Hg or above should be referred promptly to a source of medical care. All persons with blood pressures of 160/95 mm Hg or above should have the blood pressure elevation confirmed within 1 month. All persons under the age of 50 with blood pressures between 140/90 mm Hg and 160/95 mm Hg should be checked every 2 to 3 months. All persons over 50 years of age with blood pressure between 140/90 mm Hg and 160/95 should be checked every 6 to 9 months. All adults with diastolic blood pressures below 90 mm Hg should be advised to have their blood pressure checked yearly. Patient education begins at the same time the blood pressure is initially measured. Without alarming the patient, the person taking the pressure must carefully communicate the importance of following the recommended action.

Blood pressure measurements, whether by physicians or other health professionals, must be undertaken carefully. Training in blood pressure measurement should be required and conducted under the supervision of a physician or other qualified personnel. Groups or individuals who plan to measure blood pressure must insure an adequate system for repeating blood pressure measurements and for prompt referral of patients. Nonphysicians following these protocol's and specifically avoiding statements implying diagnosis should not be considered as engaging in the practice of medicine.

It is recommended that all routine pretreatment workup be limited to history, physical evaluation, and basic laboratory tests: hematocrit; urinalysis of protein, blood, and glucose (dipstick); creatinine and/or blood urea nitrogen; serus potassium; and electrocardiogram. Other tests which may be helpful include a chest X-ray, blood sugar, serum cholesterol, serum uric acid, microscopic urinalysis, and blood count.

The first goal of antihypertensive therapy is to achieve and maintain diastolic pressure levels at less than 90 mm Hg with minimal adverse effects—the patient must be treated to a defined endpoint. This can be accomplished in 80 percent to 85 percent of hypertensive patients regardless of the initial severity of the disease. Factors which influence the decision to begin drug treatment at diastolic blood pressure levels of 90 to 105 mm Hg include: Elevated systolic blood pressure; presence of target organ damage, for example, left ventrical hypertrophy; family history of the complications of hypertension; male sex; smoking habits; elevated blood cholesterol level; and diabetes.

The regimen recommended calls for initiating therapy with a small dose of an antihypertensive drug, increasing the dose of that drug, and then adding, one after another, other drugs as needed. The dose of each drug initially is low and subsequently is increased as needed to reach a predetermined therapeutic goal. Tranquilizers and sedatives are not effective in lowering blood pressure and should not be used as primary therapy.

The first step in the recommended program should ordinarily be a thiazide-type diuretic, starting with less than maximal dose. If the therapeutic goal is not achieved with the diuretic alone and a review of the possible reasons for treatment failure has been made, an additional drug should be added as the second step. There are several alternative second drugs; reserpine, methyldopa, or propranolol. When a third step is needed, hydralazine may be added to the regimen. If the first three steps of the stepped-care regimen are ineffective and the causes for unresponsiveness have been investigated, substitution or addition of guanethidine in increasing doeses for one of the step 2 drugs is indicated. Clonidine and prazosin may also be substituted for a step 2 drug.

Management of high blood pressure must be considered a lifelong endeavor, with the leve's of blood pressure the criteria of its adequacy. After normal levels are achieved, it may be possible to reduce drug therapy; however, rarely is it possible to discontinue treatment. This point should be emphasized to the patient. Once blood pressure has been stabilized at normotensive levels, followup visits in asymptomatic patients may be appropriately handled by nurses under a physician's supervision.

This information is condensed from the "Report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure" published in the Journal of the American Medical Association, January 17, 1977. While the emphasis is on drug therapy for hypertension in high risk persons, the NHLBI is also examining nutritional approaches to controlling hypertension and other cardiovascular disease. It is clear that Americans consume far greater amounts of salt than are physiologically necessary. Large numbers of Americans, perhaps as many as 25 percent, are heavier by 20 percent or more

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than their ideal weight. Both factors are associated with hypertension. Obesity especially multiplies the risk of untoward events when it occurs in conjunction with hypertension. As an additional step in an active cardiovascular nutrition education effort, the Institute plans to enlarge the scope of its hypertension program to include weight control in hypertension.

DIABETES AND CARDIOVASCULAR DISEASE

Mr. MICHEL. How much are you spending on research to determine the relationship between diabetes and cardiovascular disease?

Dr. LEVY. In 1977 we project we will be paying about $11.9 million for direct diabetes-related research and considerably larger numbers of dollars for indirect by diabetes related studies like our risk factor trials.

BLOOD

Mr. MICHEL. If I recall correctly, some of these reports around the country were to the effect that we have a shortage of blood supplies in the country, is that true?

Dr. LEVY. We think that things are better now. As you know, the national blood policy was promulgated by the Secretary to supply a safe and sufficient blood supply whenever and wherever it was needed.

There have been several improvements. The risk of hepatitis is down considerably primarily because our volunteer donations have increased and the paid donations have decreased. It is estimated that only 7 percent comes from paid donations as compared to 22 percent only a few years ago. The American Blood Commission, an organization of the private sector which includes the three major components of the blood services complex, the American Red Cross, the American Association of Blood Banks and the Council of Community Blood Centers. is moving to solve problems in regionalization and distribution. Where their interests and our interests concur, we work together.

Mr. MICHEL. Thank you.

We will submit some others for the record.

HYPERTENSION STATISTICS

Mr. FLOOD. Mr. Natcher?

Mr. NATCHER. Doctor, in your statement you advise the committee that we have 27 million people now suffering from hypertension. I believe last year your figure was 23 million. What statistical source do you use now for your information, Doctor, just as a matter of curiosity?

Dr. LEVY. The same source we used last year, the National Center for Health Statistics. The difference between 23 and 27 million people deals with the fact that in the National Center for Health Statistics survey in addition to the 23 million patients found to be hypertensive when screened, 4 million Americans were normotensive when screened but on blood pressure lowering drugs. They did not have high blood pressure at the time. We assume that they represent hypertensives on treatment.

So the total is 27 million (23 million hypertensives plus 4 million normotensives on blood pressure lowering drugs). That is patients with blood pressures of 160 over 95 or higher. Physicians in practice

often use 140 over 90 as the level or cutoff to define hypertension. If we use that cutpoint, the number of hypertensives in the United States increases to a little over 50 million.

SICKLE CELL ANEMIA

Mr. NATCHER. Tell us what you are doing as far as research is concerned in sickle cell anemia, briefly. What about your research now as far as sickle cell anemia is concerned?

Dr. LEVY. In the basic area we are still trying to understand the basic process of sickling, the gelation. We are studying the control of the hemoglobin genes so we can get the patient's blood-forming tissue to a more soluble hemoglobin. This would be fetal hemoglobin, the hemoglobin that is present in the newborn but that lasts only a short period of time. We are trying to learn how to switch its production back on.

In the clinical arena we are still evaluating antisickling drugs. Cyenate has shown some promise used outside the body extracorporeally to bathe the cells. We are beginning a study of the natural history of sickle cell disease because we don't have a carefully documented set of observations of the relationships between the different environmental influences, clinical signs, and laboratory findings that makes sickle cell disease so different in different individuals.

So we are beginning a large natural history study so that we can see what factors worsen or improve the course, the risk for crisis in the patient. Finally, of course, we have our sickle cell disease education program aimed at both the health care professional and the public attempting to define the facts and strip away the myths about this troublesome disorder.

Mr. NATCHER. How much will you spend in 1977 and how much in 1978 as far as sickle cell research is concerned?

Dr. LEVY. Extramurally, the number is about $16.2 million in 1977 and about $16.4 million in 1978.

Mr. NATCHER. Doctor, as I understand in your opening statement, you said the clinical course of sickle cell disease is poorly documented. I believe that is in your statement. You know this committee has appropriated money to your Institute for several years now as far as this particular item is concerned. How can you now tell us that the clinical course of this disease is poorly documented? What do you mean?

Dr. LEVY. Mr. Natcher, when we look at the records we see that most of our clinical information represents anecdotal information as to factors which make sickle cell patients better or worse. What we appreciate now is that we must take a systematic view of the problems of the neonate, of the child, and of the adult with sickle cell disease trying to gain some insights through controlled observations that will make us more effective in predicting outcomes. Unfortunately, when we look at the available clinical data it is found wanting. Our clinical research dollars in sickle cell disease have gone in the past to clinical trials of antisickling agents. As you know, these trials have not been productive.

BLOOD SUBSTITUTES

Mr. NATCHER. Doctor, how would you describe your efforts to develop blood substitutes?

Dr. LEVY. I would describe it as extremely promising in animals including nonhuman primates. We can keep animals alive that have had 80 percent of their blood replaced by blood substitutes. If we can perfect the blood substitutes and make them safe, the demands that Mr. Michel referred to on our whole blood system will be relieved. If we have these substitutes to carry oxygen in periods of crisis or emergency, we will be able to decrease the stockpiling or storing of bloods which become outdated when they are not used.

Mr. NATCHER. Have you used blood substitutes on humans?

Dr. LEVY. The blood substitutes are still experimental. They have been used successfully in small animals and most recently in nonhuman primates.

Mr. NATCHER. How much will you be spending in 1977 and how much will you spend in 1978 for the development of blood substitutes?

Dr. LEVY. A little under a half million dollars in 1977 and unfortunately we will stay about that same level in 1978.

TRAINING RESEARCHERS

Mr. NATCHER. In the material you submitted to the committee regarding your training program, you state that in the next few years there will be a rising demand for new entrants into heart, lung, and blood disease research. What do you mean by that now, Doctor?

Dr. LEVY. Several things: One, we see that there is a natural cycle that people are dropping out, going into practice, doing other things. One has to constantly replenish the supply of researchers who are usually most productive between the ages of 35 and 42.

Another thing is that with preventive cardiology coming into being and noninvasive instrumentation coming into vogue, there are new sophisticated techniques that have to be learned and mastered. We have to have the researchers who can evaluate these new diagnostic techniques and test them. Furthermore we need the cardiovascular epidemiologists, nutritionists, and biometricians to man our increasingly sophisticated clinical trials. These then are the bases for the statement that is in the opening statement.

Mr. NATCHER. Thank you, Mr. Chairman.

ENVIRONMENTAL RESEARCH

Mr. FLOOD. Mr. Obey?

Mr. OBEY. Thank you, Mr. Chairman.

Doctor, just a very few questions.

Your Institute conducts research on diseases of heart, lung, and blood. How much of your research is targeted at possible environmental causes of those diseases?

Dr. LEVY. Mr. Obey, when we include smoking, nutrition, and life style habits as environmental causes of disease, we would say that several of our clinical trials are targeted directly at this at a cost of well over $25 to $30 million. When we include our behavioral life style work and our work on pollutants in lung disease I could develop an answer for the record, but I would say upward of about $50 million could be considered environmental research and perhaps a larger

amount. We are, for example, doing work with trace elements in water and their effect on cardiovascular disease.

[The information follows:]

NHLBI Studies of Environmental Factors Related to Heart and Lung Disease

A variety of environmental factors are being studied as part of population studies conducted or supported by the NHLBI. The Institute's epidemiological studies have mainly sought to identify factors in the general environment that are associated with increased risk of developing heart and lung diseases.

Environmental factors in the general population included in Institute heart disease studies are: dietary factors including alcohol use, tobacco use, geographical differences, urban-rural differences, occupation, socioeconomic levels, income levels, seasonal effects, migration effects from low incidence areas to high heart disease incidence areas, acculturation effects, indices of crowding as reflected by the number of persons per room in the household and the identification of behavioral factors and environmental stress factors

Low coronary heart disease rates have been found associated with low intake of saturated fats and cholesterol, low tobacco use, the incidence of coronary heart disease is lower in Japan than it is in Japanese-Americans, it is lower in rural populations than in urban populations, it is lower in the higher socioeconomic and educational groups in this country. However, the reverse is true in studies in developing countries. The less acculturated Japanese-Americans have lower incidence of coronary heart disease than do the most acculturated.

Occupational associations with coronary heart disease are sought for in each of the epidemiological studies in which the Institute staff have direct participation, such as in the ongoing studies in Framingham, Honolulu, Puerto Rico and in Yugoslavia. The first two studies contain mainly white-collar and blue-collar workers usually found in urban areas. The Puerto Rico and Yugoslavia studies, each involving about 10,000 men who have been followed over a period of 4 to 7 years contain a large number of agricultural workers providing urban-rural comparisons. Also included in the Yugoslavia study supported under Public Law 480 foreign currencies are occupational groups such as coal miners, quarry workers, foundry and asbestos workers. Data will be available on the prevalence and incidence of heart disease and obstructive lung disease in this population in relation to duration of work in these occupations.

In addition to these environmental factors being studied in epidemiological studies of the Institute, there are components of many of the grant supported studies dealing with environmental influences on the cardiovascular system in animals and in human beings. The major proportion of these are studies of the short-term effects of environmental stresses, such as heat, cold, changes of atmospheric pressure and other influences on cardiovascular function.

A major effort is also being directed at intervention studies attempting to reduce the risk of heart attacks. The Lipid Research Clinics have an important dietary component aimed at achieving cholesterol reduction as a supplement to the cholestyramine drug being tested in this clinical trial.

Likewise, the Multiple Risk Factor Intervention Trial (MRFIT) has a major focus on achieving reduction of cigarette smoking and lowering of plasma cholesterol through reductions of saturated fat and cholesterol in the diet of the high-risk men who are participating in this clinical trial. The objective of the MRFIT is to determine whether fatal and nonfatal heart attacks can be reduced in men who have above average risk because of combinations of risk factors of high blood pressure, high blood cholesterol and cigarette smoking. A direct relation of the amount of cigarettes smoked to the measure of impaired lung function is being found in the men who have enrolled in this study. An important additional product expected from this study will be the determination of the effect of cessation or reduction of cigarette smoking on the subsequent course of lung function over the follow-up period of 6 years.

These types of studies of environmental factors related to cardiovascular disease conducted or supported by the Division of Heart and Vascular Diseases would come to approximately $30 million and those supported by the Division of Lung Diseases to about $15 million.

Mr. Obey. How much of that research would you say is concentrated in lung as opposed to heart research?

Dr. LEVY. In lung research we are evaluating cigarette smoke and other environmental pollutants and allergents. In heart research we are evaluating the risk factors smoking and nutrition, minerals, and trace elements. Certainly a good deal more "environmental" research is being done in the heart division than in the lung.

Mr. OBEY. More is being done in the heart than lung?

Dr. LEVY. That is right because all of the research on the risk factors, nutrition, and smoking and heart attack and trace metals is done out of the heart division. It is in this division that we have most of our epidemiology and biometry expertise.

Mr. OBEY. If we leave aside the dietary questions that could be related to my dairy farmers back home, let me ask you, if you are looking strictly at the impact of chemicals on disease, how much research of that nature are you doing in the heart area?

Dr. LEVY. Mr. Obey, as you know, there are several other groups, the Environmental Protection Agency, our own National Institute of Environmental Health Sciences.

Mr. OBEY. I understand.

Dr. LEVY. We have a standing relationship with the National Institute of Environmental Health Sciences that, I believe testified yesterday, covers or studies most of the effects of chemicals on different systems, demonstrating the chemicals' effect. Our Institute would then study the physiological effect of the element on the cardiovascular system or the pulmonary system after the chemical has been identified.

Mr. OBEY. The reason I ask is because I was looking at your index of current research grants and contracts administered by your shop, September 1975. When you look at the sections labeled "Environmental Health" or "Environmental Health Contamination" in general or "Occupational Health," "Occupational Diseases," "Occupational Industrial Medicine," "Occupations-Agricultural Workers," "Occupations-Industry," almost all of those relate to the lungs. I found very few which relate to heart. I was wondering why.

Dr. LEVY. That is just because of the naming of the research grants. While heart grants relate directly to environmental or occupational factors, it is not customary to think about the materials we consume or the cigarettes we smoke which affect the cardiovascular system, as environmental. They should be obviously. This is a problem of classification.

Mr. OBEY. What about items such as sulfur dioxide and nitrogen dioxide, particularly sulfate. What kind of research are you doing as far as the effect those three may have on heart disease?

Dr. LEVY. As to the effect of those three agents on heart disease, we are supporting relatively little. Dr. Rall is looking at that. We have been studying the effect of carbon monoxide, which is very readily available in the air we breathe with automobile exhausts and with smoking. There is evidence that it affects the metabolism of the heart muscle, the permeability of the blood vessel wall, and the ability of the red blood cell to carry oxygen, all three having potential serious effects on the heart's functioning.

ARTERIOSCLEROSIS

Mr. OBEY. Are you familiar with the research which indicates that arteriosclerosis may be related in its early stages to cancer and it might be caused by the same mutagenic agents?

Dr. LEVY. We support this work. The original reports were from Dr. Earl Benditt, from Seattle, Wash. It is an interesting hypothesis that has generated a lot of interest.

Looking at the entire data now, Mr. Obey, it appears that the monoclonality—that is, the similarity of cells—that suggested the possibility of carcinogenicity is probably a factor of death of some cells and the survival of others until a similar or monoclonal line in rebirth of cells dominates the plaque. Early plaques and middle-sized plaques are not monoclonal. It is only the chronic scarred plaque that is monoclonal or monotypic.

So the final word is not in, but we have come to think of another explanation for the single cell "origin" of the final plaque than mutogenic effects.

Mr. OBEY. How much more do you plan to pursue that area with research?

Dr. LEVY. The pursuit, the understanding of the basic mechanisms involved in atherogenesis is a prime target for the Institute. If we can prevent atherogenesis, we can prevent the major killer. Perhaps the most exciting thing going on now, Mr. Obey, is a demonstration of a new agent, prostycline, which dilates vessels, breaks up platelet clumping and generally appears to keep the arterial wall free of debris.

Mr. OBEY. What I meant was how much more do you plan to pursue at least the suggestion that the Benditt research would seem to imply?

Dr. Levy. We continue to support Dr. Benditt, an investigator at the University of Washington, and an investigator at the Cardiovascular National Research and Demonstration Center has become interested in the issue recently.

Mr. OBEY. How many are doing the work in addition to Benditt?

Dr. LEVY. There are four investigators with grants in this program area. I would be glad to describe the grants for the record.

[The information follows:]

MUTAGENIC AGENTS

RESEARCH SUPPORTED BY THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Research grant number, principal investigator, and grantee institution

HL-03174—Benditt, Earl P., University of Washington, Seattle, Wash.

MECHANISMS OF ACUTE VASCULAR REACTION TO INJURY

HL-141777—Thomas, Wilbur A., Albany Medical College, Albany, N.Y.

CENTER FOR THE PREVENTION AND TREATMENT OF ATHEROSCLEROSIS (SPECILIZED CENTER OF RESEARCH)

HL-17269—DeBakey, Michael E., (Dr. Trentin) Baylor College of Medicine, Houston, Tex.

NATIONAL RESEARCH AND DEMONSTRATION CENTER IN CARDIAC AND BLOOD VESSEL DISEASE

HL-18473—Heptinstall, Robert H., Johns Hopkins University School of Medicine, Baltimore, Md.

GENESIS OF ATHEROSCLEROTIC LESIONS

WATER

Mr. OBEY. You mentioned soft water. What kinds of research are you doing in that area?

Dr. LEVY. Here we have been cooperating with the Environmental Protection Agency and others trying to get a handle on the purported inverse relationship between hard water and cardiovascular disease. As you probably know, the problem is very complex because it appears that the water that comes out of the faucet is very different than the water we find in the reservoir. We are trying to define the water elements coming from the faucet. We are also trying to take advantage of serendipity, change in water systems, fluoridation, to look at cardiosvascular status and trace elements in individuals sampled before and again after a change. This is a major focus of our research.

Mr. OBEY. I know this all gets tangled up with EPA and NIEHS and NCI and all the rest. What I am curious about is what your specific role is in that area. How do you carve that problem up and how do you approach it from your end?

Dr. LEVY. In terms of role, we have the expertise in cardiovascular disease. We understand the physiology, what is known and not known about heart and blood vessel metabolism, heart attack, and sudden death.

Mr. OBEY. My question is: What does that mean in terms of specifics? Are you doing specific research in that area and if so, what?

Dr. LEVY. What it means in specifics, Mr. Obey, is we supply some of the dollars that go into doing the research projects. We pay for many analyses on hair, nails, and other substances. We design many of the protocols that are done and the Environmental Protection Agency helps in that they have the access to these different groups, to the public health groups, to the facilities and to the plumbing and thus it makes a very nice relationship in that we have the questions and they have access to places where we can get the answers.

[The information follows:]

] TRACE ELEMENTS, WATER, AND HEART DISEASE [

In response to your question concerning specific research on trace elements, soft water and heart disease, the following are examples of NHLBI conducted research.

The Seattle Study of Trace Elements from Drinking Water was launched in May 1975, to examine the relationship of trace metals in home water to their levels in human tissues and to carious cardiovascular measurements. Municipal employees and their families were to be studied both before and after the city added lime for corrosion control to water supplying part of the city. In August 1975, the city delayed the decision to lime for an indefinite period, but preliminary data from the study indicated that many of the original objectives can be met even if the post-liming part of the study is not realized. Seven hundred and fifty employees have been screened, and analysis of their home tap water samples shows good quality control in the laboratory and a wide range of concentrations of the study metals. Zinc and copper concentrations in the water samples are negatively correlated with each other (because the source of each is a different kind of plumbing). Therefore, separate effects on metal levels in tissues are expected. A selected sample of 150 men and their families have submitted hair, toenail, and serum samples.

Analysis for Trace Elements in Human Tissues: A Request for Proposal was issued by the NHLBI on March 1, 1976, to determine the levels of cadmium, copper, lead, and zinc in hair, toenails, and blood collected from subjects of the Seattle Study of Trace Elements from Drinking Water. Twenty-four proposals were received and an award was made to the University of Missouri. The results will be used to determine the importance of drinking water as a source of intake for these important metals and the possible relationship of tissue levels of these metals to cardiovascular health.

The Health and Nutrition Examination Survey of the National Center for Health Statistics began collecting home tap water samples from its examinees in July 1974, and completed its sample in September 1975. Thirty-five areas in the U.S. were included with approximately 100 examinees at each area. Water samples from home taps and from major suppliers in each area are being analyzed at Purdue by proton induced x-ray emission under control by the EPA Water Quality Research Laboratory in Cincinnati. Analysis of the relationship between examined cardiovascular measurements and bulk and trace elements in home tap water will be carried out by NHLBI.

The Boston Study of Cardiovascular Risk Factors in Relation to Lead in Drinking Water was initiated because the Metropolitan District Commission, serving water to the Boston Metropolitan area, planned to reduce lead exposure to residents by controlling the corrosiveness of the drinking water supply. Lead is hypothesized to be an agent in the association between soft water and elevated cardiovascular disease mortality. If subjects who currently have elevated levels of lead in their drinking water have reduced levels of cardiovascular risk factors as the water lead is reduced compared with controls, this will be support for the hypothesis. Therefore, effects of the change in lead exposure will be assessed before and after examinations of a population of veterans who are subjects of an already existing aging study.

Trends in Urban Mortality in Relation to Fluoridation Status: Analyses of trends in mortality since 1950 in fluoridating communities as compared with those that did not fluoridate were undertaken to assess possible long term effects of fluoridation upon total and cause-specific death rates. Urban places in the U.S. with populations of 25,000 or more in 1950 were selected for study. The overall findings were clearly negative with respect to any relation between fluoridation and observed changes in mortality over the twenty year period studied. The results of this study are being prepared for publication.

Studies of Heart Attack and Water

Mr. Obey. What does the relationship seem to be between soft water and heart problems?

Dr. Levy. There is an inverse relationship between hard water and heart attacks. The harder the water, the less the heart attack. This is best shown in studies in England and other parts of Europe. In the United States, it is not as clearcut.

Mr. Obey. What does that show in terms of the difference in incidence from the expected norm?

Dr. Levy. I can provide for the record the English data. In the United States, the question is far from clear. It is suggestive that soft water puts one at risk. But, the studies have been small, and not done as well as they might have been. But, I would be delighted to provide you with the English data, the World Health data that started the issue moving, and what we have collected thus far in the United States.

Mr. Obey. Isn't the range that has been suggested so far—doesn't that show a difference of 25 to 50 percent?

Dr. Levy. It depends on which study you accept, and whether you accept the limitations of the studies. The English studies were very suggestive initially, and very exciting. We have not seen numbers like that except from one study in the United States.

Mr. Obey. How much do you think you are devoting out of your budget to that specific area?

Dr. Levy. Directly or indirectly, probably somewhere around $300,000 or $400,000, Mr. Obey.

[The information follows:]

] WATER CONSTITUENTS AND TRACE ELEMENTS IN RELATION TO CARDIOVASCULAR DISEASES 1/ [

Significant inverse correlations between the hardness of drinking water and local cardiovascular mortality rates are found consistently in major national studies and less consistently within smaller regions. A number of bulk and trace constituents of finished water at the treatment plant show correlations with mortality of equal but not greater magnitude to the correlations of hardness with mortality. Little is known about these relationships with tap water, but levels of several trace metals of biological significance are known to vary markedly within water distribution systems and are probably related to types of pipe and the corrosiveness of the water supplied. Tap water studies and studies of localities within smaller regions are recommended to disentangle the association of water quality and health from the associations of both to other regionally distributed factors. Rainfall is one such factor which may influence the content of both drinking water and soil and thus human mineral intake. A number of other environmental and social factors seem unlikely to be intermediaries from the results of several multivariate studies.

Inverse correlations between the hardness of drinking water and local cardiovascular mortality rates have been discovered and confirmed in the United States, Canada, and in England and Wales. A recent commentary on the subject cites 49 studies from 9 countries relating regional differences in cardiovascular disease to constituents of drinking water but finds the data inadequate to discriminate between basic hypotheses. The question remains open as to whether the bulk or the various trace elements usually found in hard water are protective or whether something in soft water is harmful. The correlations may mean only that water quality is an index of something else, a factor not transmitted through drinking water. Although it has been estimated that the maximum attainable mortality reduction from optimal conditioning of drinking water is at most 15%, the absolute number of potentially preventable deaths is large, so that recent meetings of investigators have given strong endorsement to continuing research in this area.

Hardness is not a specific constituent of water but a complex characteristic measured by titration with a chelating agent and often expressed as calcium carbonate equivalent. The first reports of correlations between water hardness and cardiovascular mortality were published in 1960. Using data by the U.S. Geological Survey on finished water supplies in 1315 U. S. cities to calculate average state values and age-adjusted death rates for whites by state, negative correlations were found for all-cause and cardiovascular rates—lower death rates in states with hard water. The correlation with noncardiovascular diseases taken as a group was small and not significant. Within the cardiovascular category there were strong relationships to water hardness for arteriosclerotic heart disease (ASHD) (r=-.5) and hypertensive heart disease (r=-.6), and less of a relationship for stroke deaths (r=-.3). The negative correlation of hardness to coronary death rates was not as high when 163 large cities were studied as it was with data for entire states, despite the fact that in the city analysis water values more closely represent the exposure of the population at risk than in the state analysis. This study used water data published in 1952 and deaths from the 1949-1951 period. Using the same water data and 1960 mortality figures, a later study again found correlations for states between hardness and ASHD (r=-.5) and hypertensive heart disease (r=-.4) to be significant and stronger than that for stroke (r=-.25). Using 1962 water data and 1960 mortality data for 88 large cities, a correlation was found for ASHD of -.4. Again the city data showed a weaker correlation than the state data.

1/ A. Richey Sharrett and Manning Feinleib, Epidemiology Branch, Division of Heart and Vascular Diseases, National Heart and Lung Institute, National Institutes of Health

Other investigators using United States mortality data have confirmed the negative correlations with water hardness. Another study using 1949-1951 mortality in 135 central county areas found, not only the expected negative relationships between mineralization of city water and heart diseases and negative correlations with malignancies and cirrhosis, as earlier studies had found, but also a significant positive correlation with strokes which contrasts with the earlier finding, and other significant correlations with stomach ulcer, diseases of infancy, and gastritis. The plethora of significant findings (all of the above greater than + or - 6) cast doubt in some investigations on the specificity of any of the relationships. Another group of investigators used 1960 water and mortality data for 95 U.S. metropolitan areas and found a greater negative correlation for coronary disease than any other category of cardiovascular disease. The relationship with hypertensive heart disease was less marked than in earlier data. A negative correlation with malignant deaths shows that the correlations are not entirely specific to cardiovascular diseases. Yet another study correlated state 1960 mortality to river water analyses and found a significant negative correlation for hypertensive heart disease, a smaller negative correlation for ASHD and a nonsignificant positive correlation for noncardiovascular diseases.

The most extensive investigation of the water hardness story has been in England and Wales by a team with the Medical Research Council. They first reported analyses of mortality in 1948-1954 among 83 county boroughs. Correlation with all cardiovascular disease was of the order of -.5 for both males and females, both in the 45-64 and 65-74 age groups. But here the relationship was stronger with cerebrovascular disease than with hypertensive or coronary heart disease. Cancer again showed a significant negative correlation, but only for females. Bronchitis also was more frequent in soft water areas. These observations were repeated using death data in 1958-1964 in the 61 largest county boroughs, resulting in even larger negative correlations for the cardiovascular disease categories than before. Now, however, the negative correlation of noncardiovascular deaths with hardness was significant, with bronchitis and cancer both contributing to this relationship. In a subsequent study five towns which increased the hardness of their water between 1900 and 1955 by 50 parts per million or more had more favorable cardiovascular trends between 1951-1961 than six towns which decreased hardness, and the 72 towns with constant water were intermediate. A 1973 study, however, used the most recent mortality data for the British county boroughs (1958-1967) and found little if any relationship between cardiovascular mortality and water hardness. Stroke mortality appeared to be highest in towns with hardness between 150 and 200 ppm, as did hypertensive hear disease deaths. Correlations were not reported, but ASHD deaths were only slightly less frequent in the hard water categories which were used to classify the data. These results are in substantial disagreement with other studies of the same county boroughs. Results are presented as proportionate mortality ratios instead of standardized or age-specific rates, and it is not know whether this is the reason or whether the past relationships no longer hold with new data.

The major findings from the U.S. and U.K. are in substantial agreement, but cardiovascular death rates for white males are about 40% higher in extreme soft water than in extreme hard water areas in the U.K., and only 15% higher in the U.S. Cerebrovascular disease shows strong negative correlations with hardness in the U.K. and weak negative correlations in U.S. data. Arteriosclerotic and hypertensive heart disease mortality show consistently negative and usually significant correlations in most age-sex groups in both countries. There are negative correlations of borderline significance with cancer in both countries, but the U.S. and U.K. data for other noncardiovascular categories are completely different. Noncardiovascular diseases as a group correlate negatively with hardness in U.K. data at significant levels but this correlation is absent in the U.S. Bronchitis and cancer, both negatively correlated, seem to be the factors explaining the noncardiovascular relationship in the U.K. In the U.S. a variety of significant positive correlations and a few negative ones have been found which have no counterparts in England. The differences here support the hypothesis of a factor in water which is specific for cardiovascular diseases.

] CONCLUSIONS [

The negative correlation of the hardness of public drinking water with cardiovascular mortality is consistent in large national studies. Whether or not this association is due to any constituent of drinking water is still unknown. The fact the the association seems stronger in U.S. and Canadian data when studied by region than when studied by smaller local areas indicates that there may be regional variables affecting mortality rates which are associated with, but not contained in, hard or soft water. The relative weakness of the association between mortality and water hardness in studies confined to a single state, province, or small country may be due to sampling variation or the curtailed range of values for water hardness, but may indicate that drinking water itself is not a potent factor. To control for regional factors, more work needs to be done within small areas which have a wide range of water hardness. More emphasis needs to be placed on estimation of effects and placing confidence limits around the estimates rather than on determining the degree of correlation. Maps of mortality rates and of the independent variable being considered are more useful than coefficients of correlation for showing the consistency of the relationship and generating hypotheses.

Cities which change their water may provide "natural experiments" which should be studied. However, attribution of any subsequent changes in mortality rates specifically to changes in the water must be conditioned by changes in other factors that may occur in these cities.

Regionally distributed variables which are consistently associated with water hardness are very likely not associated by chance. For example, in both Britain and North America soft city water is associated with rainfall. This needs further investigation, not only to see if effects of water persist after statistically controlling for rainfall, but to clarify the interrelationships of rain, drinking water, and soil chemistry to human nutrition.

On the other hand, the fact that water hardness has a regional pattern invites nongeochemical hypotheses as well. Presumably a number of factors differentiate life along the American Coasts from that in the Western Plains. Cardiovascular mortality does not have a simple relationship to social class, and socioeconomic variables have not explained away the water associations, but the search should continue for nongeochemical determinants of regional mortality differences.

The evidence that calcium and magnesium levels in tissues vary with the hardness of city water is suggestive. Work should certainly be encouraged to define further the relationship of the levels of these ions in water to their levels in tissues and the effect of these tissue differences to cardiovascular disease.

Despite the apparent importance of both essential and toxic trace metals, work has scarcely begun on their epidemiology in water. Data which has been used do not attempt to define typical levels for trace metals at each city. Most values reported are for spot samples, but trace metals in city water are known to have wide day-to-day and seasonal variation. With these limited data the trace metals most strongly implicated in the water studies are lithium and vanadium. Others discussed in this view are of interest because of their associations with hardness or corrosiveness of water and their probable physiological functions. Corrosiveness certainly affects exposure to trace metals at the tap, and its use as an index in epidemiological studies is advisable. Study of corrodable trace metals in representative tissues in cities with varying corrosiveness of water may be fruitful. Finally, more work is needed on tap water, though these are the most difficult studies to conduct. Knowledge is needed both on the actual trace metal content of tap water and on the relationships to risk factors and clinical disease.

DRUGS

Mr. PATTEN. Could I ask one or two questions?

Mr. FLOOD. Yes.

Mr. PATTEN. Last night's paper had an article that certain heart drugs are available in other foreign countries that have not been approved by the FDA, except in one case, which is the oldest. Did you want to comment on that?

Dr. LEVY. I would be pleased to, Mr. Patten.

Mr. PATTEN. Just briefly.

Dr. LEVY. The drug is the beta-blocker propranolol. Though there has been a delay in approval for some drugs uses that have been a concern to us from time to time. I think that there is good reason for FDA to delay the approval of other beta-blocking agents in that several of these beta blockers have had serious toxicity when they have been in use in Europe. It is fortunate for the American public that they were not exposed to them.

These drugs have potent effects on the cardiovascular system, and we best know all we can about them before we release them in the United States.

CHOLESTEROL

Mr. PATTEN. I have another question. Cholesterol—a fellow built like I am, they tell me I am a real target. Say if you wanted to dissolve fats—every woman has to do it in her kitchen, they use chemicals. Alcohol dissolves fats. Ether dissolves fats. You can dissolve fats with benzene.

In that area, do you think there is room for us, with any of these other substances that dissolve fat, to reduce cholesterol and other fatty tissues?

Dr. LEVY. The problem with the liquid solvents you mention is they have other noxious effects. But, the exciting thing is that we can talk about biological detergents, the proteins that carry fats in the blood.

Our research center in Houston has synthesized many of these protein carrying moieties. In the future we would like to think of these biological detergents as roto rooters helping to clear lipids out of vessels. But, that is in the future.

NUTRITION

Mr. PATTEN. Well, I have a professor in the biology building up there in Rutgers—where Dr. Wakesman discovered streptomycin. He is a great fellow for preaching nutrition. Now he has a drug that relieves people with prostate gland trouble. It hasn't been approved yet by the FDA.

I have some friends that use it. They say it is marvelous. It enables them to avoid surgery.

He says they are using this in Russia, and in the Philippines, with great success. President Marcos of the Philippines is gung ho for it. Rutgers has submitted a project. There was quite a bit of publicity in a national magazine recently. I am going to send you a copy of it.

I will send you a copy of this article.

Dr. LEVY. I would be pleased to receive it.

Mr. PATTEN. Some scientists, chemists, that I met with up at Rutgers over Washington's birthday are enthused with what he is doing.

LIPID LOWERING DRUGS

Dr. LEVY. Several of the new lipid lowering drugs have been reported to have an effect on prostatic and other secretions. The question is demonstrating their primary effects on lipid lowering and their safety. I would be pleased to receive the article.

Mr. PATTEN. Yes. He emphasizes what you eat, the nutrition. You all go for that. You all say fellows like myself ought to cut down, lose weight. Cut salts and eggs and a lot of other things. So, I know he has me sold a little bit on it because some of the people using it say it has been very beneficial.

Dr. LEVY. Well, nutrition has the potential for saving a large number of lives. Our problem is first to demonstrate that altering diet will prevent heart attack, and then our harder problem, as you well know, Mr. Patten, and so do I, is how to change dietary habits, how to alter habits.

Mr. PATTEN. Well, I don't have to tell you I am going to a funeral tomorrow morning. They found the lady dead in bed yesterday. Last week I went home. A lawyer took a little trip to Spain, and they brought his body back. He died on the plane. A little medical history there. A little medical history with the woman—heart trouble. So, it occurs more frequently in my experience than anything else. Your work is very important.

SUDDEN DEATH

Dr. LEVY. Sudden death is a major problem. Over 60 percent of heart attack deaths are sudden.

Mr. PATTEN. In both cases there was medical treatment and a little history—vascular troubles.

Dr. LEVY. What we find now in sudden death is that many patients have prodiomata, signs that they often don't pay attention to. Most people who die suddenly have coronary artery disease, and usually the thing that does them in is an irregular heart rhythm, that occurs suddenly, and leads the heart to function irregularly. It is one of the things that we hope to soon control with proper drugs.

Mr. PATTEN. Thank you, Mr. Chairman.

HIGH BLOOD PRESSURE EDUCATION PROGRAM

Mr. FLOOD. Now, one may think we are giving a lot of attention to hypertension and as you know, the committee in its report on the fiscal 1977 appropriation actually directed the Institute to establish the Office of Hypertension Control and to conduct a pilot demonstration on hypertension control in from four to six States, to test the effects of it, statewide, and to coordinate large-scale efforts to control hypertension.

After all that, what is the status of this effort?

Dr. LEVY. I think you will be pleased. We have established the National High Blood Pressure Education Program Office out of which the program runs. The request for contract proposals for statewide coordinated high blood pressure was released. I am delighted

to report that in terms of a first, on February 11 we met with all the regional and State and territorial health officers. We had over 46 States represented, outlined the plan, which deals with each State coming in, or rather requires that each State applying present a plan, which must contain a survey and surveillance system to get baseline data on the number of strokes, and the number of heart attack and stroke deaths, as well as other morbidity and mortality information.

The State would then implement the plan and assess the results in 3 years repeating the baseline survey. We would give them the wherewithal to measure, to quantify, to coordinate. We hope that they will be using their 314(d) money to provide the rest. This meeting, by the way, was cosponsored by the Institute and the Health Service Administration. The enthusiasm was great. We have gotten a number of calls and inquiries already. We hope to start this program, as well as two other programs, Mr. Chairman, in the same area this year. One deals with coordinated control of blood pressure in the work setting— since men are so often more reachable in the work setting—and finally, the other would set up one or two pilot community high blood pressure control centers, so we can learn first hand about the problems of organization and health maintenance in the individual communities.

HYPERTENSION PROJECTS

Mr. FLOOD. Aren't you glad I asked you that one?

Now, Doctor, on the matter of hypertension, the demonstration projects, will these demonstration projects involve labor unions, business groups? It seems to us that the workplace is the logical setting for this type and kind of screening.

Dr. LEVY. We agree completely. That is where the men are, and not to be chauvinistic, the problem is that we are detecting—we are screening women, but we are not getting to the males with high blood pressure. Our latest surveys suggest that while the number of undetected women with hypertension has fallen to less than 20 percent, over 40 percent of hypertensive men are still unaware of their high blood pressure.

The work setting is also a place where one can hope to achieve better adherence to therapy. We are hoping our new request for work setting model programs will get business groups, industrial firms, and the unions to work together. We sponsored a national conference on blood pressure control in the work setting here in Washington in the fall. The meeting was received enthusiastically by both business and labor leaders.

What they have to do is put up some resources. What we will do will be to supply the expertise and the resources to coordinate, to measure, to evaluate what they do. They have to be willing to do it; both the labor union and the business have to be willing to work together.

We are delighted with the results we see from some pilot projects on blood pressure control in the worksetting. One very exciting project is in New York and involves several department stores. It shows that in terms of reduced absences from work, sick leave, hospital days, that the union and the industry very quickly get back their dollars. When you consider how many dollars are put into industrial

accident prevention and other health care benefits and when you consider that there are more than 50 deaths from cardiovascular disease to every one that is accidental this new direction holds great promise. We are very encouraged with the enthusiasm of labor and industrial groups. We look at the work setting as a way to achieve better blood pressure detection and control.

Mr. FLOOD. How much do you plan to spend for these hypertension demonstrations in 1977 and 1978?

Dr. LEVY. In 1977, we have put up about $750,000 for the work setting projects. We put forward approximately $2.5 to $3 million for the statewide coordinated high blood pressure efforts and approximately $300,000 for the 2 pilot community projects. How many dollars we will be able to spend in 1978 depends on whether we are going to be able to meet all our present contract commitments, which, as you know, right now does not look very good. Our projections are that we will be meeting only 90 percent of our current contract commitments.

Mr. FLOOD. Well, how do you plan to evaluate the effectiveness of these projects, these hypertension demonstration projects? Do you have a formal plan?

Dr. LEVY. That is built in as a requirement.

Mr. FLOOD. You have a formal plan?

Dr. LEVY. That is right.

Mr. FLOOD. I want that formal plan for the record.

Dr. LEVY. I will be pleased to provide for you the evaluation requests that we build into these programs, and what measures, what indicators we will be using.

[The information follows:]

HYPERTENSION EVALUATION REQUIREMENTS

For demonstration of the impact of State coordination of hypertension control, States will be asked to assess both before and after these efforts: (1) Changes in the number of hypertensive patients in or served by the States who are aware of their condition, under active care of surveillance, and who have successfully controlled their high blood pressure; (2) changes in the estimated rate at which strokes occur in the State; and (3) changes in death rates for stroke, hyperensive heart disease, and heart attack. In the short term (3 years) of the projects, we not likely to see dramatic changes in death rates, but States should experience quite measurable changes in the control status of hypertensive patients.

For demonstrations of hypertension control in the work setting, in addition to a cost analysis for achieving certain steps, projects are being asked to reflect the number of hypertensive employees detected, referred to care, entering therapy, achieving control and maintaining control. Further, we are asking for changes (hopefully reduction) in the number of employees requiring hospitalization, in the number becoming eligible for diability benefits and in absenteeism rates. Again, in the short time allowed, we should not expect dramatic changes, but we should see clear progress in each of the specified outcomes.

PEDIATRIC PULMONARY CENTER

Mr. FLOOD. All right. Now, last year, you recall, you told us you were trying to integrate your efforts with those of the pediatric pulmonary centers of the maternal and child health program.

Have you succeeded in integrating all these activities?

Dr. LEVY. We have succeeded in establishing a better exchange and dialog. Unfortunately, the lead in HSA, who was responsible for

the pedriatric pulmonary centers, Dr. O'Hare, has gone back into practice. But, using the pediatric pulmonary disease working group of our Interagency Technical Committee, we have had useful and productive exchanges of information and plans. I believe that four meetings have now been held of the working group dealing with pediatric pulmonary diseases.

Mr. FLOOD. What kind of collaborative work have you had with the pulmonary centers?

Dr. LEVY. The collaborative work has been through HSA. We have helped them evaluate projects and activities. We have also had useful discussions with them, with our pediatric pulmonary specialized centers of research, and the centers, about needs in education, and further research, for these children who are afflicted with pulmonary disease. The health care professionals at the pediatric pulmonary centers are often much more aware of immediate needs, since they are providing direct service to these children.

Mr. FLOOD. How much do you plan to spend in 1978 to support the work in these pediatric pulmonary centers?

Dr. LEVY. We do not fund those pediatric pulmonary centers directly. Our research will be used by them. We have committed $7 million in 1978 to our pediatric pulmonary specialized centers of research.

Mr. FLOOD. But not directly.

Dr. LEVY. There is no large transfer of funds. In a few cases, a specialized center of research and a pediatric pulmonary center are in the same location. What we have done then is to encourage an intermingling of staff, of resources, of facilities.

LUNG DISEASES

Mr. FLOOD. What percentage of chronic lung diseases are caused by environmental factors?

Dr. LEVY. If we include the cigarette as an environmental factor——

Mr. FLOOD. Do you?

Dr. LEVY. I would.

Mr. FLOOD. Go ahead.

Dr. LEVY. I would say better than 90 percent of chronic lung diseases is environmental in origin.

Mr. FLOOD. Do you have a specific research program, other than that one you have—the research center in Vermont—to study and identify the environmental agents which cause lung disease?

Dr. LEVY. We have several specialized centers of research in lung disease, chronic bronchitis, emphysema, asthma, pulmonary fibrosis, many are looking into environmental agents, and looking into the body's response to these environmental agents, how the body physiologically responds to these irritants, these allergens, and how to prevent this.

FUNDING LUNG RESEARCH

Mr. FLOOD. How much of your budget for lung diseases generally would you spend on basic research and to develop general knowledge about the lungs?

Dr. LEVY. Our program, which is called structure and function of the lung, is primarily a basic research program, and it received about

$14.5 million in this fiscal 1977 year, and a little bit more than that in fiscal 1978.

Of course, several of our other programs, as in pediatric pulmonary diseases, airway diseases, include basic research on collogen, elastin, on new methods of detection. So, to talk about basic research efforts as compared to clinical efforts is difficult. I would say that probably more than 40 percent of the research, probably more than 50 percent, is still in basic investigator-initiated research.

Mr. FLOOD. Now, I think you know this, but a few days ago we had here the National Institute for Occupational Safety and Health, the NIOSH group, and they are also very much interested in lung diseases, as you know.

Do you talk to these people? Have you developed any kind of a working relationship with that organization? Have you thought in any way about joint funding some of these research activities? We always get around to that. Have you thought about joint funding some of these research activities?

Dr. LEVY. We have thought about and talked about and indeed do have some minimal joint funding. Perhaps the most important thing is Dr. Merchant of NIOSH, whose expertise is in the lung area, has just been nominated to our Pulmonary Diseases Advisory Committee. Dr. Lenfant, our Director of the Division of Lung Diseases, is on the NIOSH Advisory Committee. So, with this interlocking directorate, we keep familiar with each other's activities and events.

BLOOD RESOURCES

Mr. FLOOD. Now, your budget also shows you are going to spend $10 million for what you call blood resources. Well, suppose you tell us briefly how you are going to spend that money. What kind of activity are you going to support?

Dr. LEVY. Blood resources is a new mandated area to the Institute. There is an enormous research void there. The techniques for fractionating blood into the cell elements, the red cells, the white cells, the platelets, which are used for the treatment of many diseases, the techniques for separating the plasma protiens, like antihemophilic factor for hemophilia, albumen, globulins, have not really been developed further since World War II.

What we are doing with this money is to support research to develop better fractionation processes and the preservation of platelets and white cells used for patients with bleeding problems, infections, and malignancies.

Mr. FLOOD. How long have you been at it?

Dr. LEVY. We have supported some blood resource research for about 5 years. We increased our amount of support last year. The amount of support we can give the blood resource area in the future is limited by the total budget that we have. So, it is not increasing. The opportunity and the need is great in this area. Of course, finally, we contribute to the work of several of the task forces of the American Blood Commission, which are moving forward, on the issues of safe labeling procedures, regionalization, donor recruitment, blood utilization, and blood resource data collection.

Mr. FLOOD. In the material that you did submit to the committee, you say that 25 percent of the 8 million pints of blood that are collected each year is never transfused at all, and much of the 25 percent—and this is your language—is wasted. Well, what are you doing to reduce the waste?

Dr. LEVY. What we are trying to do is to accomplish regionalization of the blood supply, better sharing of blood and blood products, and better blood resource management practices. We are also improving the shelf life of blood and blood products. For example, just about to come into law, is the adding of adenine to stored red blood cells. This will allow the lifespan of the red blood cell packs to be extended from 21 to 35 days.

I would like to amplify my answer for the record. The term "wasted" needs to be understood. It refers to the number of units of blood drawn that are not transfused. Most of the time these units are utilized for plasma fractionation, which yields such valuable products as albumin, gamma-globulin, and typing reagents. The number of units of blood actually wasted by outdating is very small although I cannot give an exact figure. Finally, there is an irreducible minimum of units that cannot be utilized because they test positive for hepatitis or syphilis, because they are accidentally contaminated, or because the container does not contain the prescribed quantity of blood.

Mr. FLOOD. We keep hearing from groups of all kinds that they cannot get blood, they cannot get blood components. The hemophiliac, you mentioned, they can't get the blood. What about this?

Dr. LEVY. The problem is that one of the other things we have to do is get better data on the requirements in blood. I would be pleased to develop for the record what we are doing to better develop the blood resources, both in research and in education.

One of the problems is that we have to educate the physician on how to use blood. Often the use of only the red blood cells and the saving of the plasma for other uses would be as effective, if not more effective, for the patient. But, it is still a common practice to give whole blood transfusions where red cells would do, so that plasma and other components become acceptable. So, it is both a research effort and an education effort that we have ahead of us.

Mr. FLOOD. Then you better do that for the record.

[The information follows:]

DEVELOPMENT OF BLOOD RESOURCES

Currently, our major effort is concentrated on the support of a National Research and Demonstration Center. This is the Puget Sound Blood Center in conjunction with the University of Washington at Seattle. This center conducts both research and education programs at the level of physicians, nurses, donor recruiters, laboratory technicians, blood donors, and the public at large. The Puget Sound Blood Center is looked on as a model of educational efforts and of proper utilization of the blood resources. Second, the Institute supports a program project currently at a level of $1.8 million at the New York Blood Center. This is the largest single blood center in the country and the one with the most extensively developed research facilities. This research involves, among other things, obtaining optimal yield of plasma and antihemophilic factor, automated procedures for labeling blood and blood specimens in a way to eliminate human errors, and research in plasma fractionation.

The Institute supports a number of contracts dealing with improved methods of plasma fractionation involving several outstanding laboratories. The Institute also supports a large contract that entails entirely new approaches to plasma fractionation and the operation of a pilot plant intended to enable blood banks

from all over the country to send plasma for processing by efficient methods. We have supported the development of a sterile connecting device which will allow the shelf life of frozen blood to be extended significantly by allowing sterile transfer after thawing and thus impacting on the utilization of the national blood resource. In addition, the research conducted with funds from our Institute on blood substitutes, as I mentioned earlier, if successful, may substantially alleviate the need for human blood.

One of the task forces of the American Blood Commission, operating under a contract from the Institute, is investigating methods of studying donor motivation and systems of donor recruitment with a view to obtaining participation of a larger segment of the population than that which constitutes the donor pool at present.

The Institute will be sponsoring a National Workshop on Logistical and Managerial Problems in Blood Banking.

ANTIHEMOPHILIAC FACTOR

Mr. FLOOD. Now, last year again we talked about—I forget the phrase you used—antihemophiliac concentrate, that the person can carry right with him, and administer to himself as he needs it, whenever it might be. What progress are you making in developing adequate quantities of this concentrate? At a reasonable cost?

Dr. LEVY. That is a problem. We have set up a pilot plant in New York that is attempting to see how cheaply, and how effectively, and how safely one can make large quantities of this antihemophiliac factor.

The problem in making the material is that there is a loss in activity during preparation. One does not recover all the effective material.

Mr. FLOOD. But there is progress in this now.

Dr. LEVY. There is progress, and we are very excited about the new potential fractionation procedures that may allow us to prepare even safer and more potent antihemophiliac factor.

BLOOD DONATION SYSTEM

Mr. FLOOD. Now, you also identify as one of your big objectives the establishment of an all-volunteer blood donation system. Well, how do you plan to do this? At what point in time do you plan to achieve this?

Dr. LEVY. We do this now primarily by encouraging the voluntary sector. The moral effects of the American Blood Commission and its groups are moving toward this. The exciting thing, Mr. Chairman, is that the amount of paid blood 5 years ago was estimated in this country as 22 percent. The amount of paid blood now, of the number of units of blood now collected, is estimated to be about 7 percent. We have this rapid reduction because more and more of the large blood collectors are moving toward voluntary blood donations, and it looks like the realization of the better safety, of the voluntary blood, is having an effect. Post transfusion hepatitis has been massively reduced. Other events are helping, too, like the new BOB regulations that will require a unit of blood to be labeled as whether it is paid or voluntary. This will hasten and speed up the movement to an all-voluntary blood donor source. We are delighted with the movement, with the decrease in the amount of paid blood and the associated decrease in hepatitis risk.

BLOOD DATA SYSTEM

Mr. FLOOD. You also state as one of your objectives the development of a national blood data system. What do you mean? Is that currently under development, or is this something you are going to start sometime in the near future or what?

Dr. LEVY. One of the four task forces that we support through the American Blood Commission is on the development of a national blood data system. It is quite clear——

Mr. FLOOD. National blood data system?

Dr. LEVY. Yes; it is quite clear that the best way to get all the data we need on our blood resource is to get the voluntary groups to go ahead and collect it. They have submitted a report now to suggest the creation of the center, so that is where we stand now. It has moved from a task force to a recommendation for the creation of a blood data center, and we will be looking over their plans I am sure over the next 3 to 6 months.

Mr. FLOOD. How much are you going to spend on this data system in 1977? How much are you going to spend in 1978?

Dr. LEVY. Right now, Mr. Chairman, in 1977 we have been supporting the task force. That cost is a little over $150,000 now. In 1978, we have no dollars available right now to help support this center.

Mr. FLOOD. All right. Do you have any idea how much it would cost when it is in full operation?

Dr. LEVY. When it is in full operation, we hope it will not cost the Government, except to get information, large amounts of dollars. We hope it will come through voluntary donations from the members of the American Blood Commission. But, it may cost us in the years in which it is being set up to underwrite it anywhere from $1 to $3 million a year.

Mr. FLOOD. Now, you have been talking a great deal about this, but how long has your organization been working on the development of a national blood policy? Again, how much of the taxpayers' money has HEW already spent on this matter?

Dr. LEVY. A national blood policy was promulgated in 1973.

Mr. FLOOD. That is HEW?

Dr. LEVY. Yes. The American Blood Commission started in 1975. We were given the mandate to get effectively involved with our renewal legislation in 1976.

The HEW itself has not spent large amounts of money. What it has done has been to serve as a policeman, a gadfy, a moralist, getting all of the collectors, providers, users of blood together, to move this field toward the goals of the national blood policy.

NATIONAL BLOOD POLICY

Mr. FLOOD. When will you be able to tell us that HEW actually has an official national blood policy?

Dr. LEVY. HEW has an official national blood policy now.

Mr. FLOOD. When is it going to be fully implemented?

Dr. LEVY. Full implementation we think will be most effective if it is done voluntarily by the groups involved in the American Blood Commission. If they do not move in the next year or two, toward the

goals—and I commented earlier that we are pleased that we are making progress, rapid progress—then more regulations, like the regulation that BOB just promulgated about labeling of blood, will be necessary to achieve all of the goals. But, we are very pleased, Mr. Chairman, with what we see.

Mr. FLOOD. All right. As long as your objective is to find ways to lower the cost of processing, storing blood, transfusing the blood——

Dr. LEVY. To lower the cost, increase the quantity, decrease the toxicity, and increase the safety of this blood.

Mr. FLOOD. The answer is yes?

Dr. LEVY. Yes, Mr. Chairman.

Mr. FLOOD. All right.

Now, in addition to your Institute, the Arthritis Institute also supports research in all kinds of blood related diseases. Can you tell us how you divide up this work? Can you tell us how the area is divided? Do you coordinate your activities?

Dr. LEVY. With the passage of the new legislation that made us the Heart, Lung, and Blood Institute last year, we set up an NIH Blood Coordinating Committee. We meet with the Institutes at the NIH that conduct or support a significant amount of research related to blood.

Actually, the largest supporters of blood research at the NIH is the Cancer Institute. We meet with these groups. We review each other's programs. This first year has been spent primarily in developing a glossary, a thesaurus of what is blood related and what is not, and how much we are all spending on it.

What we are getting down to business to now is to look at each others new initiatives, where can we work together. In several areas we are cooperating; for example we have two projects with the Cancer Institute where we are cosharing in the support of programs, just what you are interested in.

FUNDING BLOOD RESEARCH

Mr. FLOOD. We heard them at some length. That is why I asked you. What about this now? Can you think of any reason why this committee shouldn't appropriate all of the dollars now for blood related research into a single Institute? Yours, for instance?

Dr. LEVY. Mr. Chairman, I would say that——

Mr. FLOOD. That is a tough one.

Dr. LEVY. The historical perspective of the support of blood, the manpower, the expertise for specific elements of blood exists throughout the NIH——

Mr. FLOOD. Should we appropriate the funds to a single Institute, such as your Institute?

Dr. LEVY. I think for the investigator and for the scientific field, a multiplicity of sources is more effective, if the sources are effectively coordinated. That is what we aim to do.

Mr. FLOOD. Then you do this for the record. Identify your Institute's research objectives—talking in the area of blood diseases—and also identify the objectives of the Arthritis Institute in blood diseases.

Dr. LEVY. I will add to that the objective of several of the other Institutes engaged in blood research as well.

Mr. FLOOD. That is all right.

[The information follows:]

BLOOD RESEARCH OBJECTIVES

Currently, the responsibilities for research in the general field of thrombosis and hemostasis, which include the hemophilias and other clotting disorders, and the responsibility for research in sickle cell anemia and related conditions, including Cooley's anemia, rest with the National Heart, Lung, and Blood Institute. Another area which is essentially the sole responsibility of our Institute is blood resources, and this includes research on the preservation of the various blood components; on component therapy; on the safety of blood, which involves hepatitis research; and on the utilization, the logistics, and the management of the national blood resource.

The National Cancer Institute has the primary responsibility for malignant blood diseases, leukemia, Hodgkin's disease, and other lymphomas, and, because of the close relatedness of these diseases to white corpuscles, for white blood cell research also. The National Institute of Allergy and Infectious Diseases is also involved extensively with research in white blood cells because of their function in infectious diseases, and in hepatitis research, because the infectious agents are viruses.

There is comparatively little overlap between these mandates. There is considerable overlap between the concerns of our Institute and those of the National Institute of Arthritis, Metabolism, and Digestive Diseases in the area of red cell research—an overlap that is the result of historical developments. The National Institute of Arthritis, Metabolism, and Digestive Diseases has a primary interest in metabolism in general and has a long record of supporting research in red cell metabolism and related subjects. It would be difficult to discontinue or transfer such a program without a disruptive dislocation not only within the National Institutes of Health but within the scientific community that has been relying on existing support mechanisms in specific Institutes. The National Heart, Lung, and Blood Institute has established, in keeping with the mandate embodied in the Renewal Act of Public Law 94-278, a blood coordinating committee on which every Institute at the National Institutes of Health with a significant interest in the field of blood research is represented.

KIDNEY DISEASE RESEARCH

Mr. FLOOD. Now, in that material you gave us on your intramural research program that you are conducting on kidney diseases, what specifically are you doing in this area? Anything promising on the horizon?

Dr. LEVY. The kidney disease research program in intramural has been in existence for almost 20 years. The most exciting work they do is with micropuncture, looking at the factors that affect the exchange of salt of electrolytes, of materials, in the kidney nephron, learning about active energy systems that are involved in effectively helping the body get rid of waste products, salt, and water.

Mr. FLOOD. It is costing the medicare trust fund $600 million a year.

Dr. LEVY. Mr. Chairman, let me say that the extramural kidney research with renal dialysis, is supported by the Arthritis Institute.

Mr. FLOOD. Well, I know. Yes; the Arthritis Institute also has this program. By the way, so does VA.

Dr. LEVY. That is right.

COOLEY'S ANEMIA

Mr. FLOOD. Now, we talked a little while ago, not this year, about using the drug Desferal to treat Cooley's anemia. How successful is that drug? What about side effects on that one?

Dr. LEVY. The primary problem is related to the pain of the injections of the material. We are very pleased right now that continuous infusion of Desferal seems to be decreasing iron stores in the heart and other organs. We really just started funding projects in this area, and we hope, in the next 2 to 3 years, to get more definitive information.

SPECIALIZED RESEARCH CENTERS

Mr. FLOOD. Now, it was back in 1971, you started to fund the specialized research centers. You were out there. Well, how many of these are you currently supporting, and can you identify their major accomplishments? You can do some of that for the record.

Dr. LEVY. I would be pleased to develop it for the record.

Mr. FLOOD. And we would like to know how much are you going to invest in these centers, in 1977, and how much in 1978.

Dr. LEVY. $33 million in both 1977 and 1978. But we will provide that for the record.

[The information follows:]

]SPECIALIZED CENTERS OF RESEARCH[

Introduction

In 1970 the National Heart, Lung, and Blood Institute (NHLBI), announced a program to establish, on a competitive basis, a limited number of research centers devoted to specific disease problems identified by the Institute as of high priority. The objective of the Institute in establishing Specialized Centers of Research (SCORs) was to focus resources, facilities, and manpower on particular problems to expedite the development and application of new knowledge essential for improved diagnosis, treatment, and prevention of cardiovascular pulmonary and blood diseases. The initial program, undertaken after extensive planning, consisted of four groups of SCORs, each group addressing one of the following disease areas: arteriosclerosis, hypertension, pulmonary diseases, and thrombosis. In Fiscal 1975, a fifth group of SCORs, focusing on ischemic heart disease, joined the program. In Fiscal Year 1976 a total of 53 centers were active with funding totaling $32 million.

The SCOR Concept

A SCOR is an identifiable organizational unit within an institution. The specific purpose of these grant-supported centers is to advance basic knowledge and develop the most effective methods of clinical management and prevention in their designated disease areas. Programs of a SCOR may include basic, developmental, or applied projects and clinical investigations as they relate to a central theme. The SCOR concept requires that each type of SCOR be a part of a national network of Centers of Research addressing similar problem areas and that there be close coordination among SCORs within the network. To accomplish this active coordination, SCOR Directors meet regularly to review progress, discuss common interests and problems, and plan collaborative efforts. Each SCOR also has a special collaborative relationship with the NHLBI, working closely with the Institute staff to further appropriate NHLBI goals as set forth in the National Plan.

The interaction of scientists from various disciplines within a SCOR is more than a casual one brought about by mutual interests in the designated SCOR research area. There is an active collaboration of basic scientists and clinical researchers on projects of mutual interest. In addition, SCOR investigators are made aware of the entire SCOR program via seminars in which they describe their own current research activities and learn of relevant work by other investigators.

Although the maximum award period for a SCOR is five years, continuation of support, after the first year, is subject to satisfactory performance.

Evaluation of each SCOR is carried out via periodic visits of Institute staff and outside consultants to review progress. In addition, scientific progress is evaluated annually by members of the appropriate NHLBI Scientific Advisory Committee. This peer review by non-Institute scientists is an important component of the evaluation of each SCOR.

Over five years of experience with the first phase of the SCOR program has demonstrated its value for highly original basic research, for scientific communication, and for applied research in preventive and therapeutic medicine. Recently completed competitive solicitations for a second phase of SCORs should further this program aimed at the solution of specific problems of high priority.

Current Status of the Centers

Arteriosclerosis

The programmatic focus of the Arteriosclerosis SCORs is on the development and application of new knowledge essential for the improved diagnosis, treatment and prevention of atherosclerotic disease.

In the first five year phase of the SCOR program (1971-1975), 15 arteriosclerosis centers were funded. As of fiscal 1976 13 centers remained in the program, with one center converted to a regular research grant and another replaced by a National Research and Demonstration Center. The geographical distribution of the 13 centers is shown in Figure 1.

A new national competition was announced in May 1975. As a result, early in fiscal year 1977 eight SCORs were awarded including six renewals and two new Centers. The remaining seven SCORs are now in a phase-out period. It should be noted that continuation of a SCOR beyond a maximum of five-year funding is not automatic; existing centers must compete with new applications under scrutiny of the peer review mechanism. The competitive nature of center renewals extends across the entire SCOR program to insure the highest quality research directed at research problems of current significance.

Current activity is centered in three major areas with several studies within each area: clinical studies of hyperlipidemia and vascular disease, animal and tissue studies and basic laboratory investigations. Highlights of accomplishments include a community-based study of adult coronary heart disease risk factor reduction through lifestyle modification; extensive prevalence studies among 14,000 children from four different SCOR populations of risk factors such as diabetes, high blood pressure and high blood lipids; and studies of the metabolism of lipoproteins and lipids.

Hypertension

Five Hypertension SCORs were funded with the Phase One Program inaugurated in 1971. Through a national competition initiated in 1974, four centers were funded in fiscal 1976 for Phase Two of the Hypertension SCORs (Figure 2). The four Centers consist of one new Center and three renewals; two Centers were terminated.

The major thrust of the Program is a study of the renin-steroid relationships in hypertension. Much work has been done on "biochemical profiling" which relates plasma renin activity and aldosterone excretion rates to the type of hypertension in order to define groups of hypersives responsive to specific types of therapy. Steroids, which may explain some of the diuretic-responsive types of hypertension, have recently been identified. Accomplishments in the purification and crystallization of salivary renin have been made. The SCOR Program has further elucidated the differences between two types of experimental renal hypertension - "one kidney and two kidney hypertension. The one-kidney type is produced by renal artery constriction of the remaining kidney following unilateral nephrectomy and the two-kidney type, by renal artery constriction of one kidney, the other remaining intact. These two types seem to be different in their control mechanisms. New information has been generated in regard to the relationships of body fluid volume to other abnormalities that characterize hypertension. Natural history studies involve two aspects -- one of renin as a determinant of atherosclerotic complications in hypertensive patients, and the second, malignant hypertension in young black men.

Ischemic Heart Disease

From 1967 to 1974 the Myocardial Infarction Research Units (MIRU's) pioneered in developing innovative and effective techniques in basic and clinical research and treatment of heart attacks. In fiscal year 1975, after a nationwide competition, nine Ischemic Heart Disease SCORs were funded (Figure 3) with a mandate to broaden the research focus to the various manifestations of ischemic heart disease. The objective of the program is to support multidisciplinary clinical and fundamental research directed at the reduction of death and disability from ischemic heart disease.

Research in the Ischemic Heart Disease SCORs focuses on clinical manifestations and the pathophysiology, biochemistry and anatomy of ischemic heart disease. Investigations on patients with suspected or known acute or chronic ischemic heart disease are included spanning the complete spectrum of ischemic heart disease from the early detection of latent ischemic heart disease to such problems as acute myocardial infarction, sudden cardiac death, angina pectoris, congestive heart failure, emergency medical care and cardiac rehabilitation. Studies also include research relevant to ischemic heart disease in non-clinical laboratories, such as biochemistry, electrophysiology, pathology, hematology, and endocrinology laboratories.

The centers have already made a number of contributions toward protecting ischemic myocardium, quantifying infarct size, and in completing a clinical trial to test whether surgical or medical treatment is the best treatment for unstable angina pectoris.

Pulmonary Diseases

The Pulmonary Disease SCORs inaugurated in 1971 resulted in the funding of 11 centers. It was recognized, however, that these centers were weighted toward the study of chronic lung diseases. Consequently a second competition announced in September 1971 expanded the program in 1972 to 17 centers with an adequate research balance including fibrotic and immunologic diseases, environmental factors in pulmonary diseases and therapeutic interventions. A third Pulmonary Disease SCOR competition was announced in March 1975 and invited applications for both renewal of active SCORs and new SCORs. As a result of this competition the total number of centers has grown to 24 (Figure 4). Each of these centers addresses itself to one of four disease categories including chronic diseases of airways, pediatric pulmonary diseases, fibrotic and immunologic pulmonary diseases, and pulmonary vascular diseases. Within these disease categories, topics of particular interest are irreversible chronic bronchitis and emphysema; asthma, hyaline membrane disease (neonatal respiratory distress syndrome); cystic fibrosis, fibrosis, bronchiolitis and other obstructive lung diseases; identification of risk factors for fibrotic and immunologic pulmonary diseases, pulmonary hypertension and pulmonale; and pulmonary edema.

Through these SCORs it has been demonstrated that simple screening tests for pulmonary function can be used with sensitivity and specificity to diagnosis subclinical pulmonary emphysema; radiographic imaging techniques have been developed which now allow visualization of the smallest lung units; the prevention and management of respiratory distress syndrome has been improved; much basic knowledge on the ontogeny and phylogeny of the surfacant system has been developed.

Thrombosis

The Thrombosis SCORs have launched a multifaceted program of research into the etiology, pathogenesis, prevention and treatment of thromboembolic disease. Much of the work is basic in nature, elucidating various details of the highly complex coagulation mechanisms and their interrelationships with blood platelets and the vessel wall.

Phase One of the thrombosis SCOR competition established five SCORs. In 1976 a new competition resulted in the funding of three SCORs (Figure 5). Two of these Centers are renewals, and one is a new Center; three of the original Centers were terminated. Each thrombosis SCOR has its own particular mix of basic and clinical research activities, reflecting the individual talents and interests of its scientists. However, in all Centers the role of the platelet in thrombosis is one of the principal foci of activity. Platelet research has proceeded along the following lines: structural detail down to the molecular level, using electron microscopic, biochemical and immunological techniques; the relation to lipids in thrombus formation; elucidation of the mechanism of platelet aggregation and the "release" phenomenon. Of particular interest has been an intensive study of the structure of the

fibrinogen molecule and its breakdown products. The role of these products in thrombosis initiation is under study. From these studies new means of diagnosis of incipient thrombosis may be expected. In addition, the thrombosis SCOR program has encompassed such studies as noninvasive techniques to detect deep vein thrombosis; the development of laboratory techniques for the evaluation and control thrombosic therapy; and clinical trials of platelet-inhibiting drugs for prevention of thrombosis in patients at high risk.

Future Funding

As noted in the previous section, all SCOR programs except for Ischemic Heart Disease, have embarked on their second phase awarded in fiscal 1976. The Ischemic Heart Disease SCORs will not be ready for a new competition until 1979 with potential funding in 1980. The following table shows the expected expenditures for the SCOR program for fiscal 1977 through fiscal 78, and the expenditures in FY76.

SCOR Program	# Active FY76	Funds (Millions of dollars) Prior to FY76	FY76	FY77	FY78
Arterio-sclerosis	13	47.8	5.9	10.0	7.7
Hypertension	4	14.2	3.6	3.2	3.9
Ischemic Heart Disease	9	7.8	9.7	9.7	9.6
Pulmonary Diseases	24	34.7	10.3	6.8	11.0
Thrombosis	3	12.0	2.8	3.0	2.9
Total	53	116.5	32.3	32.7	35.1

Table 1. SCORs Expenditures (Projected for FY77 and 78)

ARTERIOSCLEROSIS

OBLIGATIONS	
Funding History:	
Fiscal Year 1976	$ 5,925,305
Fiscal Years 1971-1975	$47,788,577
Total Funding to Date	$53,713,882



ACTIVE ORGANIZATIONS - 1976

GRANT NUMBERS

Program Inaugurated in 1971

1. Albany Medical College, Albany, New York ..... HL 14177
2. Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina ..... HL 14164
3. Massachusetts Institute of Technology, Cambridge, Massachusetts ..... HL 14209
4. Mayo Foundation, Rochester, Minnesota ..... HL 14196
5. Rockefeller University, New York, New York ..... HL 14236
6. Stanford University, Stanford, California ..... HL 14174
7. University of California, La Jolla, California ..... HL 14197
8. University of California, San Francisco, California ..... HL 14237
9. University of Miami, Coral Gables, Florida ..... HL 14141
10. University of Iowa, Iowa City, Iowa ..... HL 14230
11. University of Southern California, Los Angeles, California ..... HL 14138

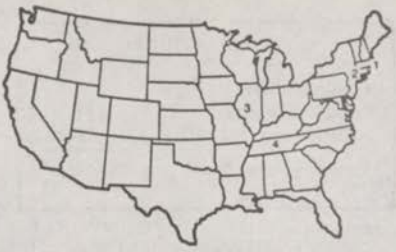
Program Expanded in 1972

12. Louisiana State University, Baton Rouge, Louisiana ..... HL 15103
13. University of Chicago, Chicago, Illinois ..... HL 15062

Figure 1. Arteriosclerosis SCORs

HYPERTENSION

OBLIGATIONS	
Funding History:	
Fiscal Year 1976	$3,580,919
Fiscal Years 1971-1975	$14,244,139
Total Funding to Date	$17,825,058



CURRENT ACTIVE ORGANIZATIONS — **GRANT NUMBERS**

Phase One Inaugurated in 1971
Phase Two Awarded in 1976

1. Boston University, Boston, Massachusetts ..... HL 18318
2. Cornell Medical School, New York, New York ..... HL 18323
3. Indiana University Foundation, Bloomington, Indiana ..... HL 14159
4. Vanderbilt University School of Medicine, Nashville, Tennessee ..... HL 14192

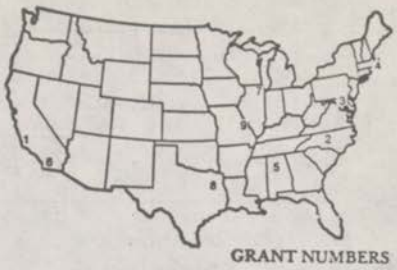
Figure 2. Hypertension SCORs

ISCHEMIC HEART DISEASE

OBLIGATIONS

Funding History:

Fiscal Year 1976	$9,736,553
Fiscal Year 1975	$7,814,421
Total Funding to Date	$17,550,974



CURRENT ACTIVE ORGANIZATIONS — GRANT NUMBERS

Program Inaugurated in 1975

1. Cedars-Sinai Medical Center, Los Angeles, California ..... HL 17651
2. Duke University, Durham, North Carolina ..... HL 17670
3. Johns Hopkins University, Baltimore, Maryland ..... HL 17655
4. Massachusetts General Hospital, Boston, Massachusetts ..... HL 17665
5. University of Alabama, Birmingham, Alabama ..... HL 17667
6. University of California, San Diego, California ..... HL 17682
7. University of Chicago, Chicago, Illinois ..... HL 17648
8. University of Texas Southwestern Medical School, Dallas, Texas ..... HL 17669
9. Washington University, St. Louis, Missouri ..... HL 17646

Figure 3. Ischemic Heart Disease SCORs

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PULMONARY DISEASES

OBLIGATIONS	
Funding History:	
Fiscal Year 1976	$10,288,532
Fiscal Years 1971-1975	$34,706,824
Total Funding to Date	$44,995,356



CURRENT ACTIVE ORGANIZATIONS — GRANT NUMBERS

Phase One Inaugurated in 1971

1. Columbia University College of Physicians and Surgeons, New York, New York ..... HL 14218
2. Johns Hopkins University, Baltimore, Maryland ..... HL 14153
3. Medical College of Virginia, Richmond, Virginia ..... HL 14251
4. University of Arizona, Tucson, Arizona ..... HL 14136
5. University of California, La Jolla, California ..... HL 14169
6. University of California, San Francisco, California ..... HL 14201
7. University of Texas Southwestern Medical School, Dallas, Texas ..... HL 14187
8. University of Vermont, Burlington, Vermont ..... HL 14212
9. University of Washington, Seattle, Washington ..... HL 14152
10. Vanderbilt University School of Medicine, Nashville, Tennessee ..... HL 14214
11. Yale University, New Haven, Connecticut ..... HL 14179

Program Expanded in 1972

12. Boston University, Boston, Massachusetts ..... HL 15063
13. Medical College of Wisconsin, Milwaukee, Wisconsin ..... HL 15389
14. Rancho Los Amigos Hospital, Downey, California ..... HL 15098
15. Tulane University, New Orleans, Louisiana ..... HL 15092
16. University of Pennsylvania, Philadelphia, Pennsylvania ..... HL 15061

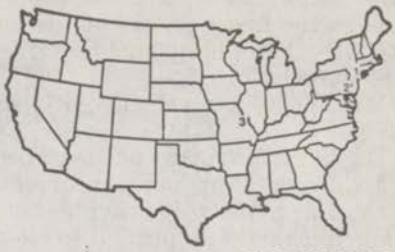
Phase Two Awarded in 1976

17. Harvard University, Boston, Massachusetts ..... HL 19170
18. Johns Hopkins University, Baltimore, Maryland ..... HL 19157
19. University of California, San Francisco, California ..... HL 19155
20. University of California, San Francisco, California ..... HL 19156
21. University of California, San Francisco, California ..... HL 19185
22. University of Missouri, Columbia, Missouri ..... HL 19160
23. University of North Carolina, Chapel Hill, North Carolina ..... HL 19171
24. University of Washington, Seattle, Washington ..... HL 19187

Figure 4. Pulmonary Diseases SCORs

THROMBOSIS

OBLIGATIONS	
Funding History:	
Fiscal Year 1976	$2,780,668
Fiscal Years 1971-1975	$12,046,667
Total Funding to Date	$14,827,335



CURRENT ACTIVE ORGANIZATIONS **GRANT NUMBERS**

Phase One Inaugurated in 1971
Phase Two Awarded in 1976

1. Cornell University Medical College, New York, New York ..... HL 18828
2. Temple University School of Medicine, Philadelphia, Pennsylvania ..... HL 14217
3. Washington University, St. Louis, Missouri ..... HL 14147

Figure 5. Thrombosis SCORs

Dr. LEVY. The sudden death program, the program on quantifying infarct size, new measurements of enzymes that can identify heart attack in the first minutes of the heart attack, have all come from the SCOR's. The pulmonary SCOR's have given us tremendous insight into the relationship——

Mr. FLOOD. Are you currently supporting everything you started in 1971?

Dr. LEVY. No; many of the projects have been completed.

Mr. FLOOD. What are you currently supporting?

Dr. LEVY. We will provide that for the record. I think, Mr. Chairman, you would be pleased to see that when the SCOR program runs a finite period of time, usually 5 years, we have competitive renewals, so that some centers that we supported initially are not being supported now, and new centers are being supported now that were not supported before.

Mr. FLOOD. All right.

GEOGRAPHIC PATHOLOGY

Mr. OBEY. Doctor, let me just ask a few more questions.

Evidently there has been some research around the country which indicates there is a correlation between the incidence of cancer and the incidence of heart disease in the same geographical area; is that correct?

Dr. LEVY. No; that is not really correct, Mr. Obey. We have gotten in the last year into geographic pathology, and I have a map here that I will supply for the record that shows the distribution of coronary heart disease, the major heart disease killer. We have recently looked at it in relationship to the cancer map. Our map is quite different from theirs. Obviously, there are a few places where there is overlap, but it does look in terms of the major heart disease forms, that the distribution of heart disease deaths and cancer deaths do not overlap each other.

[The information follows:]

Mr. OBEY. So there is no significant correlation in your judgment.

Dr. LEVY. I am sure that there may be some correlation in some industrially polluted areas. But looking at the U.S. map as a whole, the cancer hot spots do not match up with the heart disease hot spots as we are now defining them; though seeing hot spots like this, Mr. Obey, clearly gives the suggestion that there are special features about, for example, the southeastern part of the United States that have to be investigated.

CAUSES OF HEART DISEASE

Mr. OBEY. What are generally regarded as the three leading causes of heart disease?

Dr. LEVY. Smoking, high cholesterol, high blood pressure, and diabetes are the four major risk factors.

Mr. OBEY. I have heard different viewpoints on cholesterol. It appears that it is involved in some way, but it has been suggested to me by some that cholesterol may not be the cause of arteriosclerosis but rather a major factor in its later stages. What would your response be to that?

Dr. LEVY. It is clear from epidemiologic studies that the higher a subject's cholesterol, the more he is at risk.

Mr. OBEY. I am not trying to deny that. I am simply asking, is it in fact a degenerative factor.

Dr. LEVY. Atherosclerosis is a complex affair. Some studies have shown that the cholesterol carried in the blood by lipo-proteins can initiate injury, can get into the blood vessel and begin the process. There is even better evidence, however, that cholesterol is a handmaiden in the process; that the more cholesterol circulating in the blood, the more cholesterol will get into the atherosclerotic plaque and the larger the plaque will become. The major element in the atherosclerotic plaque is cholesterol. The $64 million question, as we might call it, is whether lowering cholesterol through diet or drugs will decrease atherosclerosis risk. With nonhuman primates that has been demonstrated. In man we are seeking evidence now. But I have no doubt that cholesterol is an associate factor with atherosclerosis and is involved in its genesis. Whether it is involved with the immediate etiology is not clear in that we don't understand the multifocal etiological nature of the process.

FUNDING RESEARCH ON WATER AND CARDIOVASCULAR DISEASE

Mr. OBEY. OK. The Environmental Health Science Task Force Report recommended that research should be intensified to identify the causal factor in soft water of the syndrome we are talking about. You said that you are spending about $300,000 in your shop on that?

Dr. LEVY. We are spending $300,000 in studies relating to this, direct studies in soft and hard water, with the EPA. It has been budgeted for approximately $100,000 in fiscal 1977.

ENVIRONMENTAL FACTORS

Mr. OBEY. Let me ask you this. Again, regardless of how they are characterized, and looking over this list of grants and contracts—if you just ignore the classification let me ask you this question.

If you exclude diet—I know there is an awful lot being done on cholesterol—what percentage of your budget would be devoted to research on the environmental causes, and I am talking about the direct natural environmental causes as opposed to something which we can make a conscious choice about.

Dr. LEVY. Perhaps most directly I can answer that by saying that it is hard to exclude diet, smoking, lifestyle from the heart area. In the lung area we estimate that about $9 million is invested in environmental studies that——

Mr. OBEY. Let's talk heart. My point is, if you exclude smoking, which is after all a voluntary act, and if you exclude eating 60 pounds of cheese a week, if you exclude those kinds of voluntary acts, research on those kinds of factors, what percentage of your research would be geared into the environmental agents about which people have no choice?

Dr. LEVY. I would say that probably directly related it would be—depending on definitions and leaving out those other environmental factors—probably 1 or 2 percent of the heart budget is spent on these other environmental factors—looking always for new risk factors in heart disease, in fact thinking of it that way I might say it is probably more than the 1 or 2 percent.

Mr. OBEY. Well, my only point in this questioning is this, Doctor. I recognize that in terms of environmental impact on the human body, if you are talking about the liver, the lungs or kidneys, you are talking about the organs which have a more heavy responsibility in that area, in terms of the way the body functions.

But my question is simply this.

In the light of the suggested conclusions—let me put it that way—of some of the research being done, don't you think that that item might be a little light? I understand the traditional mind-set would not lead one to explore the environment directly as a cause of heart disease. But I am wondering whether or not the amount of money you indicate perhaps isn't a little smaller than it should be in relationship to some of the more traditional research that you are doing.

EPIDEMIOLOGICAL STUDIES

Dr. LEVY. The problem is always competing priorities. But let me assure you, Mr. Obey, we have increased our interest and enthusiasm in this area.

Dr. Feinlieb, who is chief of our epidemiology and biometric activities in the Division of Heart and Vascular Diseases is intensely interested in this, both looking at specific factors such as trace metals, and extending our current epidemiological studies to try to include more and more of these environmental factors that were not thought about or measured before. I am sure we will be spending more dollars on this in the future.

Mr. OBEY. Just one last comment, Doctor. You mentioned trace metals. And yet when you indicate the small amount that is really being spent, for instance, on water—I have no idea whether that research is going to lead anywhere or not. It just seems to me that one of the most frustrating things facing any family in this country is to know that there is so much that is being suggested about the dangers found

in their own water supply, and they cannot make a conscious decision about it. You can buy bottled water and you can find out in some ways it is dirtier than the stuff that comes out of the tap. Under those circumstances, I am somewhat surprised that you are not spending more at least in that area—granted that I know precious little about it.

Dr. LEVY. We are seeking the answers. One of the most difficult things in this area are the chemical assays to measure the amount of elements in the tissues, in the blood, and until those assays can be perfected and have precision and accuracy, wider spread epidemiological studies would be like scatter guns. And so a major focus in on improving the technology here.

Mr. OBEY. Do you think that there is any more that your shop can do or do you think that this kind of research is more appropriately conducted in some other agency?

Dr. LEVY. I have no doubt that we could do more in this area. I have no doubt that we have not defined all of the factors—just looking at the cardiovascular mortality map we just looked at—suggests there are local geographic factors. Undoubtedly, many of them are in the environment, in the trace metals, silicone, other materials in the ground, in the earth, in the air we breathe. We certainly could do more looking at it from our perspective. The more perspectives that are brought into this issue, looking at it from testing chemicals or looking at it from the end result, the heart disease, the quicker we will get the information and the answers.

So, yes, I am sure we could do more, and we will do so within the limits of our budget. This is an area that our epidemiologic group has become more interested in in the last few years.

RESEARCH FUNDING

Mr. OBEY. I would be curious if you could tell me what would be the three or four most important kinds of studies that you think you could usefully perform in your shop in these areas that you cannot perform now, given your budget limitations.

Dr. LEVY. Well, the biggest problem, Mr. Obey, is undoubtedly to have the resources to take advantage of serendipity, the knowledge that a community, a town, a State, is going to change its water supply some way, to get the baseline assessments, and then to measure the subjects again. Right now we can only do this in a very small pilot-like way, because of the dollars that would be required. These experiments you might say of nature and man, however, provide a great opportunity. But we are limited in terms of availing ourselves of it at the present time. Improving the technology, the ability to measure these elements in the heart, in the body, is something that we and NIEHS are both supporting and exploring right now.

The performance of more systematic epidemiologic surveys in high-risk areas, as in the Southeast, to try to define what are the trigger factors in this area, clearly would have great promise of reward.

Dr. FREDERICKSON. One of the great problems is that the test system doesn't exist. The long-range nature of trying to discover what causes arteriosclerosis by using man as a subject is a tremendous problem. If one could assume that mutagenesis might lie at the base, one could

test a number of substances or factors by a system for determining if they are mutagenetic. I suspect that probably isn't going to be the case. But when in vitro tests, using smooth muscle cells reveal extraordinary sensitivity to a number of external variables, such as chemicals, then it might be possible to proceed here a lot faster.

So one of the problems is to get a much more sensitive and meaningful test.

Mr. OBEY. Thank you, Mr. Chairman.

Mr. FLOOD. Thank you very much.

We will adjourn until 1:30 when we will meet with the Dental Institute.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. CONTE

Mr. CONTE. What has been the progress with your hypertension detection and followup program? How many people are participating in this program, and what kind of results have you had?

Answer. The hypertension detection and followup program is a multicenter cooperative effort designed to determine the effectiveness of systematic sustained antihypertensive therapy in reducing total mortality in a wide spectrum of persons with elevated diastolic blood pressure screened from fourteen communities.

Over 158,000 persons age 30–69 were screened, of whom 26 percent were black and 74 percent white and other. 14.5 percent were found to have high diastolic blood pressure.

After a second screening at the clinic, 10,940 hypertensive persons were enrolled in the program. 44 percent were black and 56 percent were white and other.

Approximately half of these hypertensive persons have been followed and treated at the program clinics under the stepped care regimen of treatment. The other half were referred to other sources of care in the community and are seen approximately annually by program staff to assess their current blood pressure status.

After 2 years of followup, all participants were invited to come into the program clinics for a medical evaluation. This followup medical examination was successfully completed on 92 percent of all participants.

Among the Stepped Care participants, the average fall in blood pressure after the 2 years of followup and treatment was significant. We consider the degree of sustained blood pressure control as an important achievement.

Currently, approximately 80 percent of those assigned to the stepped care group receiving treatment in the program clinics are still under active treatment and over two-thirds have achieved their goal blood pressures. The plan is to continue the program until all participants have had 5 years of followup to determine whether sustained long-term treatment will reduce mortality.

Several papers have recently been submitted describing the findings at baseline and the first 2 years' experience with followup. To date 15 articles have been published. Thus, overall we believe that the program is progressing very satisfactorily.

NON-INVASIVE INSTRUMENTATION

Mr. CONTE. You mentioned dramatic advances in the development of noninvasive methods of detecting abnormal cardiac activity. Could you tell us more about these methods, how they work and how much the necessary equipment costs? Is this technique something that could be used in mass screening efforts, or only when indicated by symptoms of cardiac disease or impairment?

Answer. Ultrasound and radionuclide approaches demonstrate underlying gross anatomic abnormalities and thus have broad applicability and appeal in delineating lesions within the heart and great vessels.

Echocardiography is a painless, safe, noninvasive-technique for visualizing the heart and great vessels by means of reflected ultrasound waves. There is intense current interest in cross-sectional echocardiography, which produces a

two-dimensional or planar image rather than the unidimensional time-motion display. This is even more useful in the diagnosis and evaluation of several congenital and acquired heart conditions.

An oscillating transducer, or "scanner," is placed on the patient's chest and directs an ultrasonic beam through the intact chest wall to the section of the heart to be examined. Like X-rays, ultrasound passes readily through many bodily tissues and fluids, but a portion of the beam is reflected from the surface of the heart and from the blood-tissue interfaces within it. The returning echoes are converted electronically into a cross-sectional image of the heart, permitting detection of structural defects and assessment of their effects on heart performance.

Two-dimensional echocardiography is highly effective in diagnosing defects such as transposition of the great vessels, tetralogy of Fallot, absence of a ventricular septum, and other congenital conditions resulting in cyanosis ("blue babies"). It often provides information on these conditions that cannot be obtained by conventional X-ray visualization (angiography) and, in some instances may even obviate the need for angiography, a procedure not without hazard in critically ill infants.

Another noninvasive method of determining abnormal cardiac activity to which I was referring has the formal name "radionuclide cineangiography." A radioisotope, which remains in the bloodstream, is given as an intravenous injection. The radioisotope in the blood within the chambers of the heart can be detected by external apparatus, and a motion picture is produced on a television screen which shows the beating of the heart. There are a number of variations on this. However, basically, this makes it possible to see how completely the heart ejects blood with each beat and how uniformly the total heart wall is contracting.

One part of this apparatus is a gamma camera which detects and locates the source of the radionuclide emissions which are then converted into a picture. There still remains the problem of the moving and beating heart. This is overcome by the use of a computer. We cannot give enough isotope so that we would get a clear picture from a single heart beat. Thus, we must take each heart beat and slice it into about 60 or 100 very short time periods, and the camera records the signal from a couple of hundred heart beats. The computer is used to add up the signals from the corresponding time slot of each successive heart beat. In this way, we can get the typical picture for every fraction of the heart beat by totaling the signals from several hundred heart beats. This is then played back as a motion picture.

Such equipment, unfortunately, is not inexpensive. Present apparatus costs in excess of $100,000. At this time, we do not look upon this as a screening tool to be used in the general population, but rather as an evaluative tool in persons who are identified as being of special risk or in whom a special assessment of heart function is needed. As we get more experience to tell us precisely how much information this technique gives us, as we develop better and less expensive technology which will permit us to do this more easily and efficiently and less expensively, the indications for its use will probably become far wider.

We are, of course, developing a variety of different noninvasive techniques. Some will always be for special diagnostic or even research procedures, but others are definitely intended for ultimate screening use.

The Institute has planned a major expansion in the development of noninvasive technology for the detection, characterization and quantification of atherosclerotic lesions. Such noninvasive technology, particularly in the form of portable devices, would be of primary value in qualifying the progression or regression of lesions in large scale clinical trials or in characterizing the nature of atherosclerotic lesions and in detecting atherosclerosis in asymptomatic persons. Envisioned program expansion would also develop and assess instrumentation and techniques for the reliable measurement of such hemodynamic factors as arterial and venous blood pressure and flow, noninvasive methods for quantifying both the dimensions of the heart dynamically, and the areas of abnormal cardiac movement. Of particular interest is the development and assessment of methods for the long-term recording and data reduction of cardiovascular physiological signals during ambulatory conditions. The availability of this noninvasive technology should lead to less expensive, more accurate and more accessible diagnosis. Better diagnosis, in turn, portends early and more effective treatment of cardiovascular disease.

HYPERTENSION IN THE YOUNG

Mr. CONTE. What are you doing to identify hypertension in the young?

Answer. Elevated blood pressure has been clearly identified as a major risk factor for coronary heart disease, stroke, and congestive heart failure in adults. However, until quite recently, relatively little has been done to identify the precursors of high blood pressure, especially those precursors that may operate or be recognizable in young persons.

Accordingly, NHLBI issued a request for research grant application (RFA) on December 18, 1975, to solicit epidemiological investigations of high blood pressure in young persons and possible early precursors of adult hypertension. As a result of the RFA, 16 research grants were awarded in fiscal year 1976. Since many investigators are emphasizing that adult hypertension may have its origins in adolescence or even in childhood or infancy, the objective of this program is to conduct epidemiologic studies which will help to identify such precursors and possibly lead to methods which may be effective in the prevention of adult hypertension. It would also provide important studies to determine the extent to which suspected precursors in young persons can explain why certain subgroups (for example, blacks) have relatively higher rates of hypertension, and whether similar factors might also be important in subgroups which have not been as adequately studied (for example, Spanish-Americans).

Finally, a task force convened by the Institute has recommended proper diagnostic and treatment procedures for youngsters with high blood pressure problems. This report, entitled "Report of the Task Force on Blood Pressure Control in Children" will be published in May in a supplemental issue of the Journal of Pediatrics which will be entirely devoted to this report.

AMERICAN BLOOD COMMISSION

Mr. CONTE. Could you tell me what the American Blood Commission has done in the past year? What are the chances of developing an all-volunteer blood donor system?

Answer. The American Blood Commission (ABC), since its creation in April 1975, has been involved in bringing about a coalition of the diverse interests and divergent philosophies in this country's blood banking complex. In an effort to resolve fragmentation of services and to promote efficiency in operations, the ABC is assisting local and regional blood service units in forming regional associations that could share resources. In addressing the need for complete and accurate information about blood service operations, the ABC is developing a comprehensive data system so that blood banks may have access to essential data relative to blood supply, use, and costs for planning and for analyzing their own performance. In an effort to eliminate costly, confusing, and potentially tragic errors in labeling blood, the ABC has developed a system which will enable all blood centers and hospitals to use a standard blood-pack label. In an effort to identify the benefits of differing donor recruitment strategies used by blood banks, the ABC is collecting and assessing data on blood-related educational programs in schools, donor recognition and incentive programs, and training programs for donor recruiters.

Of the 7.3 million units of blood collected in 1971, approximately 75 percent were from volunteer donors. The current estimate of the total blood collected from volunteer donors is 93 percent. This definitely shows a trend toward the development of an all-volunteer blood system.

COOLEY'S ANEMIA

Mr. CONTE. Last year you told us about the discovery that Cooley's anemia resulted from inappropriate production of the hemoglobin beta chain. What advances have been made in the Cooley's anemia this year? Are you working with any of the other institutes on this—the Arthritis Institute, for example?

Answer. Recent research has contributed to a better understanding of the mechanism of the inappropriate production of the hemoglobin beta chain in Cooley's anemia, otherwise known as beta thalassemia. It has recently been demonstrated that in beta thalassemia the beta globin structural genes are present in the DNA but are inefficiently expressed or code mutant unstable messenger RNA's that are degraded during development. Less commonly, there is actual deletion of the beta structural genetic material from DNA or production

of mutant nonfunctional messenger RNA. This is in contrast to the defect in alpha thalassemia, where deficiency of alpha globin messenger RNA always results from deletion of the alpha globin structural material from DNA. This improved understanding of the mechanism of inappropriate hemoglobin chain production should contribute to our goal of curing thalassemia.

Also of note is the fact that NHLBI Intramural laboratory research this year has revealed that the gene that controls the synthesis of alpha chain of hemoglobin resides on chromosome 16. The gene that controls the synthesis of the beta chain is on either chromosome 9 or 11.

In the meantime, research is also being directed toward the eventually fatal problem of iron-overload in thalassemia. The Division of Blood Diseases and Resources of the National Heart, Lung, and Blood Institute has awarded five grants submitted in response to a request for applications (RFA) in the area of treatment of iron-overload in the thalassemia. These investigators are deveolping ways to treat patients with iron chelating agents in doses higher than had been formerly feasible, with resulting improvement in excretion of excess iron. In addition, these researchers are attempting to develop new and improved chelating agents.

The National Institutes of Health is the lead agency for activities concerning Cooley's anemia in the Public Health Service. Through the Interagency Cooley's Anemia Coordinating Committee it cooperates, advises, and exchanges information with the Health Services Administration, which provides screening, counseling, and education services, and the Center for Disease Control, which provides training in laboratory procedures for detecting hemoglobinopathies including the thalassemias and has conducted a Proficiency Testing Survey on hemoglobinopathies in voluntarily participating laboratories to help improve their testing capabilities. Research in the diagnosis, treatment, and prevention of Cooley's anemia is conducted at the NIH through both an intramural program and an extramural program of grants and contracts. An Inter-Institute Coordinating Committee on Cooley's Anemia facilities a cooperative approach to the support of research at the NIH. A particularly close cooperative effort has been established between the National Heart, Lung, and Blood Institute and the National Institute of Arthritis, Metabolism, and Digestive Diseases, the two NIH Institutes which have the major responsibility for support of Cooley's anemia research. For the past 4 years the Interagency Cooley's Anemia Coordinating Committee has submitted a report on the administration of Cooley's anemia programs to the President and to the Congress.

EMERGENCY MEDICAL SERVICES

Mr. CONTE. To what extent do you work with the emergency medical services program in developing techniques for the treatment of heart attack and other heart disease symptoms on an emergency basis?

Answer. We certainly work with the emergency medical services program. Indeed, the NIH representative on the Interagency Advisory Committee for that program is our Associate Director for Cardiology. The majority of the emergency cardiovascular techniques which have been and are now being implemented by the emergency medical services program developed out of such Institute-funded activities as the clinical, emergency, care-based programs in Seattle, Miami, in Nassau County, New York, and several other places. These in turn were based upon many Institute-funded fundamental investigations, often completely outside the clinical setting, ranging from the techniques of defibrillation to the use of various emergency drugs. As a part of our research in some of these emergency care systems, we have been instrumental in supporting the development not only of techniques of care, but in supporting the concept that such care can be administered by well-trained paramedical personnel.

Our current emphasis of research with respect to emergency care contains an element of therapeutic research, but our major thrust is upon the peventionof the emergencies in the first place. I am referring here not only to the fundamental prevention of arteriosclerosis, the underlying process for most cardiovascular emergencies, but also to preventing the recurrence of cardiovascular catastrophes in those who are known to have heart disease. For example, we are starting a national collaborative trial to assess the possible therapeutic efficacy of a drug to reduce the incidence of sudden cardiac death and thereby improve the life expectancy of those who have survived a previous heart attack.

I might add that the Institute last year cosponsored (other sponsors included the American Heart Association and the American National Red Cross) a study by the National Research Council Committee on emergency medical services to examine the current state of knowledge of emergency management of the upper airway. The objective of the study was to review the recent advances in techniques and devices and to evaluate the risk/benefit features of each; to recommend standards where possible and appropriate; to review the recommendations relating to airway management of a previous (1973) conference on cardiopulmonary resuscitation and emergency cardiac care; to identify the areas where further research is needed; and to recommend, on the basis of the current level of knowledge, a sequence of procedures to be applied in upper airway emergencies and how and to whom these procedures should be taught. A report on the study has been prepared by the National Academy of Sciences.

So, in summary, we work both with the Emergency Medical Services group under Dr. Boyd, and we work to try to avoid their need.

INFANTILE RESPIRATORY DISTRESS SYNDROME

Mr. CONTE. Can you tell me more about infantile respiratory distress syndrome? What are its symptoms and what is the Institute doing to find a cure? Do you see any possible connection between infantile respiratory distress syndrome and sudden infant death syndrome?

Answer. Infantile respiratory distress syndrome (IRDS) is currently the principal pediatric pulmonary disease and the major cause of perinatal mortality. There is no known connection between IRDS and sudden infant death syndrome. Almost exclusively limited to the prematurely born, IRDS accounts for approximately 12,000 neonatal deaths and 800,000 hospital days per year. The incidence of the disorder is clearly related to the degree of prematurity and ranges from about 20 percent at 33 weeks gestation to over 60 percent at 30 weeks. Intensive multidisciplinary studies in the past 5 to 7 years have enhanced our fundamental knowledge of lung maturation; this knowledge has been rapidly applied and coordinated with clinical findings. For example, basic research efforts have shown that the lack of pulmonary surface active material (surfactant) in the fetal lung may be the major cause of respiratory distress syndrome. Through a safe procedure (amniosentesis), fluid may be sampled in utero to determine fetal lung maturity and to identify infants at risk before birth. Methods and tests have been developed to monitor the function of the infant's lungs immediately after birth which have helped to lower the incidence of morbidity and mortality. At present, these sophisticated treatment programs are best carried out in special intensive care units in large hospitals; however, programs are now being developed to educate physicians and paramedical personnel in smaller communities about new advances in diagnosis and therapy. Moreover, programs for rapid transportation of newborns with infant respiratory distress syndrome to large centers have been initiated and simple guidelines for early administration of therapy during transportation are currently being developed, since the first hours in the course of the disease crucially affect the final outcome.

Although considerable progress has been made to reduce morbidity and mortality from infant respiratory distress syndrome, prevention remains a highly desirable goal and may be possible by proper use of pharmacological interbention. The most promising drugs at present are corticosteroids, which in multiple animal studies have proved effective to maturing fetal lungs when administered to the mother shortly before parturition. Data from one controlled clinical trial suggest that corticosteroids may be similarly effective in preventing infant respiratory distress syndrome in the human neonate. However, before recommending the widespread use of such drugs, careful evaluation of possible risks versus benefits must be carried out in a well-controlled clinical trial. Such a trial has recently been initiated as a collaborative effort involving six clinical centers in the United States. Over the 5 years, data will be collected to evaluate the effectiveness of corticosteroids in decreasing the incidence of infant respiratory distress syndrome and to identify short- or long-term adverse effects that may be associated with this treatment.

LUNG DISEASES

Mr. CONTE. What portion of your budget is related to lung disease?

Answer. As you know, the National Heart, Lung, and Blood Institute's authorizing legislation has required from 1973 to the present that at least 15 per-

cent of the appropriation be used in research on lung diseases and not less than 15 percent on blood diseases. In 1976, the most recent fiscal year, $57.5 million or 15.6 percent of total obligations related directly to lung disease. These figures compare with $26.3 million or 11.3 percent in 1972, the year preceding the 15 percent requirement and $7 million in 1970 the year the Institute's name changed from the National Heart to the National Heart and Lung Institute.

PERFLUOROCHEMICAL BLOOD INSTITUTE

Mr. CONTE. Can you tell me how the perfluorochemical blood substitutes work? Will they actually carry oxygen through the body?

Answer. The perfluorochemical blood substitutes are compounds that are highly efficient in carrying oxygen and carbon dioxide. The liquid fluorochemical is converted into stable, small particles that perform the functions of erythrocytes by transporting oxygen and carbon dioxide throughout the body. Considerable progress has been made in the past several years toward developing preparations of these compounds that will carry as much, or more, oxygen and carbon dioxide as will whole blood. Complete blood replacement in rats has been achieved with perfluorochemical-type substitutes. Bloodless animals so produced exhibit no abnormal behavior but go on to regenerate blood cells and plasma and continue to grow and develop. In preliminary studies, 50- to 80-percent blood replacement has been accomplished in nonhuman primates.

CYSTIC FIBROSIS

Mr. CONTE. What is the Heart, Lung, and Blood Institute doing in research on cystic fibrosis? How do you coordinate your work with the other Institutes conducting research on this disease? Do you ever jointly sponsor research projects with other Institutes?

Answer. Cystic Fibrosis, the most common lethal or semilethal genetic disease of peoples of Caucasian descent, is inherited as an autosomal recessive manner with an estimated frequency of one in 2,000 live births in white populations. Increasing survival has resulted in an estimated total of 15,000 to 20,000 afflicted persons in the United States today, 2,000 of whom are adults. An additional 800 to 2,000 patients are diagnosed annually.

Clinically, cystic fibrosis is characterized by the triad of chronic pulmonary disease, pancreatic insufficency and elevated sweat elctrolytes. Pulmonary diease, however, accounts for 90 to 95 percent of deaths. Several research programs supported by the division of lung diseases are underway to learn more about the pulmonary-related problems of this disease. For example, the division supports studies on the chemistry of mucus in order to determine why so much mucus (which clogs the airways) is secreted by patients with cystic fibrosis. Recently, the division initiated two specialized centers of research, one at Johns Hopkins, the other at the University of Missouri which have as their goal basic research on cystic fibrosis. Additional initiatives include announcement of a new program on isolation of factors from cystic fibrosis patients which inhibit mobility of cilia, joint sponsorship (with the Cystic Fibrosis Foundation) of a workshop on "Cystic Fibrosis and Chronic Bronchitis—Two Obstructive Lung Diseases of Adults," and joint sponsorship (with the NIAMDD) of a program conducted by the Cystic Fibrosis Foundation to prepare a technical report on research and clinical care in cystic fibrosis and suggestions for future research directions.

CONSTANT PROGRAM BUDGET

Mr. CONTE. You are requesting $403.6 million, about $7 million more than last year's appropriation. It appears that this is insufficient to maintain a constant program level. Would you agree? How much is needed to support activities at last year's level when inflation is taken into account?

Answer. In the regular research grant line NHLBI in 1976 had $74.7 million available for competing projects which permitted the funding of 61 percent of these approved competing projects. In fiscal year 1977 there are $58.2 million available for regular competing research grants which will allow the funding of 49 percent of approvals. For 1978 the budget projects $46.2 million for competing research grants. This will allow us to fund somewhere between 30 percent and 35 percent of approved research grants. The Institute believes it is a desirable goal to support at least 50 percent of approved competing research grants. To fund at the 50 percent level an addition of approximately $20 million would be needed.

There is a decrease in the training line of over $3 million because of the phaseout of institutional awards. To reinstate these awards at the 1977 level would necessitate restoration of at least the $3 million. In the contract line, as you know, we traditionally fund research contract continuing commitments at 100 percent; however, in 1978 we find that we will need an addition of approximately $10 million in order to meet the present contract commitments. The funding of perhaps 90 percent of our contract commitments (primarily clinical trials), which is what we could do at the budget request level, will, of course, delay the programs and reduce the scope of the clinical trials. This would be unfortunate considering how important patient and physician motivation is in the successful completion of these trials. Thus a total of $33 million above the $403.6 million would be needed to maintain a constant program level.

TRAINING

Mr. CONTE. Why are you proposing no new institutional training awards for next year?

Answer. We were responding to the decision to phase out this program. There are two primary problems in the training area. First, the frequent stops and starts in support for training that have occurred during the past several years have created serious shortfalls in the terms of the number of individuals being trained and enormous instability in our training programs. During the period between 1971, the year prior to passage of the 1972 heart, lung, and blood legislation, and 1976 the number of trainees being supported by the Institute declined by over 10 percent. In the area of cardiovascular diseases the decline in the number of trainees is about 40 percent. This decline has been somewhat offset by modest increases in the areas of lung and blood diseases; however, large shortages still remain in these two areas as well. The shortage of trainees in the blood resources area (blood banking) is critical, and it is doubtful that the national blood policy can be fully implemented until this shortage is rectified. As a conservative estimate, the Institute should be providing support for approximately 2,500 trainees per year. During 1976 it provided support for only 1,100. Stability must be brought back to the program so that highly talented physicians and scientists can be attracted into careers in biomedical research and related activities.

Second, there is a $3.1 million decrease in the budget relating to the phased termination of the institutional training program. This is particularly at the expense of new heart research training at a time when these trainees are already perilously low.

INTRAMURAL RESEARCH

Mr. CONTE. You are proposing about a $1.2 million increase for intramural research. What accounts for that increase?

Answer. The net increase of $1,189,000 provides $168,000 for within-grade pay increases and $10,000 for Wage Board pay increase for Institute staff. It provides $87,000 for payment to the NIH services and supply fund and $666,000 for payment for centrally furnished services. An increase of $298,000, or less than 1 percent, is for the increased cost of doing research. No new programs or program expansion can occur at this budget level. An offsetting decrease of $40,000 results from one less day of pay in 1978.

CONTRACT CUTBACK

Mr. CONTE. Your justification shows that research and development contracts will be maintained at about 85 percent of this year's commitments. Why the cutback?

Answer. Within the budget's constraints we either had to cutback contracts, which, as I have noted, will delay the programs and reduce the scope and effectiveness of our clinical trials, or reduce the number of funded competing research grants from approximately 30 percent of those approved to less than 10 percent of approvals. The latter was considered unacceptable.

APPROVED PROJECTS FUNDED

Mr. CONTE. What portion of your approved projects are funded?

Answer. The percentage of approved regular research grants, reviewed for funding on a priority basis and competing for funds, which are awarded has gone

from 61 percent in 1976 to 45 percent in 1977 to 30 percent in 1978. The percentage of dollars awarded compared with applications received has gone from 30 percent in 1976 to an estimated 28 percent in 1977 and 10 percent in 1978.

MR. MICHEL

BLOOD SUBSTITUTES

Mr. MICHEL. Where do we stand with the research on blood substitutes? Can you give us any timeframe as to when such substitutes might be available for human use?

Answer. Studies on blood substitutes have been in progress for only a few years, yet the accomplishments to date have been highly significant. Complete blood replacement in rats has been achieved with a perfluoro-chemical-type substitute. Bloodless animals so produced exhibit no abnormal behavior and regenerate blood cells and plasma and continue to grow and develop. Animals can also be completely exchange-transfused with a stroma-free hemoglobin solution and require no other material to remain alive. Since research on blood substitutes is relatively new it is difficult to guess a time when such substitutes might be available for human use, especially in view of potential toxicity problems and the rigors of clinical testing in human subjects. Blood substitutes once fully developed have tremendous potential value in helping to supplement and thereby conserve the natural supply of blood.

CORONARY BYPASS OPERATIONS

Mr. MICHEL. I was particularly struck by one item in your statement to the effect that there is no evidence that the many coronary bypass operations that are performed each year actually result in any increased survival. Would you elaborate in this regard? Do these operations represent a hoax on the patient and those who finance them?

Answer. I would like to respond to your further question concerning the efficacy of coronary bypass operations. When I made that statement I was specifically referring to the results of the National Heart, Lung, and Blood Institute's national cooperative study to compare medical and surgical therapy of patients with unstable angina pectoris. Unstable angina pectoris is a condition where the patient presents with either chest pain of new onset or changing pattern. About one-half of the patients who suffer an acute heart attack reveal on careful questioning that they had experienced chest pain of a variable nature occurring from 12 hours to 12 weeks before their actual heart attack.

This has lead some doctors to use the term "impending heart attack" or "threatened heart attack" in place of the term unstable angina. In the late 1960's the technique of coronary bypass surgery was introduced. Soon after this technique became available it was used in patients presenting with unstable angina. Some doctors argued that emergent coronary bypass surgery may "prevent" an incipient heart attack and result in a reduction of both immediate in-hospital mortality as well as the long-term mortality in subsequent years. In 1972, emphasizing that there was no definite evidence showing the superiority of intensive medical management or coronary bypass surgery in determining mortality and morbidity in patients hospitalized with unstable angina, some of the participating groups in the National Heart, Lung, and Blood Institute's Myocardial Infarction Research Units developed a cooperative clinical trial to compare these two different approaches to therapy: medical versus surgical. In all patients eligible for this study, coronary angiography, a procedure in which dye is injected into the coronary arteries and enables identification of any significant obstructions, was done. This procedure identified the very small number of patients who had obstruction of the left main coronary artery in which it was agreed that there was already sufficient evidence to support probable surgical therapy. Coronary angiography also identified another small group of patients who had very mild coronary artery disease or abnormal function of the heart muscle or heart valves. Between these two small groups, at the extremes, was the largest group of patients who were randomizable with unstable angina and who had at least a 70 percent occlusion of at least one of the three main coronary artery trunks. From 1972 through 1976, 288 patients were entered into this randomized clinical trial. One hundred forty-seven patients received intensive

pharmacological medical therapy and 141 comparable patients underwent coronary artery bypass surgery.

The results of the study revealed that mortality was comparable and low in both groups in the hospital—medical mortality 4.1 percent, surgical 5 percent—and in the posthospital phase, with an average followup of 24 months medical mortality 5 percent, surgical mortality 5.2 percent. During the in-hospital period the surgically treated patients had a higher incidence of heart attacks, 18 percent, compared to an incidence rate of 10 percent in the medically treated group. Most of the heart attacks in the surgically treated group were perioperative in that they occurred in relationship to the surgical procedure. In the posthospital phase of the study, with an average followup of 24 months, the incidence rate of heart attacks was equal in the medically treated and surgically treated group, 13 percent. In evaluating posthospital angina chest pain, 15 percent of the surgically treated patients were reported to have significant anginal chest pain during at least one of the followup visits, compared to 45 percent of the medical group. It must be noted, however, that general assessment of angina chest pain is difficult to evaluate postsurgery for several reasons, including the placebo effect of surgery.

Recently the principal investigators in this study were convened in Bethesda to discuss this data which in summary showed that: Mortality was low and equal in both groups; heart attacks occurred more often in the surgically treated than in the medically treated group; medical group had more persistent angina than the surgical group.

This group of experienced clinical investigators concluded that patients presenting with unstable angina may be safely treated with careful, intensive pharmacologic therapy. Those with persistent chest pain may be studied by coronary angiography and those patients with left main coronary artery obstruction, and continued intractable pain, may require surgery. Otherwise, prophylactic surgery to prevent a heart attack or death is not necesasry.

Now we must state that patients with unstable angina represent only a small portion of the total number of patients presenting for bypass surgery each year in this country. It is difficult to have an accurate assessment of what percentage of the total they represent but it is generally agreed that it would represent approximately 15 to 20 percent of the patients and would vary from institution to institution depending on their referral patterns.

This points out that we still have insufficient evidence to fully evaluate the effect of coronary bypass surgery in relationship to its effect on mortality and morbidity in the largest percentage of patients who present for operation, those with stable angina or those patients who are asymptomatic after having a heart attack.

In an attempt to find the answers for these questions for this large percentage of patients presenting for bypass surgery, the National Heart, Lung, and Blood Institute is currently sponsoring a study comparing medical therapy versus surgical therapy in this group of patients. This study is termed the coronary artery surgery study (CASS). This study currently involves 16 medical centers. At the present time much valuable data has been gathered on over 12,000 patients who have received coronary angiography at the participating institutions. A smaller number, 305, patients have been entered into the randomized trial. The present plan is to continue entering patients into the randomized trial for an additional 18 months. A followup period of 5 years is currently planned on the patients entered into this most important study.

In conclusion we have already gathered very useful revealing the proper role of the coronary bypass procedure in the clinical approach to the patient with unstable angina. It is our hope that in the future the results of our coronary artery surgery study will provide equally important data on the proper role of coronary bypass surgery in the much larger group of patients presenting with stable angina or in patients who are asymptomatic following a heart attack.

In answering your question on whether these operations represent a hoax on the patient and those who finance them, I must answer that the physicians who perform these operations do so in their own belief that they are benefiting the patient. It is very important that the results of our unstable angina study are made available to the practicing physician. The results of this study were reported on March 9, 1977, at the annual scientific sessions of the American College of Cardiology. Several thousand doctors with an interest in cardiology heard the results of this important study and the recommendations for the care of patients

presenting with unstable angina. The results also will later be published in the medical literature and many other doctors will benefit from them. We also will present this information at other programs and meetings when the opportunity arises.

NHLBI CLINICAL TRIALS

Mr. MICHEL. Would you provide for the record a list of all the clinical trials you are undertaking, their expected length, and the cost for each?

Answer. National Heart, Lung, and Blood Institute clinical trials currently funded are:

DIVISION OF HEART AND VASCULAR DISEASES

TARGETED MAJOR CLINICAL TRIALS—R. & D. CONTRACTS MECHANISM

Aspirin myocardial infarction study (AMIS)

This study will determine whether administration of aspirin to persons who have had at least one documented heart attack will result in a significant reducton in cardiovascular morbidity and mortality. AMIS was started in fiscal year 1975.

Funding:	
Through fiscal year 1977	$9,218,000
Estimated fiscal year 1978	4,006,000
Estimated fiscal year 1979–81	4,210,000
Total estimate	17,434,000

Coronary artery surgery trial (CAST or CASS)

This trial will evaluate the efficacy of coronary artery bypass surgery and its potential therapeutic effect in reducing morbidity and mortality in coronary artery disease. This program was initiated in fiscal year 1973.

Funding:	
Through fiscal year 1977	$7,546,000
Estimated fiscal year 1978	2,650,000
Estimated fiscal years 1979–84	13,500,000
Total estimates	23,696,000

Hypertension detection and follow-up program (HDFP)

This program will determine, in the general population, the extent to which mortality and morbidity associated with elevated blood pressure can be reduced by systematic antihypertensive drug management. HDFP began in fiscal year 1971.

Funding:	
Through fiscal year 1977	$48,791,000
Estimated fiscal year 1978	7,835,000
Estimated fiscal years 1979–1980	12,364,000
Total estimate	68,990,000

Coronary primary prevention trail (LRC)

This trial is designed, as part of the overall Lipid Research Clinics program, to test whether lowering cholesterol will reduce or slow the development of premature coronary heart disease in persons with elevated cholesterol levels.

Funding:	
Through fiscal year 1977	$38,820,000
Estimated fiscal year 1978	8,565,000
Estimated fiscal years 1979–84	52,408,000
Total estimate	99,793,000

Multiple risk factor intervention trial (MRFIT)

This investigation will determine whether a preventive program directed at the reduction of serum cholesterol, reduction of blood pressure, and reduction or elimination of cigarette smoking among men will significantly reduce the inci-

dence of heart attacks and death from coronary heart diseases. MRFIT was initiated in fiscal year 1972.

Funding:

Through fiscal year 1977	$61,487,000
Estimated fiscal year 1978	11,467,000
Estimated fiscal years 1979–1984	53,655,000
Total estimate	126,609,000

Unstable angina pectoris trial

This clinical trial in conjunction with CASS will assess the efficacy of early coronary artery bypass surgery versus intense medical management by randomized studies in patients with unstable angina pectoris simulating acute myocardial infarction. This study began in fiscal year 1971 and preliminary results show that there was no benefit, no prevention of heart attack, and no decrease in death rates in those patients who had the surgery.

Funding:

Through fiscal year 1977	$649,000
Estimated fiscal year 1978	94,000
Total estimate	743,000

Collaborative clinical trial of therapy to protect ischemic myocardium

This study will evaluate techniques to protect ischemic myocardium and minimize the size of heart attack. This effort will begin during fiscal year 1977.

Funding:

Estimated fiscal year 1977	$1,100,000
Estimated fiscal year 1978	2,000,000
Estimated fiscal years 1979–80	3,100,000
Total estimate	6,200,000

Propranolol antiarrhythmic drug trial

This trial will test the effect of propranolol on total mortality and sudden cardiac death in patients recovering from a heart attack. It is planned to start this effort during fiscal year 1977.

Funding:

Estimated fiscal year 1977	$750,000
Estimated fiscal year 1978	5,000,000
Estimated fiscal years 1979–83	20,300,000
Total estimate	26,050,000

DIVISION OF LUNG DISEASES

Extracorporeal membrane oxygenators

The objective of the program is to evaluate the clinical application of membrane oxygenators by means of a coordinated, limited clinical trial.

Funding: Total estimate through fiscal year 1977 $5,300,000

Clinical study of intermittent positive pressure breathing

The goal of the study is to evaluate the efficacy of long-term intermittent positive pressure breathing (IPPB) treatment when used as an adjunct to the overall care of ambulatory patients with chronic pulmonary disease.

Funding:

Through fiscal year 1977	$1,000,000
Estimated fiscal year 1978	1,200,000
Estimated fiscal years 1979–81	3,800,000
Total estimate	6,000,000

Nocturnal oxygen therapy

This is a program to design and conduct a study to evaluate the efficacy of nocturnal oxygen therapy in the treatment of patients with chronic hypoxic lung disease and corpulmonale.

Funding:

Through fiscal year 1977	$1,200,000
Estimated fiscal year 1978	1,000,000
Estimated fiscal year 1979	1,000,000
Total estimate	3,200,000

Neonatal respiratory distress syndrome trial

The primary objectives of this study are (1) to establish a randomized double-blind, controlled trial of the effect of corticosteroids, administered 24 to 72 hours before birth on the incidence of neonatal respiratory distress syndrome, and (2) to determine whether the therapy has any adverse short-or-long-term (up to 18 months) effect on the infant.

Funding:

Through fiscal year 1977	$1,100,000
Estimated fiscal year 1978	1,200,000
Estimated fiscal years 1979–80	900,000
Total estimate	3,200,000

DIVISION OF BLOOD DISEASES AND RESOURCES

Histocompatibility of antigen—poor blood

This program will determine if sensitization to histocompatibility antigens may comprise graft survival. This program was designed to develop methods for the removal of these antigens from blood and to evaluate the effect of transfusion on graft survival.

Funding:

Through fiscal year 1977	$791,234
Estimated fiscal year 1978	0
Total estimate	791,234

Maternal to infant transmission of hepatitis B

To determine whether hyperimmune gamma globulin can interrupt the transmission of hepatitis B virus infection from an infected mother to her new baby.
To carry out a baseline surveillance for a future HBV vaccine efficacy trial.

Funding:

Through fiscal year 1977	$93,711
Estimated fiscal year 1978	0
Total estimate	93,711

Cooperative study of factor VIII inhibitors

Inhibitors (antibodies) to the defective protein occur in 4–7 percent of patients with hemophilia A and 3–5 percent of patients with hemophilia B. The inhibitor study is designed to obtain information on the occurrence and natural history of these inhibitors and clinical/laboratory evaluations which may provide a clearer picture of the significance of these inhibitors in the clinical course of the disease.

Funding:

Through fiscal year 1977	$2,008,000
Estimated fiscal year 1978	809,000
Estimated fiscal years 1979–81	1,200,000
Total estimate	4,017,000

Efficacy of sodium cyanate in patients with sickle cell disease

Sodium cyanate is being studied to characterize its antisickling properties, and determine its possible usefulness in the treatment of patients with sickle cell anemia. In order to achieve these goals, the agent is being evaluated by development of extracorporeal carbamylation techniques and continued evaluation of potential cyanate toxicity in man and animals.

Funding:	
Through fiscal year 1977	$886,687
Estimated fiscal year 1978	0
Estimated fiscal years 1979–81	0
Total estimate	886,687

Mr. MICHEL. How are people selected to participate in these trials?

Answer. Several methods are used to select people to participate in clinical trials. A trial may need people who have high cholesterol, high blood pressure, or who smoke cigarettes. In such instances, screening for these conditions may take place in large businesses and factories, or in homes within census tracts. Those people who satisfy entrance criteria are asked if they would like to participate in the study. If they agree, they are enrolled.

Other trials might require people who have had a heart attack. In these cases, hospital records are reviewed and physicians are asked to contact their patients with heart disease. If a person meets eligibility criteria, he is asked if he wishes to enter the study.

In all cases, participation is strictly voluntary. Participants are fully informed concerning the study, and they may withdraw from the study at any time.

MR. ROYBAL

BLOOD DONORS

Mr. ROYBAL. We have been told that there tends to be significant differences between blood which is given by voluntary donors and blood which is given for a cash payment. Are you doing any research in this area?

Answer. Yes; it has been shown that blood from paid donors, as a class, is undesirable in that this blood is more likely to contain the infectious agents that cause hepatitis than is blood from volunteer donors. Donors who demand payment for blood are more likely to be in a lower socioeconomic status and more likely to be supporting drug and alcohol abuse habits that would result in their being carriers of hepatitis viruses than are volunteer donors. With the advent of hepatitis B testing by third generation tests, effective screening of both volunteer and paid donor blood for hepatitis B antigen is possible. Since initiation of these tests, documented cases of transmission of hepatitis B virus from donor to recipient have become extremely rare. The major problem in transfusion-transmitted hepatitis is now associated with non-A, non-B hepatitis. Until recently, it was not clear whether transmission of non-A, non-B hepatitis through blood from paid donors occurred more frequently than through blood from volunteer donors. Research sponsored by the NHLBI shows that this is the case.

BLOOD IMPURITIES

Mr. ROYBAL. Are you trying to develop techniques to take out some of the impurities that might occur in nondonor blood?

Answer. Preliminary results of research indicate that the "washing" of red blood cells before transfusion may remove hepatitis viruses. The data, however, are not definitive, for the research has been complicated by changes in testing procedures and in the donor population. Therefore, the Division of Blood Diseases and Resources of the National Heart, Lung, and Blood Institute would like to sponsor a trial that wou'd permit comparison of washed red cells and unwashed red cells. Statistical data indicate that the incidence of transfusion-transmitted hepatitis is so low in the United States that such a large number of patients would have to be entered into the trial as to make the trial unfeasible. Therefore, the Division is looking for a suitable location outside of the United States where the incidence of hepatitis is high enough that the data could be obtained with relatively fewer numbers of patients while, at the same time, the trial cou'd be adequately monitored so that the validity of the results would be assured.

LONG-TERM EFFECTS OF DRUG USAGE

Mr. ROYBAL. Are you studying the long-term effects that drug use can have on the heart, lungs, and circulatory system, even though a person subsequently gives up drugs?

Answer. The National Institute on Drug Abuse is directing those studies, with collaboration by us when necessary. The high prevalence of bacterial endocarditis—that is, infection of the heart and its valves—in those persons who take drugs in the veins, has been of great concern to this Institute and to cardiologists since the increase in drug use has come about. Research, prompted in part by the destruction of heart valves, has led to improvement of prosthetic valves as well as to studies of the unusual and lethal bacteria which drug users get into their blood streams. The short-term effect may be a shortening of life in the person who has had several valves replaced, and still may suffer from the insidious and low grade bacterial infection.

ENZYME DETECTION AND RESEARCH

Mr. ROYBAL. The National Cancer Institute indicated it believes that enzymes which are a part of cell chemistry may be a link to cancer. Certainly, they are doing research in this area. Are you involved in this research, since blood chemistry analysis would be a significant aspect of research under the National Heart, Lung, and Blood Institute?

Answer. Enzyme determination and research into these substances which are released when the heart muscle is damaged have been and continue to be an important area which cardiovascular scientists study, supported by this Institute. The relation between the types and amounts of enzyme released may lead to more certain determination of the amount of dead heart muscle. More importantly, enzyme measurement may ultimately allow very early diagnosis of suspected heart attack.

In addition, enzyme research is unlocking some of the mystery of transport of cholesterol fractions into and out of the cell. One such substance, HMg Co A reductase, appears to play a key role in that transport.

Although these studies are not directed toward cancer research, the understanding of each step in the normal enzymatic function of the cell makes the eventual diagnosis and therapy of the abnormal or diseased cell more likely. This is true whether the cell be in heart, lung, blood or blood vessel—even the skin.

RESEARCH COORDINATION

Mr. ROYBAL. Generally, do you coordinate your research efforts with other Institutes at NIH? How?

Answer. There are formal and informal machanisms used to coordinate our research efforts with other NIH components. The informal interpersonal relationships among scientists within the NIH as well as within the scientific community are a long standing tradition with us. However, there are a number of formal coordinating mechanisms. The Interagency Technical Committee on Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources even extends beyond DHLW and focuses on five major issues: Cardiovascular biomedical engineering; high blood pressure screening; pediatric pulmonary diseases; sickle cell disease education; and the nutrient composition of foods. The newest formal mechanism has been the creation fo the NIH Coordinating Committee for Blood-Related Activities. This committee includes, in addition to the NHLBI, representatives from the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, the National Institute for Arthritis, Metabolism, and Digestive Diseases, the National Institute of General Medical Sciences, the National Institute of Child Health and Human Development, the Division of Research Resources, and the Clinical Center Blood Bank. It was created in response to the mandate of the renewal of the Institute's authorizing legislation in 1976 enlarged the authority of the Institute in order to advance the national attack upon heart, blood vessel, lung, and blood diseases and to enlarge its authority with respect to blood resources, and which also changed the name of the Institute to the National Heart, Lung, and Blood Institute. The Division of Heart and Vascular Diseases currently has two task forces which act as coordinating bodies. One involves hypertension and the other is concerned with heart disease in childhood. The latter has a standing member from the National Institute of Child Health and Human Development. We also participate in a number of NIH continuing committees: Bureaus, Institutes and Divisions' Directors; Information Officers; Scientific Directors; Medical Board; Collaborative Program Directors; Executive Committee for Extramural Affairs; Executive Officers; Grant Management Advisory Committee; and the Research Contracting Committee. These standing groups meet at least

once each month. In addition there are a number of groups to cover specific scientific issues. These topics presently range from disease oriented problems such as diabetes to more encompassing research problems such as in the area of DNA research. This briefly describes how NIH research efforts are coordinated. Our goals are to avoid unnecessary duplication, define gaps, exchange information, and resolve problems.

ULTRASOUND

Mr. ROYBAL. You indicate that you now use ultrasound and a new technique called radionuclide cineangiography to view the heart. What risks to the patient do these techniques entail?

Answer. Ultrasound is a technique where sound waves are beamed across the chest wall through the heart and the echos from these sound waves are picked up and analyzed in a graphic form. This technique can be utilized to measure the thickness of the heart wall, detect collections of fluid around the heart, and evaluate the function of the heart valves. This test requires no injections into the patient and is completely free of any discomfort to the patient. The energy generated by this test is of low level and is not in any way detrimental to the patient in the present techniques utilized for cardiac exam. One of the advantages of this technique is that repeat tests can be utilized to evaluate the progress of an individual patient without subjecting them to the radiation hazards of frequently repeated X-ray techniques.

RADIONUCLIDE CINEANGIOGRAPHY

The technique of "radionuclide cineangiography" does require the injection into the vein of a small amount of a radioactive isotope bound to albumin. The radiation emitting from the blood contained in the heart is then detected by a very sensitive camera. The camera is synchronized with the heart beat to enable detailed pictures of the contraction of the heart. Movies can be made of these picures which are modified by computer analysis and can reveal very striking moving pictures of the actual function of the heart muscle. When areas of the heart are abnormally contracting secondary to disease, most commonly secondary to ischemic heart disease, these abnormal areas can be detected. The level of radiation to which the patient is exposed in this test is much lower than that when standard X-ray technique of angiography is utilized. An additional advantage is that continued pictures can be made up to 6 hours following a single injection of isotope with no additional radiation hazard to the patient. This allows the test to be utilized at rest and following exercise in patients. By adding a period of exercise to this test much additional information can be obtained about a patient.

HIGH BLOOD PRESSURE PROGRAM

Mr. ROYBAL. On page 4 of your statement, you say that your high blood pressure program has increased the awareness of the benefits of hypertension control in the work setting. How was this accomplished?

Answer. The primary activity to date has been the holding of a National Conference on High Blood Pressure Control in the Work Setting which was sponsored for us by Secretary Mathews. Overview presentations were made by the Secretary, Dr. Theodore Cooper—then assistant Secretary for Health—and Mr. Graham Ward, of the National Heart, Lung, and Blood Institute, to outline the problem of high blood pressure control in the United States and give their views of opportunities which the work setting might present. Representatives from organized labor, industry management, occupational physicians and nurses, insurance groups, and private medical practice then responded to the issues. Response from over 150 attendees was overwhelmingly positive and supportive. As a followup the National Heart, Lung, and Blood Institute is developing a working group of similar representation to extend examination of the issues involved and to assist in transmitting any conclusions reached. In addition, a request for contract proposals to support 6–10 demonstrations of hypertension control in the work setting has been released. The Third National Conference on High Blood Pressure Control—to be held at the Washington Hilton on April 13–15—has a significant portion of the program dedicated to the presentation of existing efforts in the work setting.

ORGAN TRANSPLANTS

Mr. ROYBAL. You talk about research on organ transplants. Yet, recently, there was a report that doctors are having second thoughts about organ transplants and that the number of transplants may actually be declining. What are the problems involved in organ transplants and are we any closer to overcoming organ rejection?

Answer. The problems involved in organ transplantation are partly dependent upon the organ being transplanted. The solid organs that have been transplanted include kidney, heart, and liver. The kidney transplants have been by far the most successful. Problems with solid organ transplant include technical (surgical) problems; ischemic damage to the organ if left outside the body for too long a period of time; acute graft rejection; chronic graft rejection; suppression of the immunological response of the patients resulting in increased susceptibility to infectious agents; poor wound healing and occasionally suppression of the bone marrow, where all of the essential cellular components of the blood are produced, caused by the drugs that suppress the immune response; and Prednisone, one of the drugs used in suppression of graft rejection by suppression of the immune response, has other undesirable side effects (such as causing osteoporosis, which can result in spontaneous or near spontaneous bone fractures, and a so-called cushingoid condition with undesirable fat deposition, cataracts, and hair growth, which is troubling to women, and, if inadvertantly withdrawn in an unplanned manner, can result in acute adrenal insufficiency with all of its attendant problems. In addition, the drug may contribute to amenorrhea.

The other form of transplantation, which is a nonsolid transplantation, is bone marrow transplantation. This procedure has become feasible only fairly recently as a result of advances in knowledge about tissue compatibility. Bone marrow transplantation is technically simple. Bone marrow is removed from a donor and infused into recipients in a manner similar to that for transfusing blood. The immunologic problems, however, are complex. The major problems associated with bone marrow transplantation are graft rejection; graft versus host disease (a condition in which the graft rejects the host rather than the other way around); respiratory distress of unknown etiology,which is progressive, results in death, and is peculiar to bone marrow transplantation; and severe immune suppression of the host (the patient who received the transplant), which results in greatly increased susceptibility to infections by organisms that would not ordinarily infect a normal person and that frequently result in death.

In addition to all of the above problems, there is some evidence that suppression of a patient's immune response may increase the chances for development of various malignancies, although this data is at present somewhat controversial.

However, we are closer to overcoming organ rejection. There are recent exciting discoveries related to the immunology of organ transplantation. Specifically, new methods have been developed for testing the compatibility between donor tissue and recipient tissue that before last year were not available. Tissue compatibility depends upon a group of antigens, the expression of which is closely linked on one chromosome. The new test involves testing for one of these types of antigens, which was known to exist but for which, until last year, there was no serologic test readily available for its detection. It is still too early to determine the effect these developments will have on organ transplantation.

Also, on a positive note, I would like to bring you up to date with the progress that has been made in heart transplantation in the program at Stanford University that is funded by the National Heart, Lung, and Blood Institute. You can see from these results that, although rejection continues to be the major problem in heart transplantation, progress is being made both in its detection and quantification and in improved drug regimens to suppress rejection.

A total of 120 patients have now undergone cardiac transplantation at Stanford University and currently approximately 24 patients are receiving transplants each year. These are individuals with advanced incapacitation due to cardiac disease and a limited life expectancy measured in weeks or months. As criteria for recipient selection have become more refined, only about 20 percent of all patients referred for transplant consideration are determined to be suitable. Specific factors which presently constitute contraindications to trans-

plantation include age greater than 55 years, any active infection, recent pulmonary infarction, diabetes requiring insulin therapy, elevated vascular resistance (8–10 units), or clearly identifiable psychosocial abnormalities which would prohibit rehabilitation after transplantation.

Improved recipient selection, better methods of detecting early graft rejection, and more effective immunosuppression are considered responsible for the improving 1-year survival rate, now at 79 percent. The maximum period of survival is 8½ years. There has been a considerable improvement in the 1-year survival rate from 22 percent in 1968 to 79 percent in 1977. It is not very meaningful, therefore, to consider 3- to 5-year mortality rates. However, most recent figures given to me by Dr. Stinson are as follows:

[In percent]

	Entire series (120 patients)	Since 1973 (50 patients)
1 year	53	74
3 year	35	69
5 year	26	[1] 45

[1] Projected.

In summary, rejection continues to be the major problem in heart transplantation and while progress is being made in the detection and quantitation of rejection and in improving immunosuppressive regimes, much basic work in the immunology of transplantation remains to be done before this problem can be resolved.

BLOOD SUBSTITUTES

Mr. ROYBAL. You speak about blood substitutes. Will it some day be possible to totally replace blood in a human, or are blood substitutes only to be used for short periods of time?

Answer. It is inevitable that an adequate substitute for blood will be found; however, there is no foreseeable blood substitute, in the near future, that could be used as a complete replacement for human blood. There is some evidence to suggest, for example, that stroma-free hemoglobin—the oxygen-carrying substance of blood when it is not inside the red cells—can be used to sustain life if human blood is not available; however, this hemoglobin is rapidly cleared from the blood stream and so could be useful only in an emergency as a short-term procedure until normal blood would become available for a patient. The Institute would like to sponsor research that would permit development of stroma-free hemoglobin that could be used in such situations. In addition, it is theoretically possible to conceive of a synthetic substance with oxygen-binding powers similar to those of hemoglobin, although the practical reality of developing such a substance that would be economically feasible for general use is probably not in the near future.

While blood substitutes are still experimental and until recently have been used in small animals, they have now been used successfully in nonhuman primates. Animals have been kept alive that have had as much as 80 percent of their blood replaced by substitutes. Obviously if blood substitutes could be perfected and made safe, the demands on the whole blood resources system would be relieved.

MINORITY HYPERTENSION RESEARCH PROGRAM

Mr. ROYBAL. Explain what the minority hypertension research development program accomplished. How many students and faculty were involved. How many schools and hospitals participated?

Answer. The objectives of the minority hypertension research development program are to encourage the recruitment and development of minority investigators in specialized areas of research, prevention, control, and education related to hypertension, and stimulate hypertension research, prevention, control, and education by offering minority school faculty members and graduate students the opportunity to enhance their research capabilities in these areas.

Awards are to be made to hypertension training centers competent to provide the desired training and which have established communications with minority

schools to work out plans for the identification. selection, and deveolpment of participants. The program is expected to reach many minority individuals in the developmental stages of their careers and increase the awareness of hypertension and its sequelae and of the need for further research in blood pressure as well as its control. Enhancement of the interests and skills of minority school faculty members will also make their students cognizant of research opportunities in hypertension.

The program has just completed its first round of competition and review. Another solicitation has recently been released as a result of the first competition. Twenty-two minority institutions will participate in the program beginning the summer of 1977. This will actively involve 44 individuals—34 faculty members and 10 graduate students—as participants. The seven training centers have the commitment of 55 faculty members to participate in the program, who have expertise in areas related to hypertension.

HOTLINE

Mr. ROYBAL. The Cancer Institute has a hotline that doctors can call if they need help. Do you have such a hotline?

Answer. In order to give meaningful response to the wide range of clinical questions which would arise from practicing physicians should there be a hotline, the NHLBI would have to have a staff of medical officers with a range of expertise which is not possible for us to recruit in the current market. We have elected not to offer a "hotline" through information officers whose function is to provide information to the lay public as is the case with the NCI "hotline." Rather than extend the promise of something we haven't the resource to fulfill, we have approached providing the physician with the best information we have by other means.

There is, at the NHLBI supported Baylor School of Medicine Research and Demonstration Center, a professional consultation service for the region which the center serves. Evaluation of the concept and its function is a part of that center's activities.

DISSEMINATION OF INFORMATION

Mr. ROYBAL. How do you reach the practicing physician with the fruits of your research efforts?

Answer. Reaching the practicing physician is a complex procedure and is accomplished by various means depending on the message to be conveyed. Through a series of Institute-sponsored lectures, conferences, convention exhibits, journal articles, and Institute publications aimed at specific target groups the NHLBI directly reaches a very large group.

The Institute is also committed to assisting the appropriate voluntary and professional organizations (American Heart Association, American College of Cardiology, National Hemophilia Foundation, et cetera) reach their constituents with the relevant information.

A few specific examples of such activities include a booklet the NLHBI developed, "The Dietary Management of Hyperlipoproteinemia, a Handbook for Physicians and Dieticians" which was published through the media, professional societies and any other means available. In the past 6 years over 6 million copies have been distributed by request.

We are continuing efforts, which we believe to be effective, to bring the most up-to-date knowledge of the clinical management of hypertension available to specialists and general practitioners. Over 150 national voluntary and professional organizations, some 15 Federal agencies, numerous community organizations, and virtually all State health departments cooperate in our education program to reach both the physician and the lay public. The lay public stimulates many professional requests for information.

The results of completed clinical trials indicating a change in therapy are widely broadcast through professional journals, professional meetings, professional societies, and the media. We achieve considerable success. For instance the coronary drug project, which was a 5-year clinical trial studying the effectiveness of five different drugs in the prevention of a second heart attack, showed that in terms of improved patient survival or reduction in risk from cardiovascular death the benefits of therapy from these drugs was negative. Had this trial not been conducted, thousands of patients would continue to be treated in good faith by conscientious physicians with drugs which were shown not to benefit this particular category of patients. Again, through the Institute's health

education program, knowledge of these findings was disseminated to the public, published in scientific literature, and directly communicated to physicians.

We are convinced that a major problem of continuing medical education for physicians lies not in the content area, but in the lack of effective systems for delivery. For a variety of reasons, we believe that the logical base unit for such a system is the State, linked to the appropriate national voluntary and professional organizations. Such systems should be very broad-gauged and able to deal with the vast range of medical education problems. Most physicians (especially family practitioners, internists, and pediatricians) do not deal with "heart, lung, or blood" problems but with human problems which may relate to the heart, lungs, or blood, in addition to many other areas. Effective continuing medical education systems must relate to all these areas and overcome the splintered approach followed at present.

Clearly, the work required in the whole systems building arena goes considerably beyond our limited mandate; however, we perceive the existence of such systems as being absolutely essential to the success of our mission. Therefore, we have engaged in a substantial conceptual and organizational effort to foster the development of viable systems. In large part, our efforts have been cooperative, hence there are few results we can claim exclusive credit for; however, in the past several years we have been instrumental in establishing a National Society for Directors of Continuing Medical Education, the development of four model State systems, the drafting of model State legislation supportive of continuing medical education systems, and the organization of a national conference on physician competence and education.

SUDDEN INFANT DEATH SYNDROME

Mr. ROYBAL. What are the results of your research on Sudden Infant Death Syndrome? I understand that a study is being made by the U.S. Research Program to observe the activities of seals as a way to learn more about sudden infant death syndrome. Did you fund this project? What were the results?

Answer. The National Institute of Child Health and Human Development has the primary research responsibility for the sudden infant death syndrome (SIDS). However, the National Heart, Lung, and Blood Institute supports projects which address the role of the cardiopulmonary system which may be related to this syndrome. Such studies include investigation of the electrical instability of the heart in newborn miniature pigs. Studies of this phenomenon in human newborns are only just beginning. Experiments designed to learn more about the variability in electrical conduction and heart rhythms are underway in both puppies and infants.

The study of seals being conducted by the U.S. research program, funded by NHLBI, was developed as the result of observations that the deep diving of seals produces extreme variability in heart rate. This phenomenon has been demonstrated in adult humans, in shallow diving. However, any relation, even indirect, between the "diving reflex" and SIDS is not clear at this time. Whether SIDS is related to the central nervous system, to the cardiopulmonary system or a combination of both are current major hypotheses.

ASPIRIN

Mr. ROYBAL. Last year you were doing a study to learn if regular aspirin reduced the heart attack rate. What were your findings?

Answer. Results of a preliminary study of aspirin in people with heart disease were recently published. These results were encouraging, but not clear cut. We are currently sponsoring the Aspirin Myocardial Infarction Study. This clinical trial has finished enrolling over 4,500 men and women who have had heart attacks. These people are being followed for 3 years to see if regular aspirin use reduces the rate of recurrent heart attacks and death due to heart disease. The followup period has only recently started; therefore, results of this study are not yet available.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

Amounts Available for Obligation 1/

	1977	1978
Appropriation.....	$396,661,000	$403,642,000

1/ Excludes the following amounts for reimbursable activities carried on by this account: 1977 - $180,000; 1978 - $45,000.

National Heart, Lung, and Blood Institute

Budget Mechanism
(Dollars in Thousands)

	1977 Appropriation			1978 Estimate		
	Number	FTE[1/]	Amount	Number	FTE[1/]	Amount
Grants						
Regular						
Noncompeting	1,550		$175,000	1,556		$194,526
Competing	187		26,735	165		20,946
New	300		26,239	240		20,800
Supplemental	(200)		5,300	(227)		4,551
Subtotal	2,037		233,274	1,961		240,823
Special						
Research career program	200		6,000	200		6,000
Subtotal	200		6,000	200		6,000
Total grants	2,237		239,274	2,161		246,823
Training Programs						
Individual Awards						
Noncompeting	128	128	1,953	170	170	2,476
Competing			--			--
New	165	165	2,032	180	180	2,604
Supplemental			--			--
Subtotal	293	293	3,985	350	350	5,080
Institutional Awards						
Noncompeting	151	779	15,318	138	808	14,874
Competing			--			--
New	32	121	2,685			--
Supplemental			--			--
Subtotal	183	900	18,003	138	808	14,874
Total, training programs	476	1,193	21,988	488	1,158	19,954
Research & Development Contracts	330		81,452	330		81,452
Intramural Research			33,950			35,139
Direct Operations			18,200			18,520
Program Management			1,797			1,754
Total			396,661			403,642

1/ Full-time equivalent

DHEW - National Institutes of Health

CROSSWALK - 1977 Appropriation, 1978 Congressional Justification

INSTITUTE: National Heart, Lung, and Blood
(Dollars in thousands)

Program	Regular Program		Special	Training Programs		Research & Development	Intramural	Direct	Program	
	Non-competing	Competing	Other	Indiv.	Insti.	Contracts	Research	Opers.	Mgt.	Total
Heart & vascular diseases	$114,000	$42,282	$2,300	$2,417	$11,546	$60,499	--	--	--	$233,044
Lung diseases	26,000	9,960	2,900	988	4,061	10,926	--	--	--	54,835
Blood diseases and resources	35,000	6,032	800	580	2,396	10,027	--	--	--	54,835
Intramural research	--	--	--	--	--	--	$33,950	--	--	33,950
Direct operations	--	--	--	--	--	--	--	$18,200	--	18,200
Program management	--	--	--	--	--	--	--	--	$1,797	1,797
Total	175,000	58,274	6,000	3,985	18,003	81,452	33,950	18,200	1,797	396,661

DHEW - National Institutes of Health

CROSSWALK - 1978 Column 1978 Congressional Justification

INSTITUTE: National Heart, Lung, and Blood Institute
(Dollars in thousands)

Program	Regular Program		Special	Training Programs		Research & Development	Intramural	Direct	Program	Total
	Non-competing	Competing	Other	Individ.	Inst.	Contracts	Research	Opers.	Mgt.	
Heart and vascular diseases.....	$125,200	$30,832	$2,300	$3,249	$8,817	$66,346	--	--	--	$236,744
Lung diseases.....	31,700	7,021	2,900	1,025	3,765	9,304	--	--	--	55,715
Blood diseases and resources.....	37,626	8,444	800	806	2,292	5,802	--	--	--	55,770
Intramural research.	--	--	--	--	--	--	$35,139	--	--	35,139
Direct operations...	--	--	--	--	--	--	--	$18,520	--	18,520
Program management..	--	--	--	--	--	--	--	--	1,754	1,754
Total.....	194,526	46,297	6,000	5,080	14,874	81,452	35,139	18,520	1,754	403,642

Summary of Changes

1977 Estimated Obligations	$396,661,000
1978 Estimated Obligations	403,642,000
Net Change	+6,981,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	---	$300,000	---	+$320,000
2. Wage board pay increase	---	135,000	---	+10,000
3. Federal Telecommunications System (FTS) rate increase	---	292,000	---	+19,000
4. Federal Employees Compensation Fund (FECF) rate increase	---	31,000	---	+31,000
5. NIH Service & Supply Fund	---	5,729,000	---	+116,000
6. Payment for centrally furnished services	---	17,818,000	---	+790,000
(Standard level user charge)		(435,000)		(+102,000)
Subtotal			---	+1,286,000
B. Program:				
1. Research grants, for 300 new, 187 competing renewals, and 200 supplementals converted to noncompeting in 1978	---	175,000,000	---	+59,685,000
2. Research grants, for 290 new, 165 competing renewals, and 227 supplementals to be funded in 1978	---	58,274,000	---	+46,297,000
3. Training programs, for an additional 57 Individual NRSA awards in 1978	---	3,985,000	---	+1,095,000
4. Direct operations, for additional costs of program evaluation	262	18,200,000	---	+313,000
Subtotal			---	+107,390,000
Total, increases				+108,676,000
Decreases:				
A. Built-in:				
1. One less day of pay	---	16,475,000	---	-75,000
Subtotal			---	-75,000
B. Program:				
1. Research grants, for 481 noncompeting completed or converted to competing in 1978	---	175,000,000	---	-40,159,000
2. Research grants, for 300 new, 187 competing renewal, and 200 supplemental grants in 1977 completed or converted to noncompeting in 1978	---	58,274,000	---	-58,274,000
3. Training programs, for 45 Institutional awards completed in 1977	---	18,003,000	---	-3,129,000
4. Program management, for a decrease of three positions, salaries and related costs	50	1,797,000	-3	-58,000
Subtotal			-3	-101,620,000
Total, decreases			-3	-101,695,000
Total, net change			-3	+6,981,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
82	Heart & Vascular Diseases	---	$233,044,000	---	$236,744,000	---	+$3,700,000
86	Lung Diseases	---	54,835,000	---	55,715,000	---	+880,000
89	Blood Diseases & Resources	---	54,835,000	---	55,770,000	---	+935,000
91	Intramural Res.	435	33,950,000	435	35,139,000	---	+1,189,000
	(Standard Level User Charge)		(227,000)		(276,000)		(+49,000)
92	Direct Operations	262	18,200,000	262	18,520,000	---	+320,000
	(Standard Level User Charge)		(208,000)		(261,000)		(+53,000)
92	Program Management	50	1,797,000	47	1,754,000	-3	-43,000
	Total	747	396,661,000	744	403,642,000	-3	+6,981,000
	(Standard Level User Charge)		(435,000)		(537,000)		(+102,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	747	744	-3
Full-time equivalent of all other positions	80	90	+10
Average number of all employees.	820	830	+10
Personnel compensation:			
Permanent positions	$14,700,000	$14,942,000	+$242,000
Positions other than permanent	1,300,000	1,400,000	+ 100,000
Other personnel compensation	475,000	490,000	+15,000
Subtotal, personnel compen.	16,475,000	16,832,000	+357,000
Personnel benefits	2,600,000	2,700,000	+100,000
Travel and transportation of persons	797,000	850,000	+53,000
Transportation of things	140,000	140,000	--
Rent, communications & utilities	1,500,000	1,519,000	+19,000
Printing and reproduction	700,000	700,000	--
Other services:			
Project contracts	81,452,000	81,452,000	--
Centrally furnished services	17,818,000	18,608,000	+790,000
Other	8,417,000	8,464,000	+47,000
Supplies and materials	4,000,000	4,100,000	+100,000
Equipment	1,500,000	1,500,000	--
Grants, subsidies, & contributions	261,262,000	266,777,000	+5,515,000
Total, obligations by object	396,661,000	403,642,000	+6,981,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action to be taken
1977 House Report	
1. The Committee believes that NHLBI should establish an Office of Hypertension Control and conduct a pilot demonstration program on hypertension. (page 28)	1. The NHLBI has established the National High Blood Pressure Education Program (NHBPEP) within its Division of Heart and Vascular Diseases which serves as a focus to coordinate hypertension control efforts in the nation. An example of such coordination has been the development of a national consensus on hypertension detection, evaluation, and therapy published in JAMA, January 17, 1977. In response to the Committee's belief and to the state of science, a pilot state-wide demonstration program on hypertension has been planned. A request for proposals for the program is to be issued in February, 1977, for an open competition among the states to seek support for this activity.
1977 Senate Report	
1. Committee directive that a portion of the increased amount shall be specifically for research on Cooley's Anemia and Sickle Cell disease and that the NHLBI and NIGMS conduct a closely-coordinated research and prevention effort in this area. (page 45)	1. In FY 1977 NHLBI obligations for Cooley's Anemia research are estimated at $3.2 million, compared to $3.0 million in FY 1976. Similarly. FY 1977 NHLBI obligations for Sickle Cell Disease research are estimated at $19.0 million, compared to $18.0 million in FY 1976. Following the passage of P.L. 94-278 in April, 1976, which included Genetic Diseases, under Title IV, NIH has established a Genetics Coordinating Committee. This committee is chaired by the Director, NIGMS, and the NHLBI is a member. The committee is soon to become a PHS-wide committee responsible for coordinating research, prevention, and service programs for genetic diseases, including Cooley's Anemia and Sickle Cell Disease.
2. Committee directive that the NHLBI work very closely with the Health Services Administration in locating and treating hypertension victims. (page 45)	2. Following the passage of the Health Revenue Sharing Act over a year ago, NHLBI and HSA have coordinated to provide expert guidance to states regarding procurement

Senate Report cont'd.

and usage of health revenue funds specifically earmarked for hypertension programs. To further this end, a conference jointly sponsored by NHLBI and HSA has been scheduled for February, 1977.

3. Committee directive that the appropriate amount of funds be made available to the "Blood" program to support the research programs commensurate with its new status. (page 46)

3. In FY 1977 NHLBI obligations for Blood Diseases and Resources are estimated at $54.8 million, compared to $52.5 million in FY 1976.

Authorization Legislation

Legislation	Amount Authorized	1978 Budget Request
Public Health Service Act, Title III, Part A, Section 301--Research and Investigation, In General.....	Indefinite	$385,368,000 1/
Title IV, Part I, National Research Service Award Act....	2/	18,274,000 3/

1/ Funding estimate only.
2/ Authorization expries September 30, 1977, extension legislation is pending.
3/ Funding estimate only. Excludes $1,680,000 for old training programs.

National Heart, Lung, and Blood Institute

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	160,513,000	182,000,000	160,634,000
1971	171,747,000	178,479,000	203,479,000	194,925,000
1972	195,492,000	211,624,000	252,590,000	232,627,000
1973	255,280,000	300,000,000	350,000,000	300,000,000[1/]
1974	265,000,000	281,415,000	320,000,000	289,550,000[2/]
1975	309,299,000	321,196,000	330,000,000	324,130,000
1976	292,794,000	329,059,000[3/]	379,059,000[3/]	370,013,000[4/]
1977	342,855,000	380,661,000	420,661,000	396,661,000
1978	403,642,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

3/ Excludes Fellowships and Training Grants--not considered due to pending legislation ($20,954,000).

4/ Includes $20,954,000 for training programs authorized under continuing resolution.

National Heart, Lung, and Blood Institute

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$157,846,000	$157,846,000	$165,255,000	$157,817,000
1969	160,310,000	154,695,000	162,695,000	157,502,500
1970	151,088,000	151,088,000	171,526,000	151,088,000
1971	164,923,000	169,207,000	194,207,000	186,798,000
1972	188,225,000	203,299,000	243,299,000	224,302,000
1973	246,829,000	290,538,000	340,538,000	290,538,000 1/
1974	264,754,000	281,754,000	319,754,000	286,749,000 2/
1975	309,053,000	320,950,000	329,754,000	323,884,000
1976	292,794,000	329,059,000 3/	379,059,000 3/	370,013,000 4/
1977	342,855,000	380,661,000	420,661,000	396,661,000
1978	403,642,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

3/ Excludes fellowships and training grants--not considered due to pending legislation ($20,954,000).

4/ Includes $20,954,000 for training programs authorized under continuing legislation.

Note: The figures presented in this table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts to prior years. For example, the responsibility for funding of general research support grants is not the function of this Institute in 1978. The amount originally contained in previous years for this particular program has been removed for comparability purposes.

Justification

National Heart, Lung, and Blood Institute

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Heart & Vascular Diseases	---	$233,044,000	---	$236,744,000	---	+$3,700,000
Lung Diseases	---	54,835,000	---	55,715,000	---	+880,000
Blood Diseases & Resources	---	54,835,000	---	55,770,000	---	+935,000
Intramural Res.	435	33,950,000	435	35,139,000	---	+1,189,000
Direct Operations	262	18,200,000	262	18,520,000	---	+320,000
Program Mgt.	50	1,797,000	47	1,754,000	-3	-43,000
Total	747	396,661,000	744	403,642,000	-3	+6,981,000

General Statement

From the time of its inception in 1948 as the National Heart Institute, the National Heart, Lung, and Blood Institute (NHLBI) has been committed to the concept that in order to prevent and cure diseases it is necessary to understand how and why disease processes develop, cripple, and kill. The recent decline in the death rate in coronary artery disease (nearly 15% from 1968 to 1975) is in part a product of the Institute's efforts. Had the 1970 death rate for coronary heart disease not been turned back, some 55,000 Americans who are now alive would have died last year. Also, the death rate for stroke has declined 16% in the past 6 years, hypertension deaths declined 39%, and rheumatic heart disease declined 29% in the same period. Since the Institute was founded, the death rate from all cardiovascular disease has declined 30%. The number of deaths from cardiovascular disease dropped under one million in 1975 for the first time since 1967. Yet four disease categories falling within the Institute's mandate are among the ten leading causes of death in the United States, with cardiovascular diseases first.

While recent statistics indicate the morbidity and mortality of some cardiovascular, pulmonary, and blood diseases are decreasing, the economic losses attributed to these diseases is staggering. In 1974 the national economic drain from 30 million American sufferers of cardiovascular disease--one out of every seven Americans--is estimated at more than $45 billion. For the 14 million Americans who suffer from chronic lung disease, there is an estimated annual loss to the nation of $16 billion. Blood diseases cost the country another $1 billion. That is a total annual national bill of $62 billion, which is more than one-third of the estimated $180 billion spent in the United States for health.

Future costs will continue to rise. The NHLBI's budget represents approximately 16% of the research funds of the National Institutes of Health--a figure that has remained essentially constant since 1967--despite the new major research areas of lung and blood which have been assigned to the Institute.

The program strategy employed by the National Heart, Lung, and Blood Institute for each of its disease related mandates continues to consist of an ordered sequence of: acquisition of new knowledge (applied and clinical); testing and evaluation of promising hypotheses (clinical trials); and application of new and existing knowledge (education and demonstration). The ultimate goal of the NHLBI National Program is the prevention of cardiovascular, pulmonary, and blood diseases.

Progress was and continues to be made in each area of this overall strategy. Creative research by individual investigators and by teams of investigators is leading to new knowledge about heart, blood vessel, lung, and blood diseases. Targeted research is being supported to attack problems urgently requiring solution in those situations where the base exists to make such research feasible; and imaginative new approaches are being developed and initiated to decrease the time needed for translation of this new knowledge into improved health care.

It cannot be over-emphasized that basic investigator-initiated research in search of new knowledge in areas related to normal cell mechanisms and the etiology and pathophysiology of disease is of very high priority. Such knowledge is a prerequisite for effective prevention and rational treatment of disease. No central authority can establish predetermined guidelines to obtain such knowledge. In the main, it can only be developed by individual investigators, working in small or large groups following their own leads, and pursuing problems of their own choosing. History bears out the importance of such basic nondirected research and indicates that our current level of health and disease knowledge and understanding has been provided in large part from its fruits.

The Institute is using clinical trials to ascertain the validation of existing treatment and prevention regimens and the development of new ones. Although there are serious conceptual, fiscal, and ethical problems that surround the boundary of clinical trials, the Institute would be remiss if it were not responsive to the need to conduct these definitive studies. In many instances patients are engaged in treatments for which the scientific basis and efficacy have not been demonstrated. In addition, treatments and interventions in the field of cardiovascular, respiratory, and blood diseases often can be very expensive. The current NHLBI investment in clinical trials, therefore, exceeds fifty million dollars.

Considerable knowledge has been acquired in recent years concerning many of the diseases under the NHLBI mandate. To ensure that these efforts do not go unexploited the Institute has undertaken an active program of prevention, control, and education to speed this knowledge into the mainstream of clinical medicine. The NHLBI has acted in this new area of responsibility to develop the approaches needed to carry out its mission. Advice and guidance is being sought from behavioral and social scientists, nutritionists, and others possessing skills not previously emphasized within the NHLBI.

In summary, the 1978 request would support full-funding of all noncompeting research grants, that is those grants previously recommended for support and not competing for funds in 1978. It would provide an estimated support for nearly 35% of competing research grants recommended for awards in 1978. NHLBI targeted programs (including essentially all of the Institutes multicenter clinical trials) are largely supported by research and development contracts and selected new initiatives are being started in 1977 (see categorical research description below). Funds available in 1978 would support about 90% of ensuing commitments from these and other ongoing contract programs.

Heart and Vascular Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivities:						
Arteriosclerosis	---	$63,137,000	---	$64,154,000	---	+$1,017,000
Hypertension	---	55,000,000	---	55,869,000	---	+869,000
Cerebrovascular disease	---	4,200,000	---	4,266,000	---	+66,000
Coronary heart disease	---	41,000,000	---	41,647,000	---	+647,000
Peripheral vascular diseases	---	5,010,000	---	5,090,000	---	+80,000
Arrhythmias	---	18,630,000	---	18,924,000	---	+294,000
Heart failure & shock	---	16,682,000	---	16,945,000	---	+263,000
Congenital and rheumatic heart diseases	---	8,900,000	---	9,040,000	---	+140,000
Cardiomyopathies and infections of the heart	---	3,261,000	---	3,313,000	---	+52,000
Circulatory assistance	---	17,224,000	---	17,496,000	---	+272,000
Total	---	233,044,000	---	236,744,000	---	+3,700,000
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	---	114,000,000	---	125,200,000	---	+11,200,000
Competing	---	42,282,000	---	30,832,000	---	-11,450,000
Special	---	2,300,000	---	2,300,000	---	---
Subtotal	---	158,582,000	---	158,332,000	---	-250,000
Individual awards	---	2,417,000	---	3,249,000	---	+521,000
Institutional awards	---	11,546,000	---	8,817,000	---	-2,418,000
Research & development contracts	---	60,499,000	---	66,346,000	---	+5,847,000
Total	---	233,044,000	---	236,744,000	---	+3,700,000

For more than fifty years heart and blood vessel diseases have been the major cause of death in this country. They now account for 54% of all deaths annually, more than three times the death rate from cancer, the next highest cause. Cardiovascular diseases cause two-thirds of all deaths of people over 65 years of age. An estimated 30 million Americans have diseases of the heart and blood vessels, resulting in a huge burden of acute and chronic illness and disability.

The Division of Heart and Vascular Diseases was created in 1972 as part of the general reorganization of the National Heart and Lung Institute. The Division was charged at that time with the responsibilities previously assumed by the National Heart Institute. Its mechanisms of support are research grants, training awards, and research and development contracts, the same as those of the other categorical Divisions of the Institute.

Significant progress has been made in meeting the Division's objective of increasing knowledge of the basic mechanisms and processes leading to cardiovascular disease and to close the gap between this new knowledge and the health care delivered to the patients with cardiovascular disease. Only a few examples can be identified in the limited space available.

A new kidney based substance, called big renin, has now been extracted and purified. How "big renin" is converted into the small active form and what role this transformation may have in the blood pressure regulating process remains to be resolved. In addition, an even larger molecule of renin has been isolated. The introduction of these new elements into the already complex renin-angiotensin-aldosterone system will likely open new approaches to the study of renin in blood pressure control.

Protection of ischemic myocardium (damaged heart muscle) has been the focus of a good deal of major research with several promising leads available. The ability to map the extent of damaged heart muscle is being developed and has obvious important clinical implications. These studies are being pursued by evaluation of a variety of electro-cardiographic techniques, radioisotope methods for quantifying ischemic or infarcted myocardium, as well as the utilization of more sophisticated graded exercise stress tests. Because of the rapid evolution of this field, critical review of existing activities will be conducted in 1977 in competition with potential new ones. Also in 1977 a collaborative clinical trial to evaluate techniques to protect ischemic myocardium and minimize the size of ultimate heart damage associated with acute heart attack will begin.

In the area of sudden cardiac death, studies that have direct effects upon patient care indicate that the chronic administration of beta-blocking agents may be useful in reducing mortality following a heart attack. Patients at high risk for sudden death following a heart attack can be identified as a result of the evaluation of ventricular arrhythmias. Beta-blocking agents presumably prevent sudden death by preventing ventricular fibrillation in these individuals prone to this arrhythmia. The time is ripe to test in a large-scale, collaborative study the effect of the drug propanolol on total mortality and sudden death in these patients. Coronary heart disease and its complications account for over 600,000 deaths in the U.S. each year. Survivors of heart attacks are among those with highest risk of dying. If it could be demonstrated that propranolol lowered the mortality rate in this group, it would be a major step forward in the secondary prevention of coronary heart disease. Because of possible unwarranted increased use of this drug in the next few years, it is important to establish its efficacy soon. The reported results of two European studies are very interesting. However, neither of them adequately answers the question as to whether long-term therapy with beta-blockers is beneficial in coronary heart disease prevention. The Institute proposes to begin such a trial in 1977 with its concommitant expansion in ensuing years.

Recent epidemiological studies indicate that high density lipoprotein (a complex of fat and protein molecules) levels are inversely strongly and independently correlated with the risk of developing coronary heart disease. Preliminary observation suggests that populations differ in their high density lipoprotein levels and biochemical investigations suggest that high density lipoprotein is involved in removing cholesterol from the arterial wall.

Significant progress is being made in the targeted areas identified by the Division's major clinical trials. The Aspirin-Myocardial Infarction Study is evaluating the efficacy of aspirin in reducing mortality and recurrent myocardial infarctions. The Multiple Risk Factor Intervention Trial is designed to determine whether a group at above average risk of death from coronary heart disease can be maintained in a special intervention program for six years and whether or not this intervention program will result in a significant reduction in mortality from coronary heart disease. The Hypertension Detection and Follow-Up Program is designed to determine the effectiveness of a systematic approach of antihypertensive therapy in reducing morbidity and mortality in patients with elevated blood pressures. The Coronary Primary Prevention Trial conducted by the Lipid Research Clinics is a seven-year study which began in 1973 aimed at testing whether lowering cholesterol in patients with Type II hyperlipoproteinemia will affect the disease process. Patients with this disease are at high risk of death from coronary heart disease. The Coronary Artery Surgery Trial is attempting to assess the effects of coronary artery by-pass graft surgery on morbidity and mortality in patients with coronary heart disease. A patient registry has been established whose goal is the evaluation of approximately 20,000 patients. There is an accompanying randomized study. This trial has expanded into its clinical phase in 1977.

The most significant progress in the area of Prevention, Education, and Control has been in the National High Blood Pressure Education Program which was launched in 1972. There are a number of indications that changes have taken place in public awareness and professional behavior relevant to hypertension, in part attributable to the activities and efforts of the many private and local government agencies cooperating in this national program which is coordinated by this Division. Preliminary data suggests that in 1971 only 4 million of the 23 million known Americans with high blood pressure were under adequate control. This figure now has nearly doubled. In addition, there has been over a fifty percent increase in the number of total patient visits to physicians for hypertension and hypertensive heart disease, while total patient visits for all causes increased only very slightly.

Although further research is needed to develop more physiologic control of hypertension--or even to find means for its prevention--the state-of-the-art exists now to control most hypertension and reduce its complications. In all but the most grossly medically underserved areas resources are present in adequate quantity to deliver the necessary care. The primary missing ingredient is coordination of these resources into an efficient, well organized control effort. The NHLBI, therefore, is proceeding in 1977 to establish a three-year pilot effort in four to six states to achieve and measure the impact of a large-scale coordination effort. Its objective will be to measure the effectiveness of statewide coordination of hypertension control efforts--based on management by objective derived from epidemiological and other planning data--on improving the status of hypertension control and on lowering morbidity and mortality from selected diseases.

Recent data from the Hypertension Detection and Follow-Up Program indicate that men are only one-half as likely as women to be aware that they have high blood pressure and to be under therapeutic control. The work setting, therefore, seems to be an appropriate place to reach a large segment of the male population. The NHLBI has held a national conference on Hypertension in the Work Setting sponsored by the Secretary. As a result, the Institute is initiating demonstration programs to develop tested, cost effective alternatives to controlling hypertension in the work setting.

The National High Blood Pressure Education Program has been responsible for the development of a task force concerned with high blood pressure in the young. This group has developed standards of care which are available for use by the practicing physician as well as the development of blood pressure charts to be used in the long-term follow-up of all children as regards their blood pressure. This is seen as an important step in an attempt to identify in childhood those individuals who will have hypertension as adults and provide some leads as to methods for preventing this disease.

NHLBI has entered into a cooperative program with the National Institute of General Medical Sciences and the Minority Access to Research Careers Program (MARC). The MARC Faculty Fellowship program provides opportunities in advanced research training for selected faculty members of schools that draw substantial numbers of students from ethnic minority groups. After training, fellows are encouraged to return to their sponsoring schools to do research and teach so as to inspire and assist minority students to seek careers in the biomedical sciences. The MARC Visiting Scientist Award provides financial support for outstanding scientist-teachers to serve as visiting scientists at schools where student enrollments are substantially from minority groups. The primary intent is to strengthen research and teaching programs in the biomedical sciences among students and faculty in these institutions.

The Minority Hypertension Research Development Summer Program has also been announced. This is intended to encourage the recruitment and development of minority investigators in specialized areas of research, prevention, control, and education related to hypertension and to stimulate these activities by offering minority school faculty members and graduate students the opportunity to enhance their research capabilities in these areas. Training will be offered through Hypertension Training Centers that have well-established hypertension research and training programs and are within 100 miles of a minority school or provide satisfactory alternative arrangements for communication and exchange. The Centers will collaborate with minority schools to work out plans for the identification, selection, and development of participating minority school faculty members or graduate students.

Two programs have just been initiated which will be important new directions and expansions of the Division's activities. This first is in the area of the pathogenesis of atherosclerosis in diabetes mellitus. This is in response to an identified major gap for research support for study of the mechanisms of the cardiovascular complications of diabetes. The second is a program in the epidemiology of hypertension in the young, which should provide leads for further investigation of the precursors of essential hypertension in adults. Its long range goal is the prevention of this disease. These new programs will be expanded in FY 1977 and continued in 1978.

The Institute initiated targeted activity on the development and evaluation of instrument systems for non-invasive detection, quantification, and characterization of atherosclerotic lesions approximately four years ago. It is now planned to enlarge the development of such instrumentation and to initiate its early evaluation in the clinical setting. Such instrumentation is needed to provide a quantitative assessment of the possible efficacy of therapy designed to retard or reverse atherosclerosis as well as to define prognosis in individual at risk patients.

The major thrust of circulatory assist and artificial pump development has been with pumps which have pneumatic actuation. The Institute now plans to expand the left heart assist blood pump development emphasizing longer term reliability and actuation by mechanical (as contrasted with simply pneumatic) systems. Electrical and thermal engines lend themselves much more to mechanical type linkage and thereby result in a much more efficient overall system. The configuration of constraints upon such pumps are considerably different than upon pneumatically actuated pumps.

It is also proposed that the control colonies of non-human primates for atherosclerosis, hypertension, and cerebrovascular disease be expanded. Such primates are already a scarce and threatened resource. A coordinating committee for non-human primate supply and utilization has been developed at NIH with interagency responsibilities.

The 1978 request provides for the continuation of the initiatives described above and for most ongoing programs. All noncompeting research grants will be supported and an estimated 35% of competing grants recommended for approval will be funded. The phase-out of the institutional cardiovascular training grants will continue. Research and development contracts will be maintained at approximately 85% of the 1978 commitments.

Lung Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivities:						
Structure and function of the lung	---	$14,562,000	---	$14,794,000	---	+$232,000
Pediatric pulmonary diseases	---	8,162,000	---	8,293,000	---	+131,000
Emphysema and chronic bronchitis	---	9,573,000	---	9,726,000	---	+153,000
Fibrotic and immunologic lung diseases	---	9,820,000	---	9,977,000	---	+157,000
Respiratory failure	---	6,754,000	---	6,862,000	---	+108,000
Pulmonary vascular diseases	---	5,964,000	---	6,063,000	---	+99,000
Total	---	54,835,000	---	55,715,000	---	+880,000
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	---	26,000,000	---	31,700,000	---	+5,700,000
Competing	---	9,960,000	---	7,021,000	---	-2,939,000
Special	---	2,900,000	---	2,900,000	---	---
Subtotal	---	38,860,000	---	41,621,000	---	+2,761,000
Individual awards	---	988,000	---	1,025,000	---	+37,000
Institutional awards	---	4,061,000	---	3,765,000	---	-296,000
Research and development contracts	---	10,926,000	---	9,304,000	---	-1,622,000
Total	---	54,835,000	---	55,715,000	---	+880,000

Diseases of the lung constitute a major health problem, a problem that is of increasing dimensions for some of these disorders. Lung diseases, the sixth leading cause of death in the U.S., account for more than 130,000 deaths annually. Chronic respiratory diseases affect an estimated 14 million Americans; emphysema, an estimated 1 million; chronic bronchitis, about 7 million; and asthma, approximately 6 million. Each year in the United States, lung diseases, covered by the NHLBI mandate, account for over 60 million days lost from work and 40 million days of bed restricted activity. In addition, and almost exclusively limited to premature births, respiratory distress syndrome of the neonate accounts for approximately 10,000 deaths annually. The only recent data on chronic lung diseases shows a continuous increase in death rate from chronic bronchitis and emphysema.

Six years ago the research mandate of the Institute was expanded to include the lung and the name of the Institute was changed accordingly. Research resulting from this new mandate has shown the lung to be a vastly more complex organ than previously perceived. Although the primary function of the lung is respiration--the vital function of the exchange of oxygen and carbon dioxide--it is also an important filter of environmental materials, a biochemical processor of bodily functions, and responsible for hormone production and metabolism. The goal of the new lung program is to develop effective methods for prevention and control of these acute and chronic lung disorders. The objective of the research grants and contracts in lung diseases which the NHLBI administers is to develop the basic knowledge about the lungs upon which prevention and control programs will depend.

Chronic obstructive pulmonary disease is a collection of disorders of variable cause and development characterized by the common finding of obstruction to air flow, shortness of breath, tendency to repeated infection, long-term disability, and premature death. This disease category includes emphysema, bronchitis, and chronic asthma. This group of diseases has increased in frequency over the past two decades for several reasons. In the past there were many more deaths from pulmonary infection and pneumonia, but the effectiveness of the antibiotics introduced in the 1940's and 1950's against pulmonary infections resulted in improved survival from pneumonia and the emergence of underlying chronic obstructive pulmonary disease as a public health problem.

Because the exact etiology of emphysema and other chronic lung diseases is unknown, a significant effort has been directed to identify the multiple risk factors apparent in the production of the disease and to develop more sensitive methods to detect the disease early enough for preventive measures to be effective. Basic research carried out by the Institute in the 1950's and 1960's in respiratory physiology has provided the knowledge on which this developmental research has been built. In the last five years, striking progress has occurred in the development of new tests for pulmonary function including tests of gas flow, gas exchange, tissue elasticity, and surfact tension. Application of these new tests to epidemiologic studies of special population groups will permit the identification of high risk populations and give a better understanding as to the causes and natural history of these disabling diseases.

There has emerged a vigorous and growing research program into the causes of lung disease in newborn infants and children. The pediatric pulmonary disease research program emphasizes research in hyaline membrane disease including the infantile respiratory distress syndrome, the causes of cystic fibrosis, and the relationship of a disease of the small airways in infants and children called bronchiolitis to the development of chronic lung disease in the adult. Clearly, a better understanding of lung diseases of the infant and child with improved methods of diagnosis and treatment will go a long way toward preventing life-long deterioration of lung function in the adult.

The Institute has rapidly developed an integrated lung disease program of basic and clinical research, clinical trial, demonstration, education, prevention, and control. To continue this trend two new thrusts warrant special mention: clinical trials and studies of pathogenesis.

Clinical trials have been initiated for it is clear that the current state of knowledge calls for the validation of existing regimens as well as the development of new ones. Although the Institute is well aware of the conceptual, fiscal, and ethical problems that such trials entail, it would be remiss if it were not responsive to what is clearly an acute need.

Specific examples include the establishment of clinical centers to evaluate the efficacy of antenatal steroid therapy, which involves administering steroids to the mother prior to delivery, in the prevention of neonatal respiratory distress syndrome. The primary objectives of the cooperative study are to establish a randomized, double-blind, controlled trial of the effect of corticosteroids, administered 24 to 72 hours before birth, on the incidence of neonatal respiratory syndrome and to determine whether the therapy has any adverse short- or long-term effects on the infant.

Also just initiated is a clinical study of intermittent positive pressure breathing (IPPB). The goal of this study is to evaluate the efficacy of long-term IPPB treatment when used as an adjunct to the overall care of ambulatory patients with chronic obstructive pulmonary disease. It will establish a collaborative program among several centers to obtain sufficient numbers of well-defined patients for a randomized, controlled study with uniform modes of treatment and data collection.

The 1978 request provides for the continuation of the ongoing programs in most instances. All noncompeting research grants will be supported and an estimated 35% of competing grants recommended for award will be funded. This compares with 50% in 1977. The phase-out of the institutional pulmonary graduate training grants will continue. Research and developmenc contracts will be continued at essentially the 1977 level.

Blood Diseases and Resources

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivities:						
Thrombosis and hemostatis.	---	$18,751,000	---	$19,070,000	---	+$319,000
Red blood cell disease....	---	9,266,000	---	9,424,000	---	+158,000
Sickle Cell disease.....	---	16,285,000	---	16,562,000	---	+277,000
Blood resources.....	---	10,533,000	---	10,714,000	---	+181,000
Total.....	---	54,835,000		55,770,000	---	+935,000
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting.....	---	35,000,000	---	37,626,000	---	+2,626,000
Competing.....	---	6,032,000	---	8,444,000	---	+2,412,000
Special.....	---	800,000	---	800,000	---	---
Subtotal.....	---	41,832,000	---	46,870,000	---	+5,038,000
Individual awards.....	---	580,000	---	806,000	---	+226,000
Institutional awards.....	---	2,396,000	---	2,292,000	---	-104,000
Research and development contracts.....	---	10,027,000	---	5,802,000	---	-4,225,000
Total.....	---	54,835,000	---	55,770,000	---	+935,000

This year increasing emphasis on the study of blood led to a change in the name of the Institute from the National Heart and Lung Institute to the National Heart, Lung, and Blood Institute. Blood research had been occurring within the Institute, however, for some time and had led to some very important and practical results. A good example of this is the revolution in hemophilia treatment resulting from partial purification of the antihemophilic clotting factor and its introduction into clinical practice. Current support encompasses hemophilia, thrombosis, sickle cell disease, blood fractionation and storage, development of blood substitutes, and the safety of transfused blood.

Many disorders of the blood are intimately related to cardiovascular and pulmonary diseases. The impact of clotting and bleeding disorders is considerable. Arterial thrombosis causes or complicates a great variety of diseases in all parts of the body. Thrombosis may cause pulmonary embolism which is a disorder responsible for the hospitalization of about 300,000 persons annually, approximately one-sixth of whom die. Hereditary diseases of the blood constitute a major national health problem. Approximately two million individuals, primarily black, carry the sickle cell trait. About one in every 400 black babies are born with sickle cell anemia. Twenty-five thousand Americans suffer from hemophilia. An adequate supply of high quality blood and blood products is essential for the effective treatment of many diseases and for surgical transfusions. A complex of public and private organizations acquires, processes, stores, delivers and administers blood and a variety of blood products. About 25 percent of the 9 million pints of blood collected each year is never transfused and much of this 25% is wasted.

Increasingly, the role of platelets in the genesis of atherosclerosis, myocardial infarction, and stroke is being explored. This interest has led to a detailed study of platelet structure and functio... Drugs to modify platelet function are being evaluated in man to see it they will alter the incidence and complications of these diseases.

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The focus in thrombosis and hemorrhagic disorders during the past 20 years has been on the dissection of a complex coagulation system into its individual parts in order to better understand reaction sequences and mechanisms involved. This approach has made the purification and characterization of the components possible. The trend in the foreseeable future is a resynthesis of the complex system and a study of the kinetics and regulatory mechanisms in the intact cell and whole animal.

Studies over the past several years have led to the realization that Factor VIII plays a central role in hemostasis. Much progress has been made toward its purification. It is anticipated that the purification of Factor VIII will soon be achieved, and this will permit the detailed characterization of its molecular structure. This new knowledge will offer opportunities to explore means of correcting hemostatic defects due to Factor VIII abnormalities.

Considerable progress has been made in the use of drugs that influence vascular occlusive disorders. These drugs fall into one of three general categories: (1) anticoagulants; (2) anti-platelet agents; (3) fibrinolytic agents. The next few years will see a major effort to develop the use of these agents for the prevention or treatment of vascular occlusive disorders.

Recent investigations have led to the observation that the hemoglobin molecule may be modified so as to reduce the sickling of the red cell. Agents which have been reported to have this effect include the ureas, alkylating agents, zinc, and cyanate. Cyanate has been the most promising therapeutic agent; however, there are certain toxic effects which accompany its use. New studies will add emphasis on eliminating these toxic effects as well as accelerate effort toward the development of effective new anti-sickling agents to prevent the serious complications of sickle cell anemia.

Recent advances in technology have made a significant impact on the identification and method of purification of hepatitis B virus from blood and have resulted in the production of purified non-infective antigens in chimpanzees. The virtual elimination of Hepatitis B as the cause of post-transfusion hepatitis resulting from the application of third generation tests for hepatitis B antigen makes the next urgent task the development of diagnostic tests and the etiologic characterizations of Non-A-Non-B hepatitis.

Animal studies with blood substitutes have been highly encouraging. It is hoped that increased activity in this area will lead to the development of a clinically useful blood substitute. A completely safe "physiologic" blood substitute has enormous future potential.

The thrust of the National Blood Policy poses a new challenge for the Institute. Emphasis will be placed on "management" aspects of the national blood resource in order to assure high quality, efficient blood services for all the American people. Two of the most important efforts in this endeavor will be the establishment of an all-volunteer blood donation system and the development of a national blood data system.

The 1978 request provides for the continuation of previous commitments. All noncompeting research grant commitments will be honored and an estimated 35% of competing grants recommended for award will be funded. Individual research fellows will be supported, but institutional thrombosis training grants will continue to be phased out. Research and development contracts will be continued at a reduced level.

Intramural Research

	1977 Appropriation Pos.	Amount	1978 Estimate Pos.	Amount	Increase or Decrease Pos.	Amount
Intramural Research.....	435	$33,950,000	435	$35,139,000	---	+$1,189,000

The Bethesda-based NHLBI intramural research effort plans, conducts, and directs a program of general laboratory and clinical research in heart, blood vessel, lung, and kidney diseases; certain blood diseases such as sickle cell anemia, hemophilia, hepatitis; and development of technology related to cardiovascular and pulmonary diseases.

The intramural activities maintain close communication with other programs of the Institute to facilitate early practical application of basic research findings. Areas of major interest are the biology of experimental and clinical arteriosclerosis and its manifestations; the pathophysiology of hypertensive vascular disease; functions of the lung; clinical and experimental studies on physiological and pharmacological aspects of heart, blood, and lung diseases, and a broad program of other basic research and technical developments related to them.

In 1949 a comprehensive plan was drawn up for the Institute's intramural research program. Instituted in July of that year, it provided for 3 laboratory sections, 5 laboratory-clinical sections, and 4 clinical sections. This laboratory and branch organization has changed substantially over the years, but the concept underlying that initial plan has not: the Institute's own research program should blend basic research with studies aimed directly at the solution of clinical problems posed by the cardiovascular, pulmonary, and blood diseases. Currently intramural research is organized into 6 clinical-laboratory branches and 9 research laboratories.

The productivity and accomplishments of these programs are recognized world-wide. Indeed, of the five U.S. government scientists who have been honored with the Nobel Prize in the biomedical sciences, four are or at one time were directly involved in the NHLBI intramural programs. Because of its recognized excellence, the Institute attracts many trainees, who, after accelerated and intensive training, return far better equipped for service in the medical and scientific communities. As in other Institutes, there is an active visiting scientist program which has broadened the utility of the physical facilities and intellectual environment of the NIH as a national research resource and mutally strengthened productive science throughout the world.

An immediate requirement is for clinical care services to be provided to the Clinical Center and other Institutes. The NHLBI must provide testing and consultation as needed by patients of all the clinical programs in the areas of pulmonary, blood, and cardiac diseases. The new emphasis on the NIH clinical program areas is placing a burden of clinical services on the intramural physicians which is competing with their clinical research goals.

Developments in cardiology research indicate an opportunity to examine the effects of current surgical and medical procedures in use for the treatment of coronary artery disease by utilizing newly developed nuclear scanning techniques. This could be an important

cost effective clinical tool for clinical medicine.

Promising leads in the hematology program indicate the opportunity to study blood gelation and its relationship to changes in oxygen affinity. This is expected to be highly profitable for the sickle cell anemia studies.

The budget provides for essentially the same level of activity in 1977 and 1978. The dollar change indicated is for "built-in" increases, primarily an increase for centrally furnished services.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations.....	262	$18,200,000	262	$18,520,000	---	+$320,000

This activity encompasses the majority of administrative support staff of the Institute, including activities relating to the review, award, and scientific administration of research grants, training awards, and research and development contracts. The 262 positions are located in four divisions, the Division of Heart and Vascular Diseases, the Division of Lung Diseases, the Division of Blood Diseases and Resources, and the Division of Extramural Affairs. Also included in this activity is the Office of Prevention, Education, and Control.

In 1977, it administered over 2,000 research grants, approximately 500 training awards, and over 300 contracts over a wide range of heart and vascular, lung, and blood disease and blood resource areas. The Institute's divisions have formulated plans for continued implementation of action items in the National Program Plan. Details of these plans have been submitted in past Annual Reports of the Director and its National Advisory Council. To implement the large number of new initiatives, to keep ongoing programs on target, and to develop these as planned, the Institute has made maximum use of available staff to provide adequate scientific planning, review, coordination, management, and evaluation. A continuation of the National Program Plan implementation in 1978 will be achieved to the limit of available resources. This not only includes administration of grants and contracts but coordination of the Institute's evolving programs in prevention, education, and control.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.....	50	$1,797,000	47	$1,754,000	-3	-$43,000

This activity provides the overall planning, direction, coordination, and evaluation of the Institute's programs. Included within this activity are: the Director and his immediate staff, including the Office of Administrative Management and the Office of Program Planning and Evaluation. Three administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Heart and Vascular Diseases. (Public Health Service Act, Section 301)

1977 Estimate		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$233,044,000	Indefinite	---	$236,744,000

Purpose: This activity, administered by the Division of Heart and Vascular Diseases, includes investigations of the epidemiology and etiology of heart and blood vessel diseases and studies of the basic biological mechanisms and processes involved in normal and abnormal phenomea--as well as detection, diagnosis, treatment, and preventive programs. The array of current and long-range opportunities and needs for advancement is impressive and expanding. The National Program is conducted through 10 program areas: arteriosclerosis, hypertension, cerebrovascular disease, coronary heart disease, peripheral vascular diseases, arrhythmias, heart failure and shock, congenital and rheumatic heart diseases, cardiomyopathy and infections of the heart, and circulatory assistance.

Explanation: The National Heart, Blood, and Lung Institute continues to develop and support an integrated program embracing fundamental and clinical research, clinical trials, and manpower development. It supports prevention, education, and control activities to provide for efficient and timely application of knowledge obtained through research.

Accomplishments in 1977: The largest segment of support continues to go to investigator-initiated research. Significant progress was made in the targeted areas identified by major clinical trials. These include the Aspirin-Myocardial Infarction Study, the Multiple Risk Factor Intervention Trial, the Hypertension Detection and Follow-Up program, the Coronary Primary Prevention Trial, and the Coronary Artery Surgery Trial. The most significant progress in the area of Prevention, Education, and Control continues in the National High Blood Pressure Education Program. New programs being initiated include studies of the pathogenesis of atherosclerosis in diabetes, epidemiology of hypertension in the young, a minority hypertension research development summer program, an anti-arrhythmia trial by administration of beta-blocking agents, a collaborative clinical trial to evaluate techniques to protect ischemic myocardium (damaged heart muscle) and minimize the size of ultimate heart damage associated with acute heart attack, demonstration programs in hypertension control in the work setting, demonstrations of the impact of statewide coordination of hypertension on blood pressure control and the reduction of mortality from selected diseases, further development in non-invasive instrumentation and in left heart assist blood pump development, and establishment of non-human primate colonies, among others.

Objectives for 1978: The activities enumerated above will be continued. All non-competing research grants will be supported and an estimated 35% of competing grants recommended for award will be funded. The phase out of institutional cardiovascular training grants will continue. Research and development contracts will be maintained at approximately 90% of 1978 commitments.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Lung Diseases. (Public Health Service Act, Section 301).

1977 Estimate		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$54,835,000	Indefinite	---	$55,715,000

Purpose: This activity, conducted by the Division of Lung Diseases, is responsible for overall planning, coordination and evaluation of all extramural activities relative to respiratory diseases.

Explanation: Research programs range from studies concerned with the fundamental mechanisms of lung cell metabolism to the development of instrumentation for ventilatory assist and rehabilitation. The scope of research is large as dictated by the diversity of the disease mechanisms of the lung.

Accomplishments in 1977: The Institute continued its rapidly developing lung disease program of basic and clinical research, clinical trials, and demonstration, education, prevention, and control projects. Efforts to identify risk factors in emphysema and other chronic lung diseases have been intensified. This is critical because the exact etiology of these diseases is unknown. Progress has occurred in development of new tests for pulmonary function. Programs being initiated include clinical trials for the validation of existing regimens and the development of new ones, the establishment of clinical centers to evaluate the efficacy of antenatal steroid therapy in the prevention of respiratory distress syndrome in newborns, and a clinical study of intermittant positive breathing (IPPB) to determine its efficacy for use in patients with chronic obstructive pulmonary disease.

Objectives for 1978: The request provides for the continuation of the ongoing programs in most instances. All noncompeting research grants will be supported and an estimated 35% of competing grants recommended for award will be funded. The phase-out of the institutional pulmonary graduate training grants will continue. Research and development contracts will be continued at essentially the 1977 level.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Blood Diseases and Resources. (Public Health Service Act, Section 301).

1977 Estimate		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$54,835,000	Indefinite	---	$55,770,000

Purpose: This activity, conducted by the Division of Blood Diseases and Resources, plans and directs research on blood diseases and blood resources. The program encompasses bleeding and clotting disorders, biomaterials, sickle cell disease and other disorders of the red blood cell, and blood resources.

Explanation: The Institute seeks to carry out a comprehensive program including fundamental and clinical research, professional development and training to fill projected needs, and education, prevention, and control activities to assure orderly application of the knowledge gained through research.

Accomplishments in 1977: Increasing emphasis on the study of blood led to a change in the name of the Institute from the National Heart and Lung Institute to the National Heart, Lung, and Blood Institute. Current support encompasses programs in hemophilia, thrombosis, sickle cell disease, blood fractionation and storage, development of blood substitutes, and the safety of transfused blood. Considerable progress is being made in the use of drugs that influence vascular occlusive disorders. It is anticipated that the purification of Factor VIII will soon be achieved; this will permit the detailed characterization of its molecular structure. The next few years will see a major effort to develop the use of drugs for the prevention or treatment of vascular occlusive disorders. Work will continue on modification of the hemoglobin molecule to reduce the sickling of the red cell. Continued work is planned to lead to the development of an acceptable hepatitis vaccine, as will work on blood substitutes. In blood resources two of the most important efforts will be the establishment of an all-volunteer blood donation system and the development of a national blood data system.

Objectives for 1978: The request provides for the continuation of previous commitments. All noncompeting research grant commitments will be honored and an estimated 35% of competing grants recommended for award will be funded. Individual research fellows will be supported, but institutional thrombosis training awards will continue to be phased out. Research and development contracts will be continued at a reduced level.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Intramural Research. (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
435	$33,950,000	Indefinite	435	$35,139,000

Purpose: This is a research program within the facilities of the NIH at Bethesda. Within the framework of seeking fundamental knowledge of disease processes, basic studies comprise a significant portion of the program. Such studies range from study of the subtle biochemical mechanisms controlling the central and autonomic nervous systems to a study of the basic functioning of the primitive cell. The balance and major portion of research is directed specifically toward a solution to the various forms of cardiovascular distress. Because of the recognized excellence of its programs, the Institute also attracts many trainees, who, after accelerated and intensive training, return far better equipped for service in the medical and scientific communities.

Explanation: The Institute has 435 positions for this activity, of which about half are for scientists and physicians and the remainder for technical personnel. Basic and clinical research is carried on in 16 major laboratories and branches. One hundred hospital beds are at the disposal of the clinical program. Support is given also to a vigorous out-patient clinical program with approximately 5,000 patient visits annually.

Accomplishments in 1977: The intramural activities maintained close communication with other programs of the Institute to facilitate early practical application of basic research findings. Areas of major interest are the biology of experimental and clinical arteriosclerosis and its manifestations, the pathophysiology of hypertensive vascular disease, functions of the lung, clinical and experimental studies on physiological and pharmacological aspects of heart, blood, and lung diseases, and a broad program of other basic research and technical developments related to them.

Objectives for 1978: An immediate requirement is for clinical care services to be provided to the Clinical Center and other Institutes. The NHLBI must provide testing and consultation as needed by patients of all the clinical programs in the areas of pulmonary, blood, and cardiac diseases. Developments in cardiology research indicate an opportunity to examine the effects of current surgical and medical procedures in current use for the treatment of coronary artery disease by utilizing newly developed nuclear scanning devices. There exist promising leads in the hematology program which indicate the opportunity to study blood gelation and its relationship to changes in oxygen affinity. This is expected to be highly profitable for the sickle cell anemia studies.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Direct Operations. (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
262	$18,200,000	Indefinite	262	$18,520,000

Purpose: This activity encompasses the majority of administrative support staff of the Institute, including activities relating to the review and award of grants, contracts and reimbursements to NIH for centrally furnished administrative services.

Explanation: The 262 positions in this activity are located principally in four divisions, the Division of Heart and Vascular Diseases, the Division of Lung Diseases, the Division of Blood Diseases and Resources and the Division of Extramural Affairs. Also included in this activity is the Office of Prevention, Education, and Control.

Accomplishments in 1977: Administration of over 2,000 research grants, approximately 500 training awards, and over 300 contracts was carried on over a wide range of heart and vascular, lung, and blood disease and blood resource areas. The Institute's divisions have formulated plans for continued implementation of action items in the National Program Plan. These plans have been detailed in past Annual Reports of the Director. To implement the large number of new initiatives, to keep ongoing programs on target, and to develop these as planned, the Institute has made maximum use of available staff to provide adequate scientific planning, review, coordination management and evaluation.

Objectives in 1978: A continuation of National Program Plan implementation will be achieved to the limit of available resources. This includes administration of grants and contracts, and coordination of the Institute's evolving programs in prevention, education, and control.

National Institutes of Health

National Heart, Lung, and Blood Institute

Program Purpose and Accomplishments

Activity: Program Management. (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
50	$1,797,000	Indefinite	47	$1,754,000

Purpose: This activity provides the overall planning, direction, coordination, and evaluation of the Institute's programs. Included within this activity are: the Director and his immediate staff, including the Office of Administrative Management, and the Office of Program Planning and Evaluation.

Explanation: Funding for this area provides for salaries and other operating costs for overall Institute management. Activities include the establishment of internal Institute policy for program and administrative operations, and surveillance over their execution.

Accomplishments in 1977: In 1977 leadership was provided for continuing the implementation of the National Program Plan, to "expand, intensify, and coordinate the activities of the Institute respecting heart, blood vessel, lung, and blood diseases..." This has encompassed an ordered sequence of program activities ranging from the acquisition of new knowledge to demonstration and control programs in the health care setting of the community. The emphasis on the whole continuum from basic research through clinical applications and health education has resulted in apparent significant reductions in the mortality from diseases within the Institute's purview.

Objectives for 1978: The Institute will continue the management and direction of its research programs. Emphasis will be placed on the coordination and evaluation of demonstration and control programs, including dissemination of health information. Programs primarily concerned with prevention will also be highlighted. A decrease of three positions in this activity will result in a reduction of program evaluation and analysis activities.

TUESDAY, MARCH 8, 1977.

NATIONAL INSTITUTE OF DENTAL RESEARCH

WITNESSES

DR. DAVID B. SCOTT, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. CLAIR L. GARDNER, ASSOCIATE DIRECTOR, EXTRAMURAL PROGRAMS, NATIONAL INSTITUTE OF DENTAL RESEARCH
DR. MARIE U. NYLEN, ACTING DIRECTOR OF INTRAMURAL RESEARCH, NATIONAL INSTITUTE OF DENTAL RESEARCH
DR. JAMES P. CARLOS, ASSOCIATE DIRECTOR, NATIONAL CARIES PROGRAM, NATIONAL INSTITUTE OF DENTAL RESEARCH
MRS. FRANCES H. PETTINATO, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF DENTAL RESEARCH
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
H. RICHARD MILLER, ASSISTANT DIRECTOR FOR BUDGET, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. The subcommittee will come to order.

Now we have the National Institute of Dental Research.

The presentation will be made by Dr. David B. Scott, the Director.

Doctor, we have your biographical sketch which we will place in the record at this point.

[The biographical sketch follows:]

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

BIOGRAPHICAL SKETCH

Name: David B. Scott.

Postion: Director, National Institute of Dental Research, NIH Assistant Surgeon General, PHS.

Birthplace and date: Providence, Rhode Island, May 8, 1919.

Education: A.B., Brown University, 1939; D.D.S., Baltimore College of Dental Surgery, University of Maryland, 1943; M.S., University of Rochester, 1944.

Experience

Director, National Institute of Dental Research, NIH, 1976—Present.

Dean, School of Dentistry, Case Western Reserve University, 1969–75.

Thomas J. Hill Distinguished Professor of Physical Biology, School of Dentistry, Case Western Reserve University, 1965–75.

Professor of Anatomy, School of Medicine, Case Western Reserve University, 1965–75.

Chief, Laboratory of Histology and Pathology, National Institute of Dental Research, NIH, 1956–65.

National Institute of Dental Research, NIH, 1948–65.

Dental Section, Division of Physiology, Experimental Biology and Medicine, NIH, 1944–48.

Carnegie Fellow in Dental Research, University of Rochester, 1943–44.

Association memberships

American Dental Association.

Federation Dentaire Internationale.

International Association for Dental Research.
Electron Microscopy Society of America.
Washington Academy of Science (Fellow).
American Academy of Forensic Sciences (Fellow).
American Association for the Advancement of Science (Fellow).
Ohio Academy of Science.
Society of the Sigma Xi.
Northeastern Ohio Society for Electron Microscopy.
Ohio Dental Association.
Cleveland Dental Society.
American Board of Forensic Odontology (Certified).

Special awards, citations, or publications.

Honorary membership, Finnish Dental Association, 1952.
Fellow, American College of Dentists, 1953.
Arthur S. Flemming Award (given annually to "ten outstanding young men in the Federal Service" by the U.S. Junior Chamber of Commerce), 1955.
Honorary Lecturer, Tokyo Dental College, 1959.
Award for Basic Research in Mineralization, International Association for Dental Research, 1968.
Fellow, International College of Dentists, 1969.
Annual Achievement Award, Sigma Epsilon Delta Dental Fraternity, 1976.
Honorary Member, Section of Odontology, Royal Society of Medicine (England), 1977.
Author of some 80 publications.

Mr. FLOOD. You have some people with you that you would like us to meet, don't you?

Dr. SCOTT. Yes, sir.

At the far end, Dr. Marie Nylen, Acting Director of Intramural Research. Next to her, Dr. James Carlos, Associate Director, National Caries program; Mrs. Frances Pettinato, Executive Officer. To my right, Dr. Clair Gardner, Associate Director, Extramural Programs.

Mr. FLOOD. We have your statement which we will place in the record at this point.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health
Statement by Director, National Institute of Dental Research
on
"National Institute of Dental Research"

Mr. Chairman and Members of the Committee:

I am happy to have this opportunity again to testify before this Committee on behalf of the National Institute of Dental Research. In the little over a year that I have served as Director of the Institute, I have been impressed with the progress being made by NIDR intramural and grant- and contract-supported scientists against a broad front of dental and other oral-facial diseases. Through these efforts, we are moving steadily toward our goal of effective control and ultimate prevention.

Dental Caries

In the area of caries, particularly, we are working with all due speed to develop new and improved preventive measures. One promising approach is the use of antimicrobial compounds or enzymes to dissolve plaque, the bacterial films that adhere to the teeth and gums. By thereby reducing the numbers of bacteria, we believe that nearly complete protection against tooth decay can be achieved. From over 200 such compounds screened to date by the Institute's National Caries Program, 16 advanced to animal testing during the year and two were subjected to initial human trials. One of these antimicrobials, used as a mouthrinse, reduced plaque bacteria in young adults approximately 90 percent after five days' use. Further clinical trials are planned.

Several antiseptics already in common use were shown to be effective inhibitors of the enzyme systems involved in the production of acid from sugar on the tooth surface. They have potential for caries prevention if methods could be found to prolong their period of activity in the mouth.

To increase the effectiveness of such compounds, as well as topical fluorides, the National Caries Program began research on the possible adaption of slow-release technology for intraoral use. During FY 1976, one such method was perfected to the point where it is capable of releasing prescribed, constant amounts of fluoride for 6 months in synthetic saliva. It involves an inert polymer device which can be fabricated in sizes and shapes suitable for insertion in the mouth. Tests in animals have confirmed the feasibility of this approach.

Our research on the feasibility of a vaccine against caries continues to have high priority. Studies with infant monkeys suggest that "priming" the immunologic system before it fully matures may be a promising avenue for research toward an eventual human vaccine.

Emphasis also continues on our community demonstrations of school-based fluoride mouthrinsing, begun in FY 1975. Some 25 million school-age children live in fluoride-deficient communities. If they could have the benefit of weekly fluoride mouthrinsing, caries in this group could be prevented by 30 to 50 percent. A program of information dissemination on this highly cost-effective preventive method was launched. It includes an exhibit and leaflets to be sent to meetings of educators and school-health groups, a television film for nation-wide distribution, and an instructional manual to assist communities in starting a mouthrinse program.

Following the pattern of broad program evaluation that we first established for the periodontal disease area, we next plan to evaluate the Institute's total caries research activity. Preliminary steps are underway, and it is expected that the evaluation will begin later this year.

Periodontal Disease

Studies of periodontal disease are further clarifying the different types of bacteria and immune responses associated with various forms of the disease.

In the early form known as gingivitis, in which the gums are inflamed, to date only the actinomyces have been found to evoke a specific cellular immune reaction in affected patients.

On the other hand, the form of the disease called periodontitis, which includes the loss of supporting bone around the teeth, is linked to humoral or blood immune reactions against a variety of bacteria. In this response, antibody-forming cells called B-lymphocytes produce specific antibodies against the bacterial antigens. The antibodies appear in the blood and tissues, and the B-lymphocytes themselves accumulate in the gingival tissues. When antigens of the offending bacteria seep into the gums and interact with antibodies or with the localized B-cells, complex reactions are set off. These result in the production of two potent stimulators of bone resorption called Osteoclast Activating Factor and prostaglandin. Thus, the humoral immune reaction includes two pathways for periodontal bone destruction.

Important new information is also emerging on the occurrence of extensive bone loss in rapid periodontitis and periodontosis, another severe form of periodontal disease. Scientists had isolated several bacteria, each of which could produce in otherwise germ-free animals the same severe bone loss seen in humans. New studies have shown that after the animals were infected, both types of immune activity rose for several weeks and severe bone loss developed only after their immune response declined. It was found that patients with severe periodontal disease also had defects in certain white blood cells called neutrophils, which normally migrate to the site where protection is needed and engulf bacteria or other substances. In these patients, the ability of the neutrophils to migrate and to engulf foreign substances was markedly reduced.

An on-going study of severe periodontal disease shows that tetracycline therapy, coupled with scaling and curettage treatment, has thus far prevented bone

loss for four years. However, it did not prevent the formation of bacterial plaque and the ensuing gingivitis in all patients.

To capitalize on findings from recent microbiologic, immunologic, and pharmacologic investigations, the Dental Institue plans to establish a limited number of clinical research centers devoted to periodontal disease. Their objective is to accelerate the development of new knowledge in prevention, diagnosis, and treatment.

Craniofacial Anomalies

Studies of malocclusion continue to probe fundamental growth processes to enable us to intervene earlier and more effectively when problems appear. From such research has come the recent discovery of special cells, termed myofibroblasts, and their association with growing bones and erupting teeth. It is believed that these cells play a role in orthodontic treatment in that they may be involved in the migration of muscle attachments on bones and in the movements of teeth. Subject to verification of these findings, the potential of these discoveries may be far reaching. The ability to harness the activity of special cells may eventually lead to control of certain growth processes and perhaps major innovations in therapy.

Concern with cleft lip and palate similarly embraces a wide spectrum of research, from the fundamental to the clinical. As part of the effort to improve habilitation of children afflicted with clefts, a recent study indicated that surgery during the first year of life produces scar tissue which retards facial growth. Using an animal model in an attempt to find new ways to reduce tissue contractions after palatal surgery, investigators found that wounds treated with an appropriate concentration of benzyl alcohol in normal saline effectively reduced wound contraction and fostered healing.

Although other craniofacial anomalies occur less frequently than cleft lip and palate, they are more severe and more difficult to habilitate. To make information more accessible to researchers and clinicians, a national collaborative data bank has been established at the University of Illinois. By pooling and analyzing data, it is hoped that better diagnostic techniques and more successful treatment will be developed.

Reflecting our interest in directing more attention to acquired craniofacial disfigurement, the Institute recently issued an announcement soliciting research grant applications in this area. Primary interest centers on achieving a better understanding of the nature, extent, and impact of the problem of traumatic injury to the craniofacial structures and on improving treatment procedures for injuries such as those associated with vehicular or athletic accidents. Another major concern is the physical and psychological rehabilitation of patients subjected to extensive surgery for cancer.

Restorative Materials

Research on restorative materials ranges from improving fillings to developing suitable implants to replace individual teeth and to serve as anchors for bridges and dentures. The ultimate objective of tooth implant research is to induce the body to accept an artificial implant as its own and to form a normal periodontal ligament around the implant.

From tests of various materials for implants, preliminary data indicate that bioglass has a biologically active surface which is conducive to the growth of bone and dense collagen, a major component of connective tissue. In studies on sub-human primates it was found that a structure somewhat like periodontal ligament was formed between the adjacent tissues and the implanted tooth. Although other materials are biocompatible, at present bioglass is the only one which can elicit

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specific cellular activity without causing inflammation. If it can be established that a true periodontal ligament is formed after the implantation of bioglass, we will encourage the use of this material in a limited carefully controlled clinical evaluation.

Following extensive testing of vitreous carbon implants in baboons, we have now funded our first study of artificial tooth implants in humans. During the next two years, grant-supported scientists will place implants made of this biocompatible material in a limited number of selected patients.

Oral Pain Control

Problems involving the measurement of pain in laboratory and clinical situations have been among the most difficult challenges of pain research. A new approach, known as signal detection theory, used to measure auditory and visual perception has been successfully applied to pain perception. Also, verbal descriptors have been used to develop word scales to rate the intensity and degree of unpleasantness of various oral-facial pain conditions. Both techniques are contributing to the improved clinical evaluation of pain-reducing agents.

In fundamental studies in nonhuman primates, an animal model has been developed to identify neural pathways from the face to the brain conveying nerve signals about the presence of painful stimuli. Other studies have identified descending neural circuits that shutoff pain messages before they ascend in the spinal cord to higher brain centers. One of these pathways also is activated by acupuncture and by narcotic drugs, such as morphine, which are known to suppress pain. Another pain-modulating circuit descends by a different pathway and can be activated by stress, as in the form of electric shock. Further studies of these normally present pain-suppressing pathways may ultimately aid in the development of methods of pain management not requiring repeated use of addictive drugs.

Oral Cancer

Recent improvements in the criteria for diagnosing early asymptomatic oral cancer have led to a marked increase in the detection rate. Follow-up studies suggest that despite the small size and innocuous appearance of certain lesions, over 70 percent are already invasive. These findings are being communicated to dental and medical practitioners. Further investigation is necessary to determine if cure rates are improved by early detection.

Nutrition

An important gain from nutrition research is our improved understanding of the effects of both vitamin and protein deficiencies on the metabolism and function of the tissues lining the mouth. Other progress includes the finding that small amounts of aluminum hydroxide contained in some antacids reduce phosphorous absorption and increase calcium and fluoride excretion from the skeleton. Further research, however, is required to clarify the effects of deficiencies as well as the interaction of dietary constituents and their resulting influence on the body.

Dental Research Institutes (Centers)

Now in their tenth year, the dental research institutes supported by NIDR in five different university environments continue to serve effectively as major interdisciplinary centers focusing on oral-facial problems. The principal strength of these centers has been to attract to dental research those scientists not previously engaged in this field and to develop collaborative programs.

Virology

We have previously reported to you on herpes simplex infections and viral-induced diabetes, which are part of the Institute's broad program of research in virology. Another facet of this research has now provided a new insight into how viral infections may enhance allergic reactions. This is the observation that

interferon can enhance the release of histamine, the substance in the body which accounts for many of the adverse symptoms seen in hayfever and other allergies. Interferon is produced by the body in response to viral attacks. Until recently, interferon was considered to have only the function of decreasing virus multiplication. The current findings represent a new biological role for this substance. They might explain why patients with bronchial asthma develop more severe and frequent attacks of asthma during certain infections.

Communicating Research Findings

A diversified information program is being conducted to assure that dental students, practitioners, and the general public are kept abreast of research findings that can be applied to detect, diagnose, control, or prevent dental and other oral-facial diseases. As part of this effort, an exhibit on the early detection of oral cancer was developed and shown at several professional meetings.

Two major informational thrusts during the year were the fluoride mouthrinsing program, as described in the earlier section on caries, and the sealant to protect chewing surfaces of the teeth from decay. A definitive report on clinical trials on the sealant was published in the May/June 1976 issue of the Journal of Preventive Dentistry. The findings were also highlighted in "Research News from NIDR," a monthly service to dental journals throughout the country, and in the "Dental Insider," a non-government publication distributed to 75,000 dentists. In addition, a 12-minute film on the sealant was prepared for showing to dental students and practitioners.

Public information efforts on the sealant included the preparation of a leaflet, radio spot announcements, a television spot announcement scheduled for production soon, and articles for newspapers, popular magazines, and employee house organs. Segments of the sealant film will also be shown on a nationally syndicated television documentary series.

Various preventive techniques under study by the Institute were discussed by staff from the National Caries Program at two dental schools and at annual meetings of the American Dental Association, the National Dental Association, and the American Association of Dental Schools.

Budget Request

In conclusion, Mr. Chairman, the budget request for the National Institute of Dental Research for FY 1978 is $57,981,000. I shall be pleased to try to answer any questions and supply additional information desired for the record.

RESEARCH GRANTS

Mr. FLOOD. Your budget proposes to increase the regular research grants by $3 million.

Dr. SCOTT. Yes, sir.

Mr. FLOOD. But I notice there is a reduction in the noncompeting research grants. What is the reason for that reduction? Do you have enough money now to meet all of your continuing grant commitments? Why the cut?

Dr. SCOTT. It is not a cut, Mr. Chairman. It is the cyclical nature of grant funding. There is a group of grants now expiring, so that the number of noncompetings will drop from 320 to 270. Every 3 years or so this will happen. It cycles around.

Mr. FLOOD. Is it a reevaluation of the work going on?

Dr. SCOTT. No; it is just the anatomy of the system which says that that number is expiring at this point.

Mr. FLOOD. I thought it might be reevaluation to see the work going on and drop the low-priority work?

Dr. SCOTT. Not in the noncompeting.

DENTAL RESEARCH INSTITUTES/CENTERS

Mr. FLOOD. Most of your research areas receive some increase in 1978, except the Dental Research Centers. Why is that? Is it because these centers are operating at maximum capacity? Is that it?

Dr. SCOTT. There are various reasons. One, of course, is the entire economy of the Institute and the amount we feel should be devoted to that program.

Second, there are obviously changes in the request for grant level in any given year depending on the cycle and what the site visit teams find out and recommend. In general, these institutes are now getting on their feet and attracting other grant support, and we feel they are in relatively fair shape. We would like to give them more, but we feel that with the constraints of the entire budget it would be difficult.

Mr. FLOOD. Are these centers operating at a maximum capacity?

Dr. SCOTT. I don't know what a maximum capacity is.

Mr. FLOOD. I don't know either. We often ask that question. What would you mean by it?

Dr. SCOTT. I would suspect that any good Director running a center like that would never define a maximum. He would want to expand and go into other lines of endeavor.

Our feeling is that with their constraints on space and their relationships within the university, they are not doing too badly because they do bring in extra support that you do not see here.

Mr. FLOOD. While we are on the subject of the Dental Research Centers, I believe these centers were started about 10 years ago.

Dr. SCOTT. Just about.

Mr. FLOOD. What would you identify as the major accomplishment of these centers?

Dr. SCOTT. I think the major accomplishment was bringing into research in our specialty field a rather large number of basic scientists who would not have been attracted otherwise. It made a place for them to congregate and work.

I think that is the major step forward, and that it has allowed an enormous amount of research.

Mr. FLOOD. How much have you invested in these research centers to date?

Dr. SCOTT. I don't have it at hand, but we can get it for the record.

[The information follows:]

TOTAL FUNDS FOR DENTAL RESEARCH INSTITUTES

Total investment in the Dental Research Institutes/Centers through fiscal year 1976 is $50,441,000.

FLUORIDE MOUTHRINSING

Mr. FLOOD. Currently your Institute funds projects in the fluoride mouthrinsing to prevent tooth decay. I believe it is your plan to have the communities eventually assume responsibility for funding these programs.

What incentive is there for the community to pick up all these costs on a project like that?

Dr. SCOTT. I suppose the major incentive would be the better dental health of the community. Obviously if that has been brought out in any sense by the project being there and explained and being publicized, that should be one incentive.

The second is that the cost is very low.

Mr. FLOOD. I think you will agree that this is so, given this current widespread antifluoridation sentiment, and it is widespread. Do you believe realistically that the communities will be able to successfully operate these programs faced with this?

Dr. SCOTT. I am not aware of anything controversial in the topically-applied fluorides. I think it is in fluoridation of the community water supply that the controversy exists.

Mr. FLOOD. Antifluoridation controversy generally.

Dr. SCOTT. I have not seen it anywhere except water fluoridation. Many people opposed to water fluoridation suggest that topical fluoridation would be an acceptable substitute.

Mr. FLOOD. But you don't think the sentiment would in any way affect or influence the communities in going ahead with these programs?

Dr. SCOTT. I have no feeling that it would.

VACCINES

Mr. FLOOD. We have heard a great deal of talk lately about oral vaccines which can significantly reduce the occurrence of tooth decay. It is now being tested in animals.

What is the status of the vaccine? When do you expect to initiate any clinical trial?

Dr. SCOTT. Clinical trials are not in sight yet. The results in the laboratory are more and more encouraging, but vaccines for humans are a long way down the pike. The most recent results have shown increasing amounts of antibody production by some new techniques, and certainly in subhuman primates the results of several caries trials are most encouraging.

Beyond that, however, then come all sorts of other considerations, especially when one works with a streptococally derived vaccine. This is a long research process that could take some years yet.

EVALUATION

Mr. FLOOD. Last year you provided the committee with a summary of a report prepared by the ad hoc scientific panel. They evaluated your Institute. One of the findings was that relatively little clinical research is actually being supported by the Dental Institute.

Does the budget you have before you now change that situation at all?

Dr. SCOTT. The evaluation you refer to, Mr. Flood, was on the periodontal program only. The contention of the ad hoc committee was, and quite a true one, that there was very little clinical periodontal research going on. The feeling of our staff during the year was that knowledge had reached a point by now in the basic matter of periodontal disease that it was time to push for more clinical research.

In order to do this, we made the decision to support specialized clinical research centers.

Mr. FLOOD. Does this budget change that situation?

Dr. SCOTT. This budget, as we have been able to work it out, will allow us to invest somewhere on the order of $1 million in four centers. We are hoping to start a couple this year and a couple of additional ones next year.

We did put out a request for applications, an RFA, a couple of months ago.

Mr. FLOOD. You are speaking of the calendar year?

Dr. SCOTT. No; we are speaking of the fiscal year. And we got 12 responses back, which I think is quite good, for a new venture. These will be evaluated and we hope to mesh them in with the grant cycle so that we will be able to fund the first couple.

The beginning of this program was made possible by a center grant in cleft palate dropping out, so that we will have some money left. We hope to add a couple more periodontal centers next year and by that time have four dedicated strictly to clinical research.

COOPERATIVE VENTURES

Mr. FLOOD. This ad hoc panel recommended that more research be done on periodontal diseases. One approach they recommended was the encouragement of cooperative ventures. Do you intend to act upon that recommendation? If you do, how?

Dr. SCOTT. The recommendations had a little more in them than that. They recommended expanding knowledge, mainly through microbiology and that sort of research. We are hopeful that these clinical centers actually will do a fair bit of that. We have insisted in the description of what we are after that there be a basic component in pharmacology, immunology, or microbiology.

Mr. FLOOD. How do you plan to encourage it?

Dr. SCOTT. We can recommend and encourage cooperative ventures. I think that is what we will have to do.

SEALANTS

Mr. FLOOD. There was quite a deal of talk in the past about the adhesive coatings to seal the teeth and thus reduce the caries substantially. That was your word. I notice in your budget justification that you believe the cost goes very, very high on this and you are going to restrict the use of this very valuable technique.

Why does it cost so very much? Is it material or time of the dentist or what?

Dr. SCOTT. What we actually said, Mr. Chairman, was that relative to cost effectiveness, in contrast, for example, to a fluoride mouthrinse which costs less than a dollar per year per person, the high cost of personnel in applying sealants and also some higher material costs would put the measure in a region that does not lend itself terribly well to a public health measure.

Our feeling was that this would work best in the clinic setting and in private practice. We didn't talk about restricting it.

Mr. FLOOD. Can that sealant that we were talking about be applied by a dental auxiliary? I am talking about the kind of dental auxiliary trained by the Health Resources Administration.

Dr. SCOTT. The studies demonstrated that that is indeed a possibility. One of the problems right now is the legality of doing such a thing. That is a roadblock obviously in the way of this sort of a program.

Mr. FLOOD. How does that arise?

Dr. SCOTT. It is the State practice laws for dentistry.

Mr. FLOOD. Then the so-called paramedic would be excluded by the State law you feel?

Dr. SCOTT. I think in most States that is correct.

Mr. FLOOD. Are you working on ways to reduce the cost of the sealant.

Dr. SCOTT. The cost of the sealant is not the item. It is the cost of the personnel. I doubt we can do anything about that.

But the answer to your question is "Yes." One approach is to find a different kind of a sealant which can either be self-applied or applied under different circumstances from the intricate procedure involved at present.

COSTS OF DENTAL CARE

Mr. FLOOD. With the periodontal disease a major health problem in the entire country, I wondered about the extraordinary expenses of this kind of dental care to all of our citizens. Will these current research projects that you did talk about on prevention help lower these costs? Will it correct it and lower the costs?

Dr. SCOTT. We are not as far along in prevention of periodontal disease as we are in caries. As you were just exploring yourself, it is our first view now to start some clinical centers going. So it will be a while yet.

Mr. FLOOD. We don't want to get locked into a situation where we put all this money into research and keep pushing up the costs in such a way that only a very few people can afford the results of all these costs, experiments, and research.

Dr. SCOTT. The ultimate aim is the same here, preventive methods within the reach of the community. It is a little farther in the future than caries prevention.

Mr. FLOOD. Mr. O'Brien?

INTRAMURAL RESEARCH

Mr. O'BRIEN. What is intramural research, Doctor?

Dr. SCOTT. Intramural research is the research done on the grounds of NIH in our own laboratories.

Mr. O'BRIEN. Do your studies get into the business of utilization of manpower, paradentists?

Dr. SCOTT. No, sir; they do not.

BUDGET

Mr. O'BRIEN. If this committee had a notion to cut your budget, would you have any lower priorities you would ask us to work on before we worked on others?

Dr. SCOTT. I hope the committee doesn't decide to cut the budget. We are funded in such a fashion that in my view we are dealing only with high priorities. I would hate to choose.

Mr. O'BRIEN. Thank you, Mr. Chairman.

XYLITOL

Mr. FLOOD. Now we read an article some months ago about this xylitol. It was quite a big deal at the time. At the time of the article this sweetener was tested over in Finland and was found to actually prevent tooth decay.

What is the status of this sweetener in our country and what is your opinion of the results reported by the Finnish dentists?

Dr. SCOTT. I think you have to consider those results really as an indication that nonsucrose sweeteners cause a reduction in caries because of the dietary change. It is well known that when sugars are taken out of the diet there is a reduction in caries. As far as therapeutic effects, there was a little indication of that in one of their studies, that is not terribly convincing at this point. This is being repeated by certain individuals to see what it may add up to.

Mr. FLOOD. Have you heard anything recently on it?

Dr. SCOTT. They have not reported much in Finland since. Here, we have one contract that has just become active on chewing gum with xylitol in it.

RESTORATIVE MATERIALS

Mr. FLOOD. In your research on restorative materials, as we call them, to develop strong and durable materials, that is all right. But to also be inexpensive, is that part of your goal, too?

Dr. SCOTT. Hopefully.

IMPLANTS

Mr. FLOOD. We have also talked about tooth implants. We spent all 1 day talking about tooth implants. That was in the past.

Now, Doctor, how close are you now to making this part of routine dental care?

Dr. SCOTT. As you know, implants are already in use in practice. Some years ago there was a feeling on the part of organized dentistry as well as the military and this Institute that there should be a warning to progress with due caution until more research was done in the field. The research has now progressed to the point where our Institute's first clinical study is being supported.

In other words, materials have come along which look promising, techniques look promising in animals, primarily subhuman primates. We are now supporting our first relatively small-scale clinical trial in Boston of one type of implant. There, again, I would say before widespread use could be recommended by an organization like ours it will be a little while.

PREVENTIVE DENTAL CARE PROGRAMS

Mr. FLOOD. How closely are you working with the HRA people, the Health Resources Administration, with respect to developing preventive dental care programs?

Dr. SCOTT. Health Resources is really in the manpower business as far as we know them. They have certainly had programs in prevention, but there is relatively little going on in that area at present.

So most of the preventive program development actually falls to us.

Mr. FLOOD. How are you working with these other people?

Dr. SCOTT. We are in contact with them all the time. We are right now talking over one program that they probably will be unable to support, but which may be of interest to both of us. We may be able to cooperate in that sort of project.

DIET RELATED TO DENTAL CARE

Mr. FLOOD. Do you think enough is being done by all these various agencies of the Public Health Services, quite a lot of them, to inform the public on this issue of diet in relation to dental health care?

Dr. SCOTT. Again, the question comes up as to how much is enough. Probably not at this point, sir. We are doing considerably better than we were.

Mr. FLOOD. What needs to be done?

Dr. SCOTT. I think probably what needs to be done is more effort in prevention discussion and promotion by the dental group at the Center for Disease Control, for example. They were established to do this very thing. I think they need some added support in order to do this.

We are working along those lines with caries preventive methods, which is our strongest area. But I think basically it is the same thing—the more input, the more effort comes out.

Mr. FLOOD. Mr. Early?

FLUORIDE

Mr. EARLY. Doctor, what have we done with regard to fluoride? Have you determined any alternates to fluoride?

Dr. SCOTT. Are you speaking of any kind of fluoride?

Mr. EARLY. Yes.

Dr. SCOTT. The caries program is thinking of all sorts of alternatives along the lines of antimicrobial agents, for example.

Mr. EARLY. I am thinking of self-administered fluorides rather than fluorides as we know it in Massachusetts.

Dr. SCOTT. I am not sure I follow your question.

Mr. EARLY. Did I read along the lines here that there were some experiments with mouthwash fluoride and that type of thing?

Dr. SCOTT. Yes, topically applied, either professionally or self-applied. Some of that is now in the demonstration stage, as you probably know. I refer to mouth rinsing.

There are other types of topically applied fluorides. Dentrifices are available and fluoride tablets and combinations of these approaches.

Mr. EARLY. How effective do you think these tablets are?

Dr. SCOTT. Generally less effective than communal water fluoridation. Protection varies from 30 to 50 percent.

Mr. EARLY. In Massachusetts we are having some tremendous battles over fluorides and threats about fluorides in the water. How would you assess this? In how many States is it as active as in Massachusetts?

Dr. SCOTT. Do you mean as reactive as Massachusetts?

Mr. EARLY. Reactive might be better.

Dr. SCOTT. I think I have some figures here. The way things stand now, there are about 105 million people consuming fluoridated water. Twenty-four States provide fluoridated water to over half of their populations. Fluoride is mandatory now in some 10 States. I think this includes some new positive actions in the Northwest. There are half a dozen States in which referendums are required and one State requires fluoridation unless the vote at the local level is negative.

Basically, most States are involved in positive action.

Mr. EARLY. What do the statistics show as far as the 10 States that have mandated fluoride?

Dr. SCOTT. My impression is that the States have given the different regions within their State time in which to put the fluoridation into effect. As time goes on and the deadline is reached, almost everyone is doing it, if not everyone.

Mr. EARLY. More specifically as far as the States that mandate the fluoridation, do we have any statistics as far as the effect of teeth in those States versus others?

Dr. SCOTT. I have no idea that they are doing survey work or dental studies there. The case has been proved for so long that I would doubt whether they would be investing in public health surveys.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. ROYBAL

NEW CHEMICAL TEST

Mr. ROYBAL. Recently, there were reports in the newspaper about a new chemical test that could rinse away caries instead of drilling.

(*a*) Did you help develop this chemical?

(*b*) Are you familiar with this chemical?

(*c*) When do you believe it will be on the market?

Answer. I think you are referring to a technique for removing decayed tooth substance that is being studied at Tufts University School at Dental Medicine in Boston. The research was not supported by funds from our Institute. A preliminary report was published in the December 1976 issue of the Journal of the American Dental Association. The method involves introduction of a solution, the active ingredient of which is N-monochloroglycine, into a cavity to help remove decayed tooth material during preparation for a filling. I have no idea when such an agent would appear on the market. The authors indicated that they are continuing laboratory and clinical studies on safety and efficacy in compliance with FDA regulations.

PERIODONTAL DISEASE

Mr. ROYBAL. You indicate on page 3 of your statement that defects in certain white blood cells contribute to severe periodontal disease. The Heart, Lung and Blood Institute is charged with investigating diseases of the blood.

(*a*) Are you coordinating your research efforts with that Institute?

(*b*) In what ways?

Answer. Studies of the protective mechanisms of the body, such as the white blood cells, to which you refer, and the immune system as well, are a regular part of investigations of most diseases, periodontal disease being no exception. The context of this application of knowledge about blood is in contrast to the study of identified blood diseases themselves, such as anemia or leukemia which would be in the domain of the Heart, Lung and Blood Institute. The research findings of each Institute, of course, are of interest to the others and are shared by appropriate informal contact.

CRANIOFACIAL ANOMALIES

Mr. ROYBAL. You spent a large part of your statement discussing craniofacial anomalies. A large part of the problem encountered by a person who has craniofacial anomalies is his own psychological reaction to the anomaly.

(*a*) Are you doing any studies into how best to treat this reaction?

Answer. We are indeed supporting studies on the psychological and behavioral aspects of craniofacial anomalies, both with individual grants and as integral parts of program project grants in which research on treatment is involved. We are trying to expand these studies and have recently issued a program announcement, that is, a request for grant applications, in this area.

ORAL CANCER

Mr. ROYBAL. You mention oral cancer in your statement.

(*a*) Do you do research in this area or does the National Cancer Institute?

(*b*) Have you set up ways to pool your findings?

Answer. We do support research on oral cancer, and some is also supported by agreement with the National Cancer Institute. We are in constant contact with appropriate staff of the Cancer Institute regarding programs and results. As an example, a notice appeared just last week in the Federal Register announcing a workshop on graduate education in oral oncology, jointly sponsored by the Cancer and Dental Institutes. The discussions will center on the role and function of dental specialists in oncology, as well as training needs and resources.

XYLITOL

Mr. ROYBAL. Last year you told us you were going to test xylitol, a noncarcinogenic dietary substitute.

(*a*) What were the results of your tests?

Answer. Published studies, as well as animal studies in our laboratories, have indicated that xylitol is an effective dietary substitute for sucrose in the partial control of dental caries. We have recently issued a contract to assess the effect of substituting xylitol for sucrose in chewing gum, a major snack item. We are also investigating other potential sugar substitutes.

AGING

Mr. ROYBAL. Are you developing any special programs to help the aged with their oral problems?

Answer. We do not have special programs in aging research, but we are now discussing potential areas of interest and cooperation with the National Institute

on Aging. I might add, however, that we do support several grants directly involving aging phenomena and that a very sizable portion of our work on periodontal disease, root caries, and on restorative materials is highly relevant to the aged and their dental problems.

MR. CONTE

ANTIMICROBIAL COMPOUNDS

Mr. CONTE. I believe you have two antimicrobial compounds in initial human trials for cavity prevention at the moment. Can you tell me how those trials are going? How large are your samples? How long will your trials continue? If the trials are successful, when might we see such a product in general use?

Answer. We have completed phase I clinical antiplaque trials with the antimicrobial compound, DAPA–I, and with calcium glycerophosphate which alters the pathogenic properties of dental plaque. There were short-term (15 day) studies using 40 young adult volunteers. We are now in the process of extending these studies for 1, 2, and 6 months and eventually into 2-year anticaries trials in children. Extensive toxicology studies will also be necessary to meet FDA regulations. Obviously, new drug development is a slow and expensive process. Assuming continued positive results, it will be several years before such compounds are approved for marketing.

MOUTHWASHES

Mr. CONTE. What effect do commercial mouthwashes have on the prevention of caries? Any at all?

Answer. Commercially available mouthwashes have not been shown to be of benefit in the prevention of cavities.

POLYMER INTRAORAL DEVICE

Mr. CONTE. Would you tell me more about the polymer intraoral device for slow fluoride release? How does it work?

Answer. Two of our research approaches to intraoral slow release systems appear very promising. The first involves incorporating the active compound, for example a fluoride or antimicrobial, into inert adhesive microcapsules which stick to the teeth and dissolve at a predetermined rate. The second approach is essentially a polymer sandwich, which could be cemented in place on a tooth surface or on a prosthesis and from which the active ingredient diffuses through a semipermeable membrane. Both have shown excellent release properties in artificial saliva and will shortly be tested in animals.

PERIODONTAL CENTERS

Mr. CONTE. Where do you plan to locate your clinical research centers for periodontal disease investigation? What will be done at those centers?

Answer. The applications for support under this program have just now entered the review cycle and about 3 months' time will be required before we know where the centers will be located. In our program announcement we indicated that the sponsoring institution is expected to have an adequate research base, with resources and services to support established research in areas such as microbiology, immunology, and pharmacology. We specified that the centers should develop programs to accomplish some or all of the following: Establish the causative organisms in periodontal diseases; clarify the host response to these causative organisms; perform clinical studies of therapeutic techniques and regimens; develop preventive measures.

CRANIOFACIAL DISFIGUREMENT

Mr. CONTE. What work is being done in the craniofacial disfigurement area? Are there any aspects of injury to the face and mouth which are peculiar to athletic injuries that are being investigated?

Answer. The NIDR has an established program for addressing craniofacial disfigurement of children with oral facial clefts, handicapping malocclusion, and severe syndromes. The program provides support for basic studies on etiology and for clinical research to directly address the problems of health care. Recent activities include a contract to better assess the psychosocial handicapping aspects of

facial disfigurement of severe malocclusions. A program project grant was recently awarded for comprehensive studies on the long-term effects of surgical correction of severe craniofacial defects. Studies of subhuman primates are underway to address surgical and other therapeutic influences on normal growth. Modification of surgical procedures to preserve optimal blood supply and nonsurgical orthopedic procedures to mold the growth of the craniofacial structure are also under study. An increasing number of applications related to the behavioral aspects of disfigurement have been received.

The NIDR has recently issued a program announcement requesting applications which address the biologic research questions of acquired craniofacial defects, such as disfigurements produced by accidents or inflicted injury. No projects are yet under active support, and although several applications are in process on craniofacial injuries, none are specifically addressing athletic accidents. Program staff is encouraging applications which address craniofacial injury of young people. It is recognized that the wound healing process and facial bone fractures frequently are detrimental to the normal growth pattern of a developing child. This aspect of trauma to the active youth will receive emphasis in the effort to seek research applications in this area.

BIOGLASS MATERIALS

Mr. CONTE. What is "bioglass"? And what do you mean when you say that it has a biologically active surface? What are the implications of the use of this substance for other types of replacement and implant work?

Answer. So-called bioglasses are new materials being studied in the laboratory and in animals, which show potential for use as implants in orthopedics and dentistry, and they are under investigation in both fields. They are siliceous, glass-like materials, whose chemical composition can be varied and which can be produced in various solid shapes or can be applied as coatings to hard core substances such as ceramics, steel, cobalt-chromium or other metal alloys. Interest in the bioglasses stems from their biologically active surface chemistry. Implants release ions such as sodium, calcium, and phosphorus, and these encourage nature to deposit bone-like substances and connective tissue fibers at the surface of the implant. The scientists working with this system feel that the more true to life relation between implant and recipient tissue may well improve the success rate of implants with respect to healing and retention.

TOOTH IMPLANTS

Mr. CONTE. How will patients be selected for your study of tooth implants made of biocompatible substances?

ANSWER. As mentioned in our opening statement, we are now supporting our first clinical study of implants. This is being carried on at Harvard, where successful animal studies with vitreous carbon implants have been going on for several years.

The first call for patients was issued recently by the transplant unit at the Harvard School of Dental Medicine in the form of an announcement in the newsletter of the Massachusetts Dental Society. Assistance in securing by referral 50 patients living within 25 miles of Boston was requested. Background of the study was given, and the clinical situation required for eligibility was described. It was also stated that each patient will give informed consent and will be free to withdraw consent and discontinue participation without prejudice. Should the yield not be sufficient, we would expect the next step to be through news releases about the study in the public media. Individuals interested in participating would respond directly and would be screened by the investigators. Those presenting appropriate clinical situations would be invited to join the study.

PAIN CONTROL

Mr. CONTE. In the area of pain control, is any work being done on the development of more effective equipment and technology for so-called "painless" drilling for caries repair and restoration?

ANSWER. Most of our research on pain control involves new or improved sedation procedures, using drugs, inhalation sedation, and various behavioral techniques. Equipment for drilling is already at a highly advanced state, but the mechanical equipment and preparatory techniques are, as would be expected, subject to continued updating.

ORAL CANCER

Mr. CONTE. What is the prevalence of oral cancer in the United States? What are the current treatments, and how successful are they? What is the recovery rate?

ANSWER. Oral cancer accounts for 3 to 4 percent of all cancers occurring in the United States with over 24,000 new cases occurring each year. The highest incidence occurs in individuals over 40 years of age.

It has been firmly established that the stage of development more than any other parameter influences the survival rate of oral cancer. If a mouth cancer is diagnosed early, the lesion will be locally invasive and amenable to surgical removal. For example, lip lesions, because of their greater visibility, are usually detected early and respond well to surgery. About 85 percent of males show full recovery and are alive 5 years after surgery. Oral cancers in the floor of the mouth, anterior pillar, and ventrolateral portion of the tongue show a higher mortality rate, which is probably due to the lack of early detection, and to metastasis to other sites in the body.

DENTAL RESEARCH INSTITUTES

Mr. CONTE. Where are your dental research institutes located? What sorts of collaborative programs are conducted there?

ANSWER. The dental research institutes are located at the University of Alabama (Birmingham), the University of Michigan (Ann Arbor), the University of North Carolina (Chapel Hill), the University of Pennsylvania (Philadelphia), and the University of Washington (Seattle). There are research projects at the dental research institutes that involve collaboration of (1) investigators within the same center, (2) investigators within the center and outside the center within the same institution, and (3) investigators within the center and at other institutions. An example of each of the above categories is as follows: (1) At the Center for Research in Oral Biology, University of Washington, a project to evaluate neutrophil chemotaxis in patients with severe periodontal disease is a collaborative effort between the periodontal disease group and a group studying chemotaxis. (2) At the University of North Carolina, a study of post-traumatic trigeminal sensory neuropathy involves collaboration between the neural mechanisms group of the Dental Research Center and investigators from the departments of neurosurgery, oral surgery, anesthesiology, medicine, and psychiatry of the University. (3) A project to identify newly isolated micro-organisms from the advancing front of the periodontosis lesions and from human supragingival plaque of normal patients involved collaboration between investigators from the Center for Oral Health Research at the University of Pennsylvania and investigators at the University of Massachusetts, Amherst University, and the Forsyth Dental Center.

RESEARCH GRANTS

Mr. CONTE. Would you explain why you are projecting a decrease in noncompeting regular grants and an increase in competing regular grants for next year?

ANSWER. The explanation is a very simple one. An unusually large number of noncompeting grants are presently in their terminal year and will expire. Availability of these funds will permit activation of a larger number of competing grants than usual. The net increase in the entire program, on the other hand, is not very large, and the events in question will not repeat themselves for a few years.

TRAINING AWARDS

Mr. CONTE. It appears from your justifications (p. 101, vol. II) that you are phasing out new training awards. Is that the case, and if so, would you explain why?

ANSWER. As mentioned earlier, the reduction in our training effort reflects a decision to phase out institutional awards, which were a major source of investigators. Serious needs still exist, especially for clinical researchers, and we have adjusted upwards the funding for individual fellowships.

MANAGEMENT FUND

Mr. CONTE. You are requesting a $364,000 increase in payment for centrally furnished services. Would you tell me what those services are, and why this fairly significant increase is necessary?

ANSWER. The increase for centrally furnished services represents increased services and increased cost of services provided by the NIH Management Fund in support of the NIH research program. Some of these include: Clinical Center operation and patient care; building maintenance and utilities; scientific and technical review of research and training grant applications; and standard level users charge (payment to General Services Administration for rental of space).

MR. MICHEL

DENTAL ADVANCES

Mr. MICHEL. After reading your statement, the impression I get is that while there are numerous areas where potential advances may be forthcoming, there is, with possibly a couple of exceptions, very little in the way of concrete advances which have been finalized as yet. Is that a fair characterization of the state of research at present?

ANSWER. The characterization may be a bit strong, for we have in application now several effective agents for caries control and have developed or improved various restorative materials. Better methods for the treatment of developmental anomalies, especially cleft palate, have also evolved. The fact that progress is being made is also brought out by the clinical studies we have begun on antimicrobial agents for plaque control, our limited clinical trials on implants, and, of considerable importance, our new program in which clinical periodontal research centers are to be developed.

SEALANTS

Mr. MICHEL. One of the areas where we have apparently reached the application stage relates to the development of a sealant to protect chewing surfaces of the teeth from decay. Would you describe this sealant for us, telling us how it is applied, who applies it, how long it lasts, etc.?

Answer. Sealants are plastic materials which are applied to the chewing surface of the posterior teeth—premolars and molars. The surfaces are cleaned and etched lightly to provide a retentive site, after which the sealant is applied in liquid form and allowed to polymerize into a coherent adhesive film. Most commonly, polymerization is effected by means of ultraviolet light, focussed on the surface, but there are also self-curing plastics available. In practice, the sealants are applied by a dentist, but our studies have suggested that auxiliaries can be trained in the technique. The time required for a treatment depends, of course, on the number of surfaces there are to be sealed, and as much as half an hour may be needed. In children, where new teeth are erupting over a several-year period, recall visits are required, and periodic inspections for retention are also advisable. Studies have shown that under favorable conditions sealants can be retained intact for several years. It has been demonstrated that in such cases protection against caries is complete, and, in fact, a significant effect is also obtained when the superficial part of the sealant has been lost but the part that has impregnated the etched surface has been retained. There is no question that this is a safe and effective procedure. Our field studies suggest, however, as we have said earlier, that from the standpoint of cost-effectiveness, application is best made in clinics or in the private dental office rather than in community public health programs. We have been doing a good bit in publicizing the measure by publications, a motion picture for teaching purposes, and also television and radio material.

DENTAL FLOSS

Mr. MICHEL. Some dentists recommend the use of dental floss and others do not. Is there any kind of developing consensus in the dental community in this regard?

Answer. Dental floss as part of the armamentarium for oral hygiene has long been accepted by the dental community, and it is generally being promoted. I would point out that for effective removal of plaque, the daily procedure required is detailed and requires both acquired skills and more time than one might expect. Our most recent clinical studies, carried out in school children under careful supervision in a 3-year study, indicated a small but statistically significant reduction in gingivitis, or gum inflammation, but the effect on dental caries was equivocal.

FLUORIDE MOUTHRINSING

Mr. MICHEL. Has fluoride mouthrinsing been proven to be effective? I note in your statement you indicate that caries could be prevented by 30 to 50 percent through a weekly mouthrinsing.

Answer. Fluoride mouthrinsing has been proven effective, and the figures you quote are accurate. The facts were obtained in clinical trials completed before our current demonstration program was initiated.

Mr. MICHEL. Is this mouthrinsing solution on the market? Can it be done in the home? Why the emphasis on doing it in the schools?

Answer. Fluoride solutions for mouthrinsing are now on the market, available on prescription by a dentist or physician. The procedure can be performed at home, and, of course, that is what is intended when it is prescribed. The purpose in our demonstration program in schools is, first of all, to acquaint the public with a simple preventive procedure. Second, programs in schools permit large numbers of children to be reached, many of whom do not visit the dentist, and they insure that the rinse is actually used regularly and properly. We feel that from both the ease of application and the cost-effectiveness standpoint this is an excellent public health measure.

ANTIMICROBIAL AGENTS

Mr. MICHEL. Another mouthrinse you are experimenting with would substantially reduce plaque bacteria and could provide nearly complete protection against tooth decay. Where do we stand with this research at present? About how long do you think it might be before it could become available to the public?

Answer. I think you are referring to our work with antimicrobial agents. Here, we are screening a large number of candidate compounds, and about a dozen have thus far been identified for short-term clinical trials against plaque. Once it is established that a type of compound is useful, it will be necessary to perform the necessary safety tests, and then field trials against dental caries. All of this requires several years.

PAIN CONTROL

Mr. MICHEL. You are conducting some research on the question of pain control. Is the research concerned with all types of pain, or simply oral pain?

Answer. Our studies extend directly over both oral and facial pain, including the temporomandibular joint.

Mr. MICHEL. Would the ultimate findings likely to be applicable to all types of pain?

Answer. Many of the findings would have application in other types of pain. This would include the basic neurobiology of pain, various agents and techniques for sedation and pain control, pain measurement techniques, and various aspects of behavior.

CLINICAL TRIALS

Mr. MICHEL. How are patients or participants normally selected to participate in your various clinical trials and for care in your centers?

Answer. In most of our large scale clinical trials, the investigator identifies a population with the characteristics required in the research protocol, for example, living in a nonfluoridated area, a known level of disease, an appropriate assortment of age groups, etc. He then makes the proper approaches to the community and its officials. Once the arrangements for a study have been made, individual participation is voluntary and only on the basis of written informed consent. For smaller studies, where specific types of patients may be needed, most of these individuals are already in the care of the investigators or are referred to the study by practitioners or university clinical departments as a result of dissemination of information about the project. Again, informed consent is required.

TRAINING PROGRAMS

Mr. MICHEL. I note your budget provides for a substantial reduction in the amount spent for training programs. Does this indicate that the supply of research personnel is better than it was and is reaching or exceeding the need?

Answer. The reduction in our training budget is due to the fact that funding of new institutional training grants was not permitted. These programs are our most productive and successful source of researchers. We have budgeted for

what we expect the demand for individual grants to be. So far as the supply of research personnel is concerned, it is better than it was some years ago, but it has definitely not reached or exceeded the need. A major shortage still exists in clinical investigators.

CLINICAL TRIALS

Mr. MICHEL. How much are you budgeting for clinical trials?

Answer. We do not have a specific budget item for clinical trials. In fiscal year 1976, our various programs supported about 30 projects for a total approximating $2 million. We expect the amount to be similar in the 1977 fiscal year and for fiscal 1978 we anticipate that expenditures will show a moderate increase.

RESEARCH GRANTS

Mr. MICHEL. What percentage of the grant applications in the dental field received during the current year will be funded, and in turn, what percentage approved by the study groups will be funded?

ANSWER. Eighteen percent of the grant applications received during the current year will be funded, and 34 percent of the applications approved by study sections will be funded.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Dental Research

Amounts Available for Obligation

	1977	1978
Appropriation.....	$55,573,000	$57,981,000

National Institute of Dental Research

Mechanism Table

Grants	1977 Appropriation No.	FTE[1]	Amount	1978 Estimate No.	FTE[1]	Amount
Regular						
Noncompeting	320		$17,700,000	270		$15,708,000
Competing	25		1,675,000	70		3,475,000
New	51		1,850,000	97		5,060,000
Supplemental	(8)		120,000	(9)		140,000
Subtotal	396		21,345,000	437		24,383,000
Special						
Dental Research Institutes	5		7,200,000	5		7,200,000
Research Career Program	25		615,000	25		626,000
Subtotal	30		7,815,000	30		7,826,000
Total Grants	426		29,160,000	467		32,209,000
Training Programs						
Individual Awards						
Noncompeting	11	11	228,000	44	44	848,000
Competing			0			0
New	33	33	620,000	8	8	131,000
Supplemental			0			0
Subtotal	44	44	848,000	52	52	979,000
Institutional Awards						
Noncompeting	29	196	2,603,000	17	144	1,995,000
Competing			0			0
New	7	47	680,000	0		0
Supplemental			0			0
Subtotal	36	243	3,283,000	17	144	1,995,000
Research & Development Contracts	70		5,408,000	70		5,408,000
Intramural Research			10,625,000			11,159,000
Direct Operations			5,144,000			5,137,000
Program Management			1,105,000			1,094,000
Total	576		55,573,000	606		57,981,000

[1] Full time equivalent.

DHEW - National Institutes of Health

CROSSWALK - 1977 COLUMN OF 1978 JUSTIFICATION

INSTITUTE: National Institute of Dental Research

In Thousands

PROGRAM ACTIVITY	Research Grants: Regular Program: Non-Comp.	Research Grants: Regular Program: Comp.	Research Grants: Special Programs: Multi-discip. Centers	Research Grants: Special Programs: Other	Training Programs: Indiv.	Training Programs: Inst.	Res & Develop. Contracts	Intramural Res.	Direct Opers.	Program Mgmt.	Total
Caries	3,931	765		111	137	286	3,313		1,824		10,367
Periodontal Diseases	4,320	911		75	183	1,056	616				7,161
Restorative Materials	1,901	360		47	85	329	400				3,122
Craniofacial Anomalies	5,008	838		114	213	628	600				7,401
Pain Control and Behavioral Studies	812	401		67	57	252	100				1,689
Soft Tissue Stomatology, and Nutrition	1,728	370		201	173	732	379				3,583
Dental Research Institutes			7,200								7,200
Intramural Research								10,625			10,625
Direct Operations									3,320		3,320
Program Management										1,105	1,105
Total	17,700	3,645	7,200	615	848	3,283	5,408	10,625	5,144	1,105	55,573

DHEW - National Institutes of Health

CROSSWALK - 1978 COLUMN OF 1978 JUSTIFICATION

INSTITUTE: National Institute of Dental Research

In Thousands

PROGRAM ACTIVITY	Research Grants: Regular Program: Non-Comp.	Research Grants: Regular Program: Comp.	Research Grants: Special Programs: Multi-discip. Centers	Research Grants: Special Programs: Other	Training Programs: Indiv.	Training Programs: Inst.	Res & Develop. Contracts	Intramural Res.	Direct Opers.	Program Mgmt.	Total
Caries.....	3,511	1,689		113	235	122	3,213		1,845		10,728
Periodontal Diseases.....	3,892	2,371		76	236	775	616				7,966
Restorative Materials.....	1,636	969		48	90		400				3,143
Craniofacial Anomalies.....	4,208	2,219		116	47	488	600				7,678
Pain Control and Behavioral Studies	892	460		68	86	122	200				1,828
Soft Tissue Stomatology, and Nutrition.....	1,569	967		205	285	488	379				3,893
Dental Research Institutes.....			7,200								7,200
Intramural Research.....								11,159			11,159
Direct Operations.....									3,292		3,292
Program Management..										1,094	1,094
Total..	15,708	8,675	7,200	626	979	1,995	5,408	11,159	5,137	1,094	57,981

Summary of Changes

1977 Estimated obligations	$55,573,000
1978 Estimated obligations	57,981,000
Net change	+2,408,000

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within grade increases		$85,000		+$75,000
2. FECF		11,000		+13,000
3. FTS increase		17,000		+1,000
4. Service and supply fund increase		744,000		+104,000
5. Payment for centrally furnished services		3,123,000		+364,000
(Standard level users charge)		(175,000)		(+25,000)
Subtotal				+557,000
B. Program:				
1. Research grants:				
a. Noncompeting grants-continuing support of 76 grants from 1977		17,700,000		+3,645,000
b. Support of 167 Competing grants		3,645,000		+8,675,000
c. Special grants-increase in stipend		615,000		+11,000
2. Training:				
a. National Research Service Award - 33 individual awards converting to non-competing status		620,000		+620,000
b. National Research Service Awards - 7 institutional awards converting to non-competing status		680,000		+680,000
c. National Research Service Award - 8 new individual awards		848,000		+131,000
3. Contracts:				
a. 7 new contracts converting to noncompeting status		5,408,000		+500,000
b. Support of 16 new and competing contracts		5,408,000		+1,200,000
4. Travel increase		236,000		+70,000
Subtotal		---		+15,532,000
Total, increases		---		+16,089,000

Decreases:				
A. Built-in:				
1. One day less pay.....		22,000		-22,000
2. Decrease in positions...	282	0	-1	-19,000
Subtotal.....		---	-1	-41,000
B. Program:				
1. Research grants:				
a. 126 Noncompeting grants completed, converted, or terminated.....		17,700,000		-5,637,000
b. 76 Competing grants converting to non-competing status.....		3,645,000		-3,645,000
2. Training:				
a. National Research Service Award - 33 individual awards converting to non-competing status....		2,843,000		-620,000
b. National Research Service Awards - 7 Institutional awards converting to non-competing status....		2,843,000		-680,000
c. Training - phase-out - 15 awards of old Training program.....		1,288,000		-1,288,000
3. Contracts - 23 contracts terminating, completed or converting to non-competing status.....		5,408,000		-1,700,000
4. Other Services.....		2,103,000		-70,000
Subtotal.....		---		-13,640,000
Total, decreases.....		---	-1	-13,681,000
Total, net change.....		---	-1	+2,408,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
113	Caries	39	$10,367,000	39	$10,728,000	--	+$361,000
115	Periodontal Diseases		7,161,000		7,966,000		+805,000
117	Restorative Materials		3,122,000		3,143,000		+21,000
119	Craniofacial Anomalies		7,401,000		7,678,000		+277,000
121	Pain Control and Behavioral Studies		1,689,000		1,828,000		+139,000
123	Soft Tissue Stomatology and Nutrition		3,583,000		3,893,000		+310,000
125	Dental Research Institutes		7,200,000		7,200,000		0
127	Intramural Research	178	10,625,000	178	11,159,000	--	+534,000
	(Standard Level User Charge)		(131,000)		(156,000)		(+25,000)
129	Direct Operations	34	3,320,000	34	3,292,000	--	-28,000
	(Standard Level User Charge)		(44,000)		(44,000)		(0)
130	Program Management	31	1,105,000	30	1,094,000	-1	-11,000
	Total obligations	282	55,573,000	281	57,981,000	-1	+2,408,000
	Standard Level User Charge		(175,000)		(200,000)		(+25,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	282	281	-1
Full-time equivalent of all other positions	41	41	0
Average number of all employees	326	325	-1
Personnel compensation:			
Permanent positions	$6,554,000	$6,579,000	+$25,000
Positions other than permanent	873,000	878,000	+5,000
Other personnel compensation	249,000	250,000	+1,000
Subtotal, personnel compensation	7,676,000	7,707,000	+31,000
Personnel benefits	1,173,000	1,176,000	+3,000
Travel and transportation of persons	236,000	306,000	+70,000
Transportation of things	45,000	45,000	0
Rent, communications & utilities	492,000	493,000	+1,000
Printing and reproduction	87,000	87,000	0
Other services	2,103,000	2,150,000	+47,000
Project contracts	5,408,000	5,408,000	0
Payment for centrally furnished services	3,123,000	3,487,000	+364,000
Supplies and materials	1,222,000	1,222,000	0
Equipment	717,000	717,000	0
Grants, subsidies & contributions	33,291,000	35,183,000	+1,892,000
Total obligations by object	55,573,000	57,981,000	+2,408,000

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act		
Section 301--Research and Investigation, in general	Indefinite	
Title IV, Part C--National Institute of Dental Research	Indefinite	$57,981,000 2/
Title IV, Part I--National Research Service Awards	1/	$ 2,974,000 2/

1/ Authorization expires September 30, 1977, extension legislation is pending.

2/ Funding estimate only.

National Institute of Dental Research

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$28,982,000	$28,982,000	$30,744,000	$28,978,000
1969	29,189,000	28,328,000	29,191,000	28,758,000
1970	28,064,000	28,064,000	30,654,000	29,658,831
1971	33,575,000	34,054,000	35,054,000	34,198,000
1972	37,890,000	40,757,000	43,757,000	42,317,000
1973	39,280,000	45,805,000	52,814,000	45,805,000 1/
1974	38,417,000	44,096,000	46,965,000	43,924,000 2/
1975	43,928,000	44,357,000 3/	50,969,000	49,833,000
1976	43,536,000	45,794,000 4/	45,794,000 4/	51,427,000 5/
1977	52,207,000	54,573,000	59,573,000	55,573,000
1978	57,981,000			

1/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by Public Law PL 93-192.

3/ Excludes R&D contracts not considered by House due to lacking authorization.

4/ Excludes fellowships and training grants--not considered due to pending legislation ($5,497,000).

5/ Includes $5,497,000 for training programs authorized under the continuing resolution.

National Institute of Dental Research

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	29,289,000	32,000,000	28,754,300
1971	34,563,000	35,257,000	36,257,000	35,440,000
1972	38,829,000	41,828,000	44,948,000	43,388,000
1973	44,415,000	46,991,000	54,000,000	46,991,000 1/
1974	38,452,000	44,131,000	47,000,000	43,959,000 2/
1975	43,959,000	44,388,000 3/	51,000,000	49,864,000
1976	43,536,000	45,794,000 4/	45,794,000 4/	51,291,000 5/
1977	52,207,000	54,573,000	59,573,000	55,573,000
1978	57,981,000			

1/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by Public Law PL 93-192.

3/ Excludes R&D contracts not considered by House due to lacking authorization.

4/ Excludes fellowships and training grants--not considered due to pending legislation ($5,497,000).

5/ Includes $5,497,000 for training programs authorized under the continuing resolution.

Justification

National Institute of Dental Research

Page Ref.	1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
Caries	39	$10,367,000	39	$10,728,000		+$361,000
Periodontal Diseases		7,161,000		7,966,000		+805,000
Restorative Materials		3,122,000		3,143,000		+21,000
Craniofacial Anomalies		7,401,000		7,678,000		+277,000
Pain Control and Behavioral Studies		1,689,000		1,828,000		+139,000
Soft Tissue Stomatology and Nutrition		3,583,000		3,893,000		+310,000
Dental Research Institutes		7,200,000		7,200,000		0
Intramural Research	178	10,625,000	178	11,159,000		+534,000
Direct Operations	34	3,320,000	34	3,292,000		-28,000
Program Management	31	1,105,000	30	1,094,000	-1	-11,000
Total obligations	282	55,573,000	281	57,981,000	-1	+2,408,000

General Statement

The National Institute of Dental Research is the predominant supporter of dental research and research training in the United States. The Institute's intramural and extramural programs are major determinants of how the oral health of Americans can be improved through the development of more effective treatment and preventive methods. At the same time, the Institute's basic studies to achieve a better understanding of the causes and control of various oral-facial diseases have had an impact on broader medical problems.

In addition to basic research, the Institute currently gives high priority to six categorical program areas: dental caries, periodontal diseases, soft tissue stomatology and nutrition, craniofacial anomalies, restorative materials, and pain control and behavioral studies.

The Institute also provides grant support to five dental research institutes/centers in university environments. These centers are contributing to the scientific underpinning necessary for the control of oral-facial diseases as well as to applied efforts.

The National Institute of Dental Research is committed to accelerating the development of more effective therapy as well as preventive measures. As knowledge in the research continuum approaches the point of application, steps are taken promptly to test first the efficacy and second the cost-effectiveness of the proposed agents and techniques.

At present, the state of knowledge is most advanced in the area of dental caries, or tooth decay. Accordingly, a variety of clinical trials as well as demonstrations of school-based preventive measures are being pursued vigorously.

Opportunities are now also beginning to emerge in the area of periodontal (gum) disease. Following the recommendations of an ad hoc evaluation committee, more intensive efforts will be made to stimulate clinical studies of the various forms of this disease. To help spur needed research, a limited number of periodontal disease clinical centers will be established.

In terms of frequency, caries and periodontal disease represent the predominant dental problems afflicting Americans. Although not as frequent, craniofacial malformations present more severe handicaps. The most common of these problems is malocclusion, with cleft lip and cleft palate ranking second. Other craniofacial anomalies include both those present at birth and disfigurements acquired through accident or radical surgery. Research supported by the Institute focuses on the etiology, pathology, treatment, and prevention of these defects.

In the area of soft tissue diseases, primary emphasis is on herpes simplex virus infections, recurrent aphthous stomatitis, and oral cancer. Broad advances in virology hold hope for developing appropriate treatment and for preventing disease caused by the herpes virus. This virus not only causes fever blisters of the lips but is also responsible for many cases of blindness. Recurrent aphthous stomatitis, commonly referred to as "canker sores," may also involve extraoral sites such as the genital mucous membranes and portions of the eye. The etiology of this condition is unknown. In oral cancer, research focuses on early detection of the malignant lesion.

Almost all Americans during their lifetime experience the need for treatment of diseased oral tissue. Research on restorative materials seeks improved and new materials and procedures to repair those tissues. One facet of such research is directed toward developing silver amalgams with more stable physical properties, non-precious metal casting alloys as gold substitutes, and more durable composite filling materials. Artificial tooth implants are also being investigated as optimum replacements for missing natural teeth.

Research on pain control involves both the pain associated with chronic, debilitating conditions such as facial neuralgias and the anxiety and fear of pain involved with dental treatment procedures. More emphasis is also being placed on initiating studies to determine how to motivate practitioners and the public to utilize adequately all available oral health measures. As biomedical research develops effective means of prevention and treatment of oral disease, the behavioral factors involved in their acceptance and utilization assume critical significance.

Caries

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Caries	39	$10,367,000	39	$10,728,000	--	+$361,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting		$3,931,000		$3,511,000		-$420,000
Competing		765,000		1,689,000		+924,000
Special		111,000		113,000		+2,000
Training Programs						
Individual		137,000		235,000		+98,000
Institutional		286,000		122,000		-164,000
Research and Development						
Contracts		3,313,000		3,213,000		-100,000
Direct Operations		1,824,000		1,845,000		+21,000
Total		10,367,000		10,728,000		+361,000

Introduction

Dental caries is the most common chronic disease in children and causes progressive loss of teeth at all ages. Despite partial protection of some populations by controlled fluoridation of water supplies, the American public spends over $2 billion each year to have teeth restored or extracted. To repair all lesions that occur, however, is estimated to cost $8 billion.

The National Caries Program was created by Presidential Initiative to develop the means to prevent this disease as a public health problem. The Program is a targeted research and development effort: (1) to identify new approaches for caries prevention through investigations of disease etiology, (2) to transform these approaches into practical technics through applied research, (3) to test and finally demonstrate those that are suitably cost-effective, and (4) to encourage their widespread utilization.

To carry out these objectives, the National Caries Program supports work on oral microbiology, epidemiology, biometry, antimicrobial and antiplaque agents, nutrition, secretory immune mechanisms, vaccine development, clinical trials, early caries detection, tooth remineralization, and on behavioral and communication factors in acceptance and utilization of preventive procedures.

Budget Policy, 1978

Investigations of cariogenic microorganisms will continue in an attempt to devise methods to interfere with their adhesion to tooth surfaces.

Since evidence is increasing that microorganisms in addition to the previously implicated Streptococcus mutans are important in human dental caries, several laboratory and clinical studies have been initiated to help identify them and explain their role.

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Occlusal, or chewing, surfaces though representing only 12% of the total surfaces at risk, account for 50% of the caries in children. Recent information from five clinical trials of the use of adhesive coatings to seal the pits and fissures suggest that costs will restrict use of this valuable technic to private practice settings. To obtain a more cost-effective method, tests will be made of self-applied sealants as they are developed.

Experiments have shown that most fermentable carbohydrates are cariogenic, particularly if small amounts of sucrose are present. Non-cariogenic sweeteners of various types are being developed for home use or in commercial food preparation.

Identification of potential anticaries agents is continuing through stages of pre-clinical tests and short-term clinical trials. The first stage utilizes a battery of in vitro and animal tests to identify compounds with cariostatic potential. The second consists of a three-week clinical trial to provide data on plaque control and to bring possible side effects to light.

A common experience with agents used intermittently in mouthrinses is that they do not show the antiplaque or anticaries effectiveness that would be expected on the basis of animal tests. Considerable effort is going into the development of improved delivery systems. Ideally a system would combine suitability for self-application, adhesion to oral disease sites, and slow release of prescribed levels of the agent. One system currently being assessed applies cellulose microcapsules to caries susceptible areas where they slowly release low levels of fluoride. Another system being tested in animals utilizes small prosthetic devices designed for easy attachment to the tooth and for slower release of anticaries agents.

A major program advance has been the achievement of caries immunization in several animal models. Experiments with monkeys suggest that long-term and largely complete immunization is possible. Other experiments suggest the possibility of immunizing with antigens in tablet form. In 1978 and several years thereafter, research in this area will focus on isolating and purifying microbial antigens, on animal testing of alternative immunization routes, vaccines, and regimens, and on establishing mechanisms of action.

Cost-effectiveness comparison of school water fluoridation and school-based daily fluoride tablet programs probably will be completed by 1978; however, clinical trials will be continued to check possible advantages of another fluoride compound, sodium fluorophosphate, and several alternative fluoride concentrations and dosing routines. Also a new tablet design that releases a small fraction of its fluoride in the mouth and the remainder over many hours in the gastro-intestinal tract will probably be ready for clinical trials.

School-based fluoride mouthrinsing has been established as an inexpensive, effective method for children's caries prevention in communities where municipal fluoridation of water supplies is not feasible. In 1975, a three and a half year, nationwide program of community demonstrations of this technic was established with approximately 85,000 children at 16 sites in the United States and one in Guam. In 1977, the program was expanded to test the feasibility of mouthrinsing in high schools. As data on costs and caries prevention achieved under local conditions become available, activities will be intensified to disseminate information about mouthrinsing to other communities. Brochures and television programs will be utilized to describe the advantages of the technic and detailed instruction manuals and workshops will be made available to community leaders to assist them in starting rinse programs. It is anticipated that by 1978 two other regimens will be ready for demonstration; these are a fluoride rinse program for areas with fluoridated water and a fluoride tablet program for young children in nonfluoridated areas.

Periodontal Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Periodontal Diseases....		$7,161,000		$7,966,000		+$805,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting.....		$4,320,000		$3,892,000		-$428,000
Competing.....		911,000		2,371,000		+1,460,000
Special.....		75,000		76,000		+1,000
Training Programs						
Individual.....		183,000		236,000		+53,000
Institutional.....		1,056,000		775,000		-281,000
Research and Development						
Contracts.....		616,000		616,000		0
Total.....		7,161,000		7,966,000		+805,000

Introduction

The mission of the Periodontal Diseases Program is to develop knowledge leading to the prevention and eradication of periodontal diseases. A major health problem throughout the world, periodontal diseases have already caused millions of adult Americans to lose their teeth and many more will become edentulous unless effective preventive measures can be developed. In the basic disease process bacteria colonize at the necks of the teeth, inflammation develops in the adjacent gingiva (gums), the bone and tissue fibers supporting the teeth are destroyed, and the teeth themselves become loosened and eventually lost. To achieve its mission, the Program supports research in a variety of disciplines on the cause, nature, diagnosis, treatment and prevention of these diseases.

Budget Policy, 1978

Clinical studies will be initiated to confirm and amplify recent findings implicating specific bacteria in the causation of the different periodontal diseases. Detailed microbiologic and immunologic studies will be carried out to identify suspect organisms and to determine how they may cause disease. The direct action of bacterial enzymes and toxins on soft tissues and bone will be examined; the specific host immune response to each pathogenic bacterium will be characterized; and the predominant host immune response in each clinical disease entity will be established.

Germ-free animals will be used to aid in establishing the pathogenicity of specific organisms and to determine the nature and extent to the host response. Preliminary studies have shown that about a dozen different bacteria can cause periodontal disease when inoculated individually in germ-free rats, and limited immunologic studies indicate that each type of organism evokes a different immune response. For example, one of the most destructive organisms appears to suppress the humoral and cellular immune responses, whereas other organisms such as the Actinomyces appear to enhance the immune response.

The Institute will continue to support studies on immune mechanisms which may result in tissue destruction. Thus far these studies have revealed specific mechanisms for the breakdown of cells, fibers and bone. Recent findings have made it clear that the immune system brings about elevations in both prostaglandin and Osteoclast Activating Factor, two potent stimulators of bone resorption.

Early results also suggest that patients with severe types of periodontal diseases have defects in their neutrophils, white blood cells which normally migrate to the site where protection is needed and engulf bacteria or other substances. Therefore, attention will also be given to the underlying causes of this lack of response.

Further study of the Osteoclast Activating Factor will determine its exact structure and activation sequence so that therapeutic methods of blocking its bone resorption activity can be developed. Conversely, efforts will be made to characterize biochemically bone inducer substances, in the hope that such substances may eventually be applied therapeutically. Laboratory and clinical testing of antibacterial preventive agents, particularly for the control of the severe periodontal diseases will also be expanded.

To accelerate work in these important areas, the Institute will initiate one or two clinical periodontal research centers during Fiscal Year 1978. Meanwhile the Institute will continue to support its strong ongoing programs of basic research on the biologic processes underlying oral health and disease.

Restorative Materials

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Restorative Materials.....		$3,122,000		$3,143,000		+$21,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting.....		$1,901,000		$1,636,000		-$265,000
Competing.....		360,000		969,000		+609,000
Special.....		47,000		48,000		+1,000
Training Programs						
Individual.....		85,000		90,000		+5,000
Institutional.....		329,000		0		-329,000
Research and Development						
Contracts.....		400,000		400,000		0
Total.....		3,122,000		3,143,000		+21,000

Introduction

The goal of the Restorative Materials Program Branch is to provide the materials and techniques for restoring oral and facial tissues lost or damaged by disease, congenital anomalies, and accidents. Recent statistics indicate that almost 23 million adults in this country have lost all their teeth and about half of the remaining 90 million adults have 18 or more decayed, missing or filled teeth. In addition, surgical procedures and accidents account for vast numbers of oral facial defects and injuries which require treatment based on suitable materials. To develop and improve such materials the Program supports research in materials science, metallurgy, polymer chemistry, physics, pathology, and related sciences.

Budget Policy, 1978

Since vitreous carbon and bioglass ceramic dental implants have shown promise in animal experiments, controlled clinical trials will be undertaken to determine the safety and efficacy of these devices in humans. Bioglass is of special interest because it has an active surface which is not only harmless to tissues but actually stimulates the growth of new bone and collagen. To optimize the design of future dental implants, scientists will employ finite element analysis, a mathematical technique used to analyze stresses in structural parts of the body, such as the femur and other bones. In finite element analysis, functional stresses and strains can be predicted and the design altered accordingly. Theoretically, the method will make it possible to avoid bone resorption in the jawbone from stress and strain on implants.

Silver amalgam is the most widely used filling material in dentistry, but many of these fillings fail because they fracture at the margins. When tested in the laboratory these fractured amalgams show a tendency to spread or creep when subjected to constant stress, and thus are said to have a high creep value. Since amalgams with high or low creep values also show variations in composition and structure it is difficult to tell whether they fracture because of creep or because of their composition and structure. Therefore, scientists will carry out a coordinated laboratory and clinical project in which each variable is measured separately and correlated with the marginal fractures.

Institute-supported laboratory and clinical studies have developed highly successful composite fillings for front teeth, but these fillings lack the mechanical strength needed for the chewing surfaces of the molar teeth. To gain the needed strength investigators will study new methods of combining the acrylic resin matrix and the hard glass particles which make up composites.

Several recent clinical studies have shown that the highly susceptible chewing surfaces of back teeth can be protected against decay by coating them with a plastic sealant. This method is suitable for individual application, but it is too costly and time-consuming for widespread public health application. Therefore, scientists will seek to devise new, low cost, easily applied, retentive sealant materials and techniques which can be made available to all children.

Craniofacial Anomalies

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Craniofacial Anomalies....		$7,401,000		$7,678,000		+$277,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting.....		$5,008,000		$4,208,000		-$800,000
Competing.....		838,000		2,219,000		+1,381,000
Special.....		114,000		116,000		+2,000
Training Programs						
Individual.....		213,000		47,000		-166,000
Institutional.....		628,000		488,000		-140,000
Research and Development						
Contracts.....		600,000		600,000		0
Total.....		7,401,000		7,678,000		+277,000

Introduction

Each year 6,000 newborns are afflicted with clefts of the lip and/or palate and 1,200 have other severe deformities. Malocclusion affects three of every four children in the United States and half of these have it so severely that treatment is indicated. In addition, thousands of craniofacial deformities are acquired each year through surgery and accidents. To reduce the frequency of these conditions and to alleviate the suffering and discomfort they cause, the Program supports basic and clinical research on the disorders themselves and on the normal growth and development processes underlying their clinical manifestations.

Budget Policy, 1978

The Institute will expand studies on the relationship between drug-induced craniofacial anomalies and specific protein receptor sites. In recent studies scientists have shown that the cleft-producing reactions brought about by corticosteroids in susceptible mice occur in the cell nucleus, where cortisone forms chemical complexes which interfere with protein synthesis. Attempts will now be made to localize cortisone receptors in the cells of human infants with and without cleft palate, and to search for receptor sites of other cleft-producing substances such as tranquilizers.

Because of the widespread use of polychlorinated biphenyls (PCB) and tetrachlordibenzo-p-dioxin (TCDD) in industry, it is important to determine the effects of these environmental pollutants on oral-facial structures in higher animals. Such studies will be carried out in Rhesus monkeys. Preliminary results indicate that low levels of these substances may cause malformed or missing teeth.

The Institute will continue studies on the connective tissue cell which scientists believe is involved in the tissue movements necessary for the development and maintenance of tissue architecture during growth and adulthood. The newly discovered cell, called a myofibroblast, was identified in situations where teeth and bones were moving, such as in tooth eruption and orthodontic movement. Through further study of these cells, scientists may learn more about the regulation of growth and development processes involving oral structures.

The Institute will also support studies on the newly discovered factor which prevents the growth of new blood vessels. Found in the fluid of cultured cartilage tissues, the new substance is a low molecular weight sugar-containing protein, which appears to exert its effect on the surfaces of the cells which form the new vessels. Full exploitation of these findings may lead to a practical way to favorably influence wound healing.

The long-term effects of comprehensive treatment in patients with specific disfiguring craniofacial anomalies will be studied. Corrective procedures will be performed in patients of varying ages to establish optimal timing for surgery. Patients will also receive orthodontic and prosthetic treatment, speech therapy, and psychotherapy as needed. At periodic intervals after treatment, the investigators will assess the physical and mental well-being of each patient. They will also study the role of genetic factors in the etiology of these syndromes.

To better assess the results of maxillofacial surgery, dentofacial prosthesis, and orthodontics, the Institute will support studies on the automatic optical scanning of physioprints for recording soft tissue facial patterns. The physioprint is obtained by projecting a grid onto the face and recording the distortion produced by the round contours of different parts of the face. The location and extent of the distortions provide a facial pattern which can be compared with other physioprints. Scientists hope to develop the method into a practical system which may reduce the need for X-rays.

Psychosocial studies will be carried out to confirm and amplify recent findings that children with clefts of the lip or palate exhibit more tension, more adjustment difficulties and less creativity than unaffected children.

Pain Control and Behavioral Studies

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Pain Control and Behavioral Studies.....		$1,689,000		$1,828,000		+$139,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting.....		$812,000		$892,000		+$80,000
Competing.....		401,000		460,000		+59,000
Special.....		67,000		68,000		+1,000
Training Programs						
Individual.....		57,000		86,000		+29,000
Institutional.....		252,000		122,000		-130,000
Research and Development						
Contracts.....		100,000		200,000		+100,000
Total.....		1,689,000		1,828,000		+139,000

Introduction

The goals of the Program are to develop the means to prevent or alleviate oral facial pain and to improve oral health by behavioral modification. Pain is a major problem which interferes with every aspect of human existence and can be disabling. Its psychological costs are incalculable and its economic costs are estimated to run from forty to fifty billion dollars annually in the United States. In dentistry, pain is a central problem which pervades the whole spectrum of prevention and treatment. It is estimated that at least ten percent of the American population do not even seek dental treatment because they fear pain and discomfort, and many others demand only minimal care because of fear. Thus it is imperative that research on specific problems of oral facial pain be expanded. Since advances in behavioral science could be of benefit in overcoming the dental fear and anxiety syndrome and other problems in dentistry, such as poor oral hygiene and poor dietary habits, it is also important to develop research in this field.

Budget Policy, 1978

Recent pain research has provided investigators with a new methodology called signal detection theory (SDT) analysis for studying human pain. Since SDT analysis separates and measures the objective and the subjective components of human pain, it should be useful in interpreting data from different types of investigations on human pain. For example, SDT analysis of preliminary data indicate that acupuncture reduces both the physical and emotional response to painful stimuli. The Institute will support studies to validate the use of this promising approach in the hope that this technique or a similar one will aid investigators in establishing the true nature of human pain and in developing new mechanisms for its relief.

Specific studies to be carried out include projects on the relief of pain by drugs, by electroanalgesia and by biofeedback techniques. The drug studies will combine intravenous sedation with inhalation anesthesia to develop safer and more efficacious pain control regimens for outpatients. With sedation, the investigators expect to use less inhalation anesthetic and thereby reduce hazards associated with the usual inhalation dosages. In these studies the depth of anesthesia will be correlated with untoward postoperative effects.

The Institute will also support electroanalgesia studies to develop a safe and effective technique for anesthetizing teeth without having to resort to an injection. In these investigations, scientists will subject animal teeth to pain-preventing electric currents, and subsequently will make comprehensive chemical and microscopic studies of the tooth pulp, or nerve-containing tissue.

Biofeedback studies will concentrate on the treatment of patients with intractable pain in the hinge joint of the jaws. Such patients show severe tension and pain in the main jaw muscles. By means of an electronic biofeedback system, patients will be taught to become aware of their muscle tension, a body function they may not normally sense. Subsequently, they will be trained to relax the muscles, first in a laboratory setting and then in a home environment.

Other behavioral science studies will be initiated to determine the role of emotional stress in certain forms of acute, severe periodontal disease, in recurrent Herpes simplex virus infections (fever blisters), and in bruxism (unconscious tooth grinding). In other studies, investigators will seek to eliminate the fear and anxiety associated with dental treatment, and will explore techniques for improving patient acceptance of new preventive measures. Since there is little ongoing behavioral research, staff will continue their efforts to stimulate interest and enthusiasm about the behavioral approach to oral health among both dental and nondental behavioral researchers.

Soft Tissue Stomatology and Nutrition

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Soft Tissue Stomatology and Nutrition.....		$3,583,000		$3,893,000		+$310,000
Budget Mechanism:						
Research Grants						
Regular						
Noncompeting.....		$1,728,000		$1,569,000		-$159,000
Competing.....		370,000		967,000		+597,000
Special.....		201,000		205,000		+4,000
Training Programs						
Individual.....		173,000		285,000		+112,000
Institutional.....		732,000		488,000		-244,000
Research and Development Contracts.....		379,000		379,000		0
Total.....		3,583,000		3,893,000		+310,000

Introduction

Oral soft tissue diseases cause pain and discomfort to millions of Americans and serious problems to thousands. Oral cancer alone causes 8,000 deaths in the United States each year and the virus which causes fever blisters of the lips (herpes simplex virus) is also responsible for many cases of blindness. Since normal salivary secretion, adequate systemic nutrition and proper mineral metabolism are all essential for the growth and maintenance of healthy oral tissue, it is important to understand these areas of oral biology. Therefore, the Program seeks to develop basic information on the cause, treatment and prevention of canker sores, fever blisters, oral cancer, and other oral disorders; and in addition, to develop new knowledge on nutrition, salivary secretions and mineral metabolism.

Budget Policy, 1978

In a recent prospective oral cancer study, investigators carefully noted the appearance, location and size of the lesions, and developed new diagnostic criteria to improve the detection and cure of oral cancer. The study identified the high risk regions of the mouth and the clinical and microscopic characteristics of early lesions. Seventy percent of early asymptomatic lesions were found to be malignant. These studies will now progress to a new phase which will include refinement of diagnostic criteria and confirmation of the findings in other population groups. Since a high percentage of the early lesions were found to be locally invasive, scientists will initiate long-term studies to establish whether surgical removal of these lesions actually increases survival rate.

To control herpes simplex virus-caused fever blisters, investigators have sought new chemotherapeutic agents, and have evaluated the feasibility of vaccination. Until recently, neither approach seemed promising because the virus localizes in nervous tissues where it is protected from drugs and immune cells and because virus nucleic acids in the vaccines may cause cancer. However, recent preliminary studies have shown that immunization before initial infection will protect animals completely, and early laboratory studies indicate that a vaccine without the virus nucleic acid can be effective. In view of these findings, investigators will now systematically test a series of specially prepared nucleic acid-free vaccines. They will also modify the vaccines chemically to further enhance the body's defense mechanisms against this specific virus.

In recent studies blood copper concentrations showed a positive correlation with the severity of periodontal disease, and both zinc and copper levels were found to be high in inflamed gums. To study the exact relationship of these metals to disease, scientists will now determine the effects of graded levels of dietary copper and zinc on experimental periodontal disease, and on tissue metabolic processes involving copper and zinc. The relationship of these metals to the immune response will also be examined.

Since malnutrition can cause decreased resistance to disease, animal studies will assess the influence of poor nutrition on the specific oral immune response to cariogenic (decay-causing) bacteria. In these studies salivary antibodies will be measured, bacteria will be counted and caries will be scored in animals on both normal and on protein-deficient diets. Malnourished children will also be studied.

A number of studies have reported that sodium fluoride affects the metabolism of glucose and cyclic-AMP in bacterial and mammalian cells. Since cyclic-AMP is involved in many biological processes, including tooth eruption, salivary secretion, bone remodeling and gingivitis, these studies will be pursued further.

Dental Research Institutes

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Dental Research Institutes		$7,200,000		$7,200,000		0
Budget Mechanism: Research Grants Special		$7,200,000		$7,200,000		0
Total		7,200,000		7,200,000		0

Introduction

The Dental Research Institutes and Centers Program supports five university-based institutes and centers which conduct broad programs of research covering the entire range of oral health investigations. They were initiated in 1967 to provide a stimulus to dental research by creating favorable environments which would attract high quality scientists from different disciplines to work as teams on oral problems. Now in their tenth year, the Institutes and Centers have established strong basic science programs which include highly effective collaboration with leading scientists throughout the world. Currently, the institutes are beginning to develop coordinated clinical research capabilities.

Budget Policy, 1978

Support will be provided for approximately 200 ongoing laboratory projects spanning a wide range of oral health research. In addition, the centers will give special attention to projects with clinical relevance. Several of these clinically oriented projects are outlined in the following paragraphs.

Investigators at one institute will complete a clinical trial on the effectiveness of a topically applied chemical agent called Ara-A in preventing or alleviating herpes simplex virus infections of the lips (fever blisters). The study, involving approximately 175 subjects, will be conducted in a double-blind, randomized fashion. The investigators expect to observe and follow several hundred infectious episodes. In preparing for the current clinical trial, the investigators carried out a study which showed that twenty percent of the subjects in a professional school population contracted the disease and had an average of 1.3 recurrent infections. The study also established that the time lapse from the earliest tingling sensations of the lips to the actual appearance of blisters averaged 12 hours.

At another center studies will be carried out on the mechanisms of posttraumatic craniofacial pain. The purpose of the studies is to clarify the pathophysiology of pain and to develop more effective means of managing it. Both acute and chronic posttraumatic pain will be studied in patients who have sustained known types of accidental or surgical trauma.

Biomaterials investigators at one center will seek to develop a self-activating, spring-driven device to expand maxillary (upper jaw) segments in babies with a bilateral cleft palate.

Another study will concentrate on the nervous system degeneration which occurs in diabetes mellitus. Using genetically diabetic mice, scientists will attempt to correlate craniofacial neuropathy with salivary function and oral sensory defects.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Research.....	178	$10,625,000	178	$11,159,000		+$534,000

Introduction

The Institute's Intramural laboratory and clinical research studies are directed toward a better understanding of the causes of dental and oral facial diseases and disorders and the development of treatment, control and preventive measures.

The predominant diseases and abnormalities of the oral facial region are dental caries, periodontal disease, benign and malignant soft tissue lesions as well as congenital and acquired anomalies. Varied approaches and modalities of study are required. The investigative tools presently employed are those of biochemistry, biology, biophysics, immunology, microbiology, neurophysiology, virology, behavioral science, and clinical dentistry.

Budget Policy, 1978

A major effort of the Institute's laboratory programs is directed toward understanding the biosynthesis, structure and chemistry of the mineralized tissues which are involved in both caries and periodontal disease.

Recent studies have advanced our understanding of mineral formation in bones and teeth, providing a basis for studying the effect of fluoride and other trace elements on this process. Another projected area of inquiry is to assess the effects of fluoride on the physiology and morphology of bone. Efforts are also under way to investigate the organic framework of the mineralized tissues and its role in initiating and controlling the mineralization process.

Two of the organic elements, collagen and proteoglycans, are also major components of most soft connective tissues. The Intramural program has contributed in a major way to knowledge about the biosynthesis and chemistry of collagen while the proteoglycan studies represent a recent addition. The kinds, composition, and relative proportions of these substances, and interactions among them are critical to tissue function and health. Special emphasis will be placed on following the collagen-proteoglycan interactions in soft tissue and collagen-mineral interactions in tooth and bone.

A major commitment to oral microbiology and immunology continues to be an essential component of the Intramural program since both caries and periodontal disease result from complex interactions between bacteria, host factors, and the oral environment.

A new and promising approach is the study of bacterial plasmids. These extrachromosomal elements, known to code for characteristics of significant clinical interest such as toxin production and antibiotic resistance, have been found in various strains of oral bacteria. A model system has been developed which makes it possible to study their role in bacterial pathogenicity, as well as the significance of in vivo plasmid transfer between bacteria within the oral cavity.

Another advance has been the development of a fluorescent antibody technique for identification and quantification of specific bacteria (Actinomyces) implicated in periodontal disease. This technique will be used to examine the role of these organisms in human periodontal disease as part of a combined clinical and laboratory program.

The activities in immunology are broadly based, with emphasis on understanding cellular and humoral immunological parameters of periodontal disease. Of particular interest is the finding that cellular responses to microbial products are under genetic control. Further laboratory studies will help define this genetic basis, while clinical studies will explore the existence of a possible immuno-genetic factor in severe periodontal disease.

Research into soft tissue diseases will continue with emphasis on the etiology and pathogenesis of oral aphthous ulcers, herpes simplex virus infections, and diseases of the salivary gland and pancreas. Studies will be initiated into the etiology of human oral and laryngeal papillomas, benign tumors which nevertheless may become life threatening because of the danger of suffocation.

To aid in the study and diagnosis of salivary gland diseases, a radioimmunoassay has been developed for measuring salivary amylase in serum. A similar assay technique is being developed for pancreatic amylase. These assays will provide new means for studying various disorders of both glands.

Viruses induce the production of interferon, which interferes with virus multiplication. Recent in vitro studies demonstrated that interferon enhances histamine release from leucocytes, suggesting an explanation for more frequent attacks of bronchial asthma during certain viral infections. The possible effects of interferon on other biological processes will be explored.

Studies of normal and abnormal development of oral-facial structures are primarily directed toward understanding the formative process at the biochemical level. Birth defects are being studied and attempts are being made to determine the relative importance of environmental insults and genetic factors.

Another line of investigation explores abnormal mouth and throat anatomy of infants and young children as well as their coordinated performances of feeding, breathing and crying. These observations increase our understanding of handicapping abnormalities in function.

Research effort on oral and facial pain continues with the application of fundamental knowledge about pain mechanisms to clinical studies of acute and chronic pain. A word scale has been developed which quantifies both the amount of pain experienced and the amount of unpleasantness associated with it. This scale will be used in describing various oral-facial neuralgias and to rate the efficacy of new pain control techniques. Other clinical studies will evaluate new sedative drugs employed to control anxiety and apprehension associated with ambulatory dental procedures. Laboratory research will focus on the role of pain-suppressing pathways in controlling behavior associated with anxiety or painful stimuli. Insights into such pain-suppressing systems may lead to the development of new pain-control methods.

Procedures which facilitate early X-ray detection of tooth decay and periodontal disease are under study. Experimental X-ray systems are being modeled to determine the quality and quantity of information required for a specific diagnostic situation. Of particular interest is the development of methods which improve diagnostic performance while at the same time minimizing X-ray exposure.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations.....	34	$3,320,000	34	$3,292,000		-28,000

Introduction

This activity provides for the overall administration, direction, and coordination of the Institute's grant and contract programs.

Also funded in this activity are the computer section, which analyzes and evaluates the programs of the Institute and the office of scientific communications which collects and publishes program information.

Budget Policy, 1978

National Institute of Dental Research review and approval activities include the Associate Director for Extramural Programs, a Deputy Associate Director, and assistant for special programs, 14 scientific program professionals, and 8 technical and clerical support staff. Personnel of this activity are repsonsible for the planning and developing of scientific evaluation and fiscal management of the Institute's extramural programs. These responsibilities include development of various mechanisms for support grants in 6 major program areas.

Program chiefs and their scientist administrators are responsible for all aspects of program planning, administration and individual project and program review which require scientific competency. Technical and clerical staff are required to supplement the efforts of scientific staff in achieving the Institute's goals.

The National Institute of Dental Research's contract program includes an Associate Director, 3 contract specialists, a staff assistant, and 3 clerical support staff. Personnel of this activity are responsible for the development, implementation, and evaluation of research and development contracts in the program areas of caries, periodontal diseases, restorative materials, craniofacial anomalies, soft tissue stomatology and nutrition, and pain control and behavioral studies.

This activity will continue to administer, manage, and review the grants and contract program, and provide analyses and evaluation.

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Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.....	31	$1,105,000	30	$1,094,000	-1	-$11,000

Introduction

This activity supports the overall administration, coordination, and direction of the varied programs and activities of the National Institute of Dental Research. The Office of the Director provides for the planning, direction, management, and coordination of all Institute activities; the review of current and proposed programs, dissemination of new knowledge to the dental profession and the public to encourage the application and use of preventive and therapeutic measures, as well as the provision of technical and administrative data on dental research and statistical information on dental and oral-facial disease, and the supervision of administrative support services.

Program Plans for 1978

The staff supported by this activity will continue to provide program guidance and administrative management to the Institute's staff, in the furtherance of the Institute's programs.

One administrative position has been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Caries. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
39	$10,367,000	Indefinite	39	$10,728,000

Purpose: In 1971, additional funds were authorized to create the National Caries Program (NCP), a highly organized research and development effort intended to develop methods to eliminate caries as a major health problem.

Explanation: The programs of this activity are carried out by support of research grants, research contracts, graduate training grants, fellowships, research career awards, and direct operations.

Accomplishments in 1977: Over 200 anticaries agents were screened, 16 advanced to animal testing and two to initial human trials. To improve effectiveness of such compounds, as well as topical fluorides, slow-release technology for intraoral use is under study. One method was perfected to where it released prescribed, constant amounts of fluoride for 6 months. Animal tests confirm the feasibility of this approach.

Research on a vaccine against caries showed that when infant monkeys had received a dose of decay-causing streptococci by stomach tube, a single subsequent vaccination induced very high and persistent blood antibody titers against these bacteria. Apparently this resulted from "priming" the immunologic system before it fully matured, and suggests a promising avenue for research toward an eventual human vaccine.

To publicize their ease and cost-effectiveness, we continued a Community Demonstration of school-based fluoride mouthrinsing at 16 sites across the country and released a film for use by television stations. Requests for information on how to start a caries-preventive program were answered with a detailed instruction manual.

Approximately 88 research grants, 5 career awards, 8 individual awards, 3 institutional awards and 43 research and development contracts will be supported in 1977.

Objectives for 1978: Research and development will continue on all approaches to caries prevention including antimicrobials, plaque dissolving agents, immunization, non-cariogenic sweeteners, and topical and systemic fluoride. Emphasis will increase in the areas of delivery system development, clinical trials, cost-benefit evaluation and dissemination of information on and demonstration of tested technics for caries prevention.

Approximately 95 research grants, 5 career awards, 11 individual awards, 1 institutional award, and 43 research and development contracts will be supported in 1978.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Periodontal Diseases. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$7,161,000	Indefinite	---	$7,966,000

Purpose: To develop new knowledge on the cause, treatment and prevention of periodontal diseases, the major cause of tooth loss in adults, so that the natural dentition can be maintained throughout life.

Explanation: Research programs are carried out by support of grants, contracts, individual awards, institutional awards, and career awards.

Accomplishments in 1977: Bacteria of the genus Actinomyces were implicated in gingivitis because they evoke a specific cellular immune response in patients with gingivitis, whereas other bacteria do not. Patients with the severe diseases periodontosis and rapid periodontitis were shown to have defective white cells unable to migrate or engulf foreign materials normally. Moreover, animals infected with bacteria from these patients had a striking depression of both cellular and humoral immune responses. Prostaglandins were found to prevent normal fibroblast cells from forming collagen. The fibroblasts from diseased periodontal tissues failed to produce normal collagen, but instead, synthesized an unknown, weaker type. In ongoing studies on treatment, tetracycline therapy and mechanical treatment have thus far prevented periodontal bone loss for four years.

Support in 1977 will include approximately 97 regular research grants, 8 contracts, 10 individual awards, 12 institutional awards, and 4 career awards.

Objectives for 1978: Clinical studies will be initiated to confirm findings implicating specific bacteria in the causation of the different periodontal diseases. Studies will be supported to determine whether the suspect organisms can cause disease by the direct action of their enzymes and toxins, or through specific host immune mechanisms. The predominant host immune response in each clinical disease entity will also be established. In addition, the osteoclastic substance Osteoclast Activating Factor and the osteogenic substance Bone Morphogenetic Protein will be studied to determine their biochemical structure and activation sequence. The testing of antibacterial agents will also be expanded. To accelerate these investigations, the Institute will initiate one or two clinical periodontal research centers.

Support in 1978 will include approximately 106 regular research grants, 8 contracts, 4 career awards, 14 individual awards, 7 institutional awards, and 2 multidisciplinary centers.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Restorative Materials. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978	Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$3,122,000	Indefinite	---	$3,143,000

Purpose: To develop and test new biomaterials and devices so that oral and facial tissues damaged by dental disease, congenital anomalies, and accidents can be restored to desirable function and appearance.

Explanation: These activities are accomplished by utilizing research grants, contracts, institutional fellowships, individual fellowships and research career awards.

Accomplishments in 1977: In animal experiments, metal alloys, vitreous carbon and bioglass were the most promising materials for dental implants. Uniquely, bioglass implants stimulated the growth of bone and connective tissue adjacent to the implant. The composite filling developed through Institute research has become the most widely used filling for front teeth. It is estimated that the new composites save the public $284 million per year.

Approximately 42 research grants, 2 career awards, 5 individual awards, 3 institutional awards, and 5 research and development contracts will be supported in 1977.

Objectives for 1978: During 1978 staff will develop definitive plans for long-term clinical tests of dental implants already in clinical use, and will also initiate new studies on the efficacy of vitreous carbon and bioglass implants in humans. Finite element analysis will be employed to optimize implant design, so that functional stress and strain can be minimized and bone resorption can be avoided. Coordinated laboratory and clinical studies of amalgam fillings will be carried out to determine the exact cause of clinical failure. Scientists will develop new formulations to increase the hardness and durability of composite fillings so that they can be employed on the chewing surfaces of molar teeth. To develop a cost/effective sealant to protect the chewing surfaces of the teeth against decay, investigators will seek to devise durable, retentive materials which can be easily applied to large numbers of children.

Approximately 48 research grants, 2 career awards, 5 individual awards, and 5 research and development contracts will be supported in 1978.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Craniofacial Anomalies. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$7,401,000	Indefinite	--	$7,678,000

Purpose: To conduct research on the treatment and prevention of such craniofacial disorders as cleft lip/palate, malocclusion of the teeth and jaws, and disfigurements acquired through accidents or surgical procedures, so that the impact of these conditions will be lessened.

Explanation: Research programs are accomplished by utilizing research grants, contracts, institutional fellowships, individual fellowships and research career awards.

Accomplishments in 1977: Scientists have shown that the specific cleft-producing reactions brought about by corticosteroids in susceptible mice occur in the cell nucleus. Cortisone reacts with nuclear receptors to form chemical complexes which interfere with normal protein synthesis. Recent studies indicate that palatal shelf rotation, a critical event for normal palate development, results from neuromuscular activity which can be depressed or enhanced by specific drugs. In psychosocial studies, cleft palate children showed more inhibition, more tension, and more adjustment difficulties than unaffected children. They also made lower achievement scores and were less creative. A new factor which prevents the growth of new blood vessels was discovered in the fluid of cultured cartilage cells. The new substance is a sugar-containing protein, which is believed to act on the surfaces of the cells which form blood vessels. New evidence indicates that a special contractile cell, the myofibroblast, brings about the cell and tissue movement necessary for normal growth.

Support in 1977 will include approximately 109 research grants, 4 career awards, 12 individual awards, 7 institutional awards, and 8 research and development contracts.

Objectives for 1978: Scientists will examine animal and human cells to localize specific chemical sites where drugs, such as cortisone, react with the body in causing cleft palate. Rhesus monkeys will be studied to determine the effects of the industrial poisons, polychlorinated biphenyls (PCB) and tetrachlordibenzo-p-dioxin (TCDD) on oral facial structures. In long term studies of patients afflicted by disfiguring craniofacial anomalies, the optimal age for surgical correction will be established, and the efficacy of comprehensive treatment will be assessed. Genetic factors will also be studied.

Approximately 116 research grants, 4 career awards, 3 individual awards, 4 institutional awards, and 8 research and development contracts will be supported in 1978.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Pain Control and Behavioral Studies. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$1,689,000	Indefinite	---	$1,828,000

Purpose: To develop new methods and approaches for preventing or alleviating dental and oral facial pain, for modifying behavior detrimental to oral health, and for achieving public acceptance of new preventive measures.

Explanation: These activities are accomplished by utilizing research grants, contracts, institutional fellowships, individual fellowships, and research career awards.

Accomplishments in 1977: Recent research provided new knowledge on pain measurement and pain relief. In pain measurement studies, investigators employed signal detection theory (SDT), a new methodology which enables scientists to separate and measure the objective and subjective components of human pain. SDT analysis showed that acupuncture and nitrous oxide not only affected the physiologic sensitivity to pain, but also produced an attitudinal change which made the subjects less willing to admit painful stimuli. Codeine, a narcotic prescribed for pain after dental surgery, was found to be no more effective than aspirin, or its substitute acetaminophen. When children were shown video taped films depicting well-behaved, cooperative children receiving dental treatment, the children viewing the films improved their own behavior in the dental chair.

Approximately 22 research grants, 2 career awards, 3 individual awards, 2 institutional awards, and 1 research and development contract will be supported in 1977.

Objectives for 1978: During FY 1978 studies on the relief of pain by drugs, by electroanalgesia and by biofeedback techniques will be supported. To develop safer, more effective pain control for dental outpatients, scientists will test combinations of intravenous sedation and inhalation anesthesia. In the electroanalgesia studies scientists will examine the effects of pain-preventing currents on the dental pulp, or nerve-containing tissue of the tooth. By means of electronic biofeedback techniques, patients with intractable pain in the joints and muscles of the jaws will be made aware of their muscle tension, and trained to obtain relief by relaxing. To stimulate behavioral science research, staff will convene regional conferences and will publish descriptions of program interests in professional journals.

Approximately 24 research grants, 2 career awards, 5 individual awards, 1 institutional award, and 1 research and development contract will be supported in 1978.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Soft Tissue Stomatology and Nutrition Program Branch. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$3,583,000	Indefinite	--	$3,893,000

Purpose: To develop basic information on the cause, treatment and prevention of canker sores, fever blisters, oral cancer, and new knowledge on oral disorders related to nutritional imbalance, to abnormal salivary secretions, and to disturbed mineral metabolism.

Explanation: These activities are accomplished by utilizing research grants, contracts, institutional fellowships, individual fellowships and research career awards.

Accomplishments in 1977: By carefully noting the appearance, location and size of early oral cancer lesions, investigators were able to develop new diagnostic criteria which should improve the detection and cure rate of oral cancer. Recent nutritional studies have shown that "normal doses" of aluminum hydroxide-containing antiacids result in reduced absorption of phosphorus and increased excretion of calcium and fluoride. Scientists have found an effective blocking agent which specifically prevents the pain and excessive salivation experienced by patients being treated with the anti-tumor chemical cyclocytidine.

Approximately 38 research grants, 8 career awards, 10 individual awards, 9 institutional awards, and 5 research and development contracts will be supported in 1977.

Objectives for 1978: Oral cancer researchers will refine newly developed diagnostic criteria and will initiate studies to confirm recent findings on the early detection of oral malignancies and to determine survival rates after early surgery. Attempts to prevent fever blisters by vaccination have not seemed promising because the causative herpes virus localizes in nervous tissues and remains protected from immune cells, and because virus nucleic acids in the vaccines may cause cancer. Since recent studies indicated that immunization early in life may safely prevent infection, scientists will now study the efficacy of a series of nucleic acid-free vaccines. Since copper and zinc seem to be related to the manifestations of periodontal disease, animal studies will be carried out to determine the exact role of these metals to disease. Scientists will assess the influence of poor nutrition on the oral immune response to cariogenic (decay-causing) bacteria in animals and in children. Investigators will also study the effects of fluoride on cyclic AMP and glucose metabolism in a variety of mammalian tissues.

Approximately 46 research grants, 8 career awards, 14 individual awards, and 4 institutional awards, and 5 research and development contracts will be supported in 1978.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Dental Research Institutes. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$7,200,000	Indefinite	---	$7,200,000

Purpose: To carry out coordinated multidisciplinary oral health research which utilizes the full resources of the biological, physical, and social and clinical sciences in a university setting.

Explanation: The programs of this activity are supported by research grants.

Accomplishments in 1977: Investigators at the five Institutes and Centers, working in interdisciplinary teams, carried out research activities covering nearly all phases of oral health, and published their findings in more than 500 scientific papers.

Objectives for 1978: During FY 1978 support will be provided for approximately 200 ongoing laboratory projects spanning a wide range of oral health problems. In addition, the centers will devote special efforts to the development of projects with clinical relevance.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
178	$10,625,000	Indefinite	178	$11,159,000

Purpose: The laboratory and clinical research studies of the Institute are concerned with the causes, prevention, and treatment of diseases and disorders of the oral cavity and facial region, e.g., dental caries, periodontal disease, oral soft tissue diseases, congenital and acquired defects and pain.

Explanation: The Intramural Program is carried on in 7 laboratories and branches. A dental clinic is maintained for clinical research, and also provides service for certain patients participating in the NIH Clinical Center Programs.

Accomplishments in 1977: Evidence is mounting that genetic factors play an important role in many of the diseases under investigation. A genetic basis was found for the immunological response to microorganisms implicated as etiologic agents of periodontal disease. Further, viral induction of a diabetes-like syndrome in mice was shown to be genetically determined. Genetic factors were also implicated in Sjögren's syndrome, a disease characterized by dry mouth.

Significant advances were made toward understanding specific steps of the immune reactions which lead to the destruction of the tissues that hold the tooth in the jaw. Two classes of chemical factors were identified which control the complex interactions between cells of the immune system. It was also shown that microbial products stimulate host cell to secrete a factor which induces bone destruction.

Advances in research on oral-facial pain and pain control included development of a word scale used to evaluate the effect of anxiety-reducing drugs on patients undergoing oral surgery. It was found that the drugs produced a more relaxed, cooperative patient who usually did not recall the surgical procedure.

Objectives for 1978: High priority will be given to strengthening clinical research programs, especially those concerned with periodontal disease. The program will be coordinated with present laboratory efforts to gain further insight into systemic, microbial and immunological factors involved in the human disease process.

Another priority objective is to augment present efforts in fluoride research. A tremendous expansion has taken place in our understanding of biological processes during the last decade. This new knowledge and modern technology will now be applied to questions concerning metabolic and cellular effects of fluoride.

Current programs will continue along the general lines indicated under the preceding long narrative.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
34	$3,320,000	Indefinite	34	$3,292,000

Purpose: This activity supports the scientific and administrative management of NIDR's grant and contract programs, and the computer section.

Explanation: This office is responsible for the review, development, implementation, evaluation and fiscal management of the Institute's extramural programs.

Accomplishments of 1977: The staff supported by this activity continues to provide scientific and administrative management of the Institute's research grant and contract activities.

Objectives for 1978: This activity will continue to administer, manage, and review the grants and contract program, and provide analyses and evaluation.

National Institutes of Health

National Institute of Dental Research

Program Purpose and Accomplishments

Activity: Program Management. (Public Health Service Act, Title IV, Part C)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
31	$1,105,000	Indefinite	30	$1,094,000

Purpose: This activity supports the overall planning, direction, coordination and evaluation of the programs of the National Institute of Dental Research.

Explanation: This activity supports the Director and his immediate staff, Program planning and evaluation office, office of scientific and health reports, research data office, financial management office, general administration and personnel office.

Accomplishments in 1977: The staff supported by this activity provided the leadership, program guidance, and overall administration for the programs of the Institute, as well as conducting a broad program of information dissemination directed to scientists, dental practitioners and the public.

Objectives in 1978: This activity will continue to provide the direction, coordination and administration of the Institute's programs.

TUESDAY, MARCH 8, 1977.

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

WITNESSES

DR. G. DONALD WHEDON, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. BENJAMIN T. BURTON, ASSOCIATE DIRECTOR FOR PROGRAM ANALYSIS AND SCIENTIFIC COMMUNICATION, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
F. L. MILLS, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
DONALD F. CYPHERS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES
H. RICHARD MILLER, ASSISTANT DIRECTOR, BUDGET, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER
DR. GEORGE BROOKS, ASSOCIATE DIRECTOR FOR EXTRAMURAL PROGRAM ACTIVITIES
DR. NANCY CUMMINGS, ASSOCIATE DIRECTOR FOR KIDNEY, UROLOGIC, AND BLOOD DISEASES
DR. LESTER SALANS, ASSOCIATE DIRECTOR FOR DIABETES, ENDOCRINE AND METABOLIC DISEASES
DR. HAROLD ROTH, ASSOCIATE DIRECTOR FOR DIGESTIVE DISEASES AND NUTRITION

Mr. FLOOD. Now we will have the National Institute of Arthritis, Metabolism, and Digestive Diseases.

That presentation will be made by Dr. G. Donald Whedon, the Director.

We have your biographical sketch which we will place in the record at this point.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: Dr. G. Donald Whedon.

Position: Director, National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD).

Birthplace and date: Geneva, N.Y., July 4, 1915.

Education: A.B., 1936, Hobart College; M.D., 1941, University of Rochester School of Medicine; Sc.D. (hon.), 1967, Hobart College.

Experience: Director, NIAMDD, 1962–present; Assistant Director, NIAMDD, 1956–62; Chief, Metabolic Diseases Branch, NIAMDD, NIH, 1952–65; (organizer for DGMS program of multicategorical clinical research centers, now in DRR, 1959–61); physician, outpatient department, New York Hospital, 1947–52; assistant physician, outpatient department, New York Hospital, 1944–47; assistant professor of medicine, Cornell University Medical College, 1950–52; instructor of medicine, Cornell University Medical College, 1944–50; assistant in medicine, Uni-

versity of Rochester School of Medicine, and assistant resident physician in medicine, Strong Memorial Hospital, 1942–44; intern in medicine, Mary Imogene Bassett Hospital, Cooperstown, N.Y., 1941–42.

Association memberships: Association of American Physicians; the Endocrine Society (postgraduate committee, 1962–65); American Rheumatism Association; American Diabetes Association (Board of Directors ,1970–76, Postgraduate Education Committee, 1971); American Federation for Clinical Research; New York Academy of Sciences; American Association for the Advancement of Science; American Physiological Society; The Gerontological Society; American Institute of Nutrition; Pan American Medical Association; American Gastroenterological Association; Aerospace Medical Association; Orthopaedic Research Society; American Academy of Orthopaedic Surgeons (honorary member).

Special awards, citations, publications, or activities: PHS Superior Service Award, 1967; Citation to Alumni Award, University of Rochester, 1971; NASA Exceptional Scientific Achievement Medal, 1974; Endocrine Society Ayerst Award, 1974; Certified, American Board of Internal Medicine, 1950; Certified American Board of Nutrition, 1968; Special Postdoctoral PHS Fellowship, New York Hospital-Cornell Medical Center, January 1–June 30, 1951; Subcommittee on Calcium, Committee on Dietary Allowances, Food and Nutrition Board, National Research Council. 1959–64; Editorial Board, Journal of Clinical Endocrinology and Metabolism, 1960–67; Editorial Board, Calcified Tissue Research, 1967–76; Scientific Council of the Maryland Academy of Sciences, March 1965–71; Council, National Program for Dermatology, 1971–75; principal investigator of Calcium-Nitrogen Metabolic Balance Study on NASA Gemini-VII Space Flight, December, 1965, and for similar studies on Skylab series of NASA space flights, 1973–74; Consultant to Space Medicine Division, Office of Manned Space Flight, NASA, Nov. 1963–74; University of Rochester University Alumni Council and Medical Alumni Association Council, 1971–76; University of Rochester Trustees Council, 1971–76, Chairman, 1974–75; American Institute of Biological Sciences Medical Program Advisory Panel to NASA, Chairman, 1971–75; Chairman, Life Sciences Committee, NASA, 1974–present; member, Space Program Advisory Council, NASA, 1974–present.

Dr. Whedon is the author of over 60 scientific papers on metabolic and physiologic studies of convalesence, immobilization, paralytic poliomyelitis, diseases of bone particularly including osteoporosis, human energy metabolism and space medicine.

Mr. FLOOD. Do you have some people with you that you want us to meet?

Dr. WHEDON. Yes, sir.

With me are Dr. Benjamin T. Burton, Associate Director for Program Analysis and Scientific Communication; Mr. Francis Mills, Executive Officer; Donald Cyphers, Financial Management Officer; Dr. George Brooks, Associate Director for Extramural Program Activities; Dr. Nancy Cummings, Associate Director for Kidney, Urologic and Blood Disease, Dr. Lester Salans, Assistant Director for Diabetes, Endocrine and Metabolic Diseases, and Dr. Harold Rath, Associate Director for Digestive Diseases and Nutrition.

Mr. FLOOD. We have your statement, Doctor, and we will place that in the record.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health

Statement by Director, National Institute of Arthritis, Metabolism, and Digestive Diseases
Public Health Service

on

"National Institute of Arthritis, Metabolism, and Digestive Diseases"

Mr. Chairman and Members of the Committee:

I welcome this opportunity to appear before you to report on the progress of the research programs of the National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) and to testify to the needs of these programs for fiscal year 1978. The very wide range of categorical disease responsibilities of NIAMDD include arthritis and connective tissue diseases, diabetes and other metabolic disorders, disorders of the endocrine glands, digestive diseases and nutrition, diseases of the kidney and urinary tract, diseases of the blood, bone, and skin, and the field of orthopedic surgery.

The magnitude and severity of health problems presented by these diseases is extreme, and the urgency of the enormous efforts yet to be made in reducing their toll of premature death, disability, and suffering is very great. These serious problems have been addressed in the recommendations of the National Commissions on Diabetes and Arthritis in their "national plans" submitted to the Congress in December 1975 and in April 1976. The Congress has indicated concurrence with such plans by recent legislation establishing National Diabetes and Arthritis Advisory Boards, and has expressed concern for another important set of diseases by establishing a National Commission on Digestive Diseases. We welcome these new emphases; we agree that the needs in these areas are great and we shall do all within our budgetary and manpower resources to carry out the recommendations for increased and expanded efforts conveyed to us by the Congress.

At this time I wish to describe the ways in which we are meeting the challenge of our responsibilities. In order to present a broader descrip-

tion, however, than is possible in this brief presentation of the background as well as progress and directions of our research, we have prepared Special Reports in a number of major fields. I shall, of course, be glad to discuss in greater detail any points which members of the Committee may wish to raise.

Arthritis, Rheumatic Diseases, and Orthopedic Surgery

Arthritis and rheumatism, terms that refer respectively to inflammation and destruction of joints and to disease affecting tissues surrounding the joints, head the list of chronic diseases in the United States today in terms of social and economic importance. We are now collecting considerable evidence which suggests that there may be a common origin to various arthritic diseases, such as a possible inherited susceptibility to infectious agents which remain to be identified. It is now well established, for example, that there is a remarkable association between some of these disorders and an inherited tissue component found in white blood cells known as antigen HLA-B27. Previously we have found a high frequency of stigmata for ankylosing spondylitis, a disabling rheumatic inflammation of the spine, in apparently healthy B27-positive men. More recent studies have revealed a similar association in women, while a number of other of these so-called histocompatibility antigens have now also been linked to systemic lupus erythematosus, a severe disorder also in the rheumatoid arthritis family. Continuation of these studies will not only intensify our basic understanding of these crippling disorders but may enable us to find cases earlier for more effective treatment or perhaps to identify individuals at risk of developing these diseases in an earlier phase potentially amenable to preventive procedures.

In keeping with the goal of identifying a possible infectious agent in rheumatoid arthritis, Institute-supported investigators will continue their studies of the so-called "Lyme arthritis," a new form of arthritis named after the location where it first emerged in the Connecticut River valley in the form of a circumscribed local epidemic. Further research of this newly-

recognized illness of suggested infectious origin may provide better knowledge of the poorly understood causes and early stages of other forms of arthritis.

In other developments, Institute investigators and scientists of the Soviet Union have begun their first cooperative trial in the field of arthritis and will carry out identical studies on the use of the drug D-penicillamine in the treatment of rheumatoid arthritis. This calendar year we shall also begin funding of new multipurpose arthritis centers, in keeping with the Arthritis Plan developed by the National Commission on Arthritis. The prime purpose of these centers will be to foster an optimal combination of arthritis research, professional and allied professional training, and patient education, in both cities and in outlying communities. To facilitate and coordinate these increased and broadened efforts, this past year the Institute appointed an Associate Director for Arthritis, Bone and Skin Diseases, a man who is a world authority on lupus erythematosus and a demonstrated leader in the field of arthritis as a past President of the American Rheumatism Association.

Diabetes and other Metabolic Diseases

Last year this Committee provided this Institute with a large increase in funds for activities related to diabetes and we are mobilizing all of our resources to carry out your recommendations for increased and expanded efforts. To manage this extremely important responsibility during the past year the Institute has appointed an Associate Director for Diabetes, Endocrine and Metabolic Diseases, a scientist with extensive medical research experience in diabetes and obesity. In order to deal effectively with the two and one-half-fold increase in research grants in diabetes provided by Congressional action, we have formulated and distributed a Request For Applications for support of research on a wide variety of aspects of diabetes, including its possible viral etiology, genetic factors, normal and

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abnormal hormonal action and metabolic regulation, the relationship of diabetes to nutrition and obesity, the vascular, neurologic and renal complications of the disease, and potential, future new treatment methodologies, such as transplantation of insulin-producing cells and automatic blood glucose regulating assist-devices.

In parallel with the greatly expanded research grant effort, we have also widely disseminated a Request For Applications for a new multipurpose diabetes centers program, as proposed by the National Diabetes Commission and supported by this Committee. These two actions have stimulated tremendous interest among biomedical investigators in the field of diabetes, and we look forward to a very beneficial impact upon this disease problem from these new efforts.

Diabetes is now much more widely recognized as a serious and complicated disorder ranking high on the list of diseases causing death and disability in this country. Our efforts continue to focus on the fundamental questions about diabetes that must still be answered, including an understanding of the underlying basic impairment of insulin action. An emerging research opportunity that will receive intensive effort will evolve around the finding of spontaneously appearing, and spreading, diabetes in a colony of guinea pigs, with pathology resembling that of human juvenile diabetes. Although the contagious nature of the animal disease has been verified, attempts thus far to determine the precise nature of the infectious agent have been unsuccessful.

We are equally concerned with seeking better methods of treatment and with suppressing development of the serious complications of the disease. As an example of the latter effort, a finding which may shed light on the development of the characteristic vascular lesions of diabetes and how they develop was the demonstration that healthy kidneys transplanted into diabetic patients develop such lesions de novo in their new but metabolically abnormal

environment. Transplanted healthy kidneys in non-diabetic control patients of the same age and tissue type were found to remain unaffected during the same time period.

In the meantime, we are also pursuing our research on a number of other metabolic diseases, including cystic fibrosis, a grave familial disease of the young. Here, we are pleased to report that we have recently activated a contract-supported major project, to be carried out by the Cystic Fibrosis Foundation, for a comprehensive national study of the state of the art in cystic fibrosis and future activities in this disease. This study will require a minimum of one year for completion and we shall make a comprehensive report to you at that time.

Endocrine Disorders

Endocrinology, study of the internal glandular secretions of the body, of the glands which elaborate and discharge these secretions, and of the effect of these secretions or hormones on the body's vital functions such as growth, metabolism, and reproduction, has great potential value to man's health. Because of the importance of endocrine hormones as regulators of life processes both in health and disease, the Institute maintains a strong program of basic and clinical research in this field. I wish to emphasize how truly intertwined our research efforts in endocrinology and metabolism and endocrine and metabolic diseases are with each other and with diabetes. As an example, I recall testifying before this Committee last year on the newly-recognized importance of the pancreatic hormone, glucagon, which is an apparent antagonist to insulin (the impaired activity of which plays a central role in diabetes). Endocrinologic research in recent years brought forth a new hormone, first found in the pituitary gland, called somatostatin because of effects relative to growth. Newly evolving knowledge of somatostatin now suggests the possibility of development of a new tool with which to suppress partially the elaboration of glucagon and to amelio-

rate its anti-insulin effects. This new information does not have immediate practical usefulness in therapy of diabetes but it represents a fresh, new step in that direction.

Digestive Diseases and Nutrition

Diseases of the intestinal tract, gallbladder and liver are among our most frequent chronic and disabling afflictions. Among the more important of these diseases, peptic ulcer strikes about 10% of all adults in the United States at some time in their lives. High on the list of research interests are studies on inhibitors of stomach acid secretion, and last year I reported to you about cimetidine, a new antihistamine drug. Continuing research has substantiated that this compound is an effective inhibitor. In recent related research, one of our grantees has found that a synthetic analogue of a certain prostaglandin, a naturally occurring hormone-like fatty acid, can also effectively inhibit gastric acid secretion in patients with duodenal ulcers. Both cimetidine and the new prostaglandin analogue seem to improve the healing rate of peptic ulcers and warrant further controlled therapeutic trials in ulcer patients to determine long-range effectiveness and safety. Our augmented research attack on peptic ulcers includes the continued support of a very productive comprehensive peptic ulcer center with multidisciplinary expertise.

In gallbladder disease research, we are continuing support of a multi-year, long-range cooperative program to evaluate the safety and effectiveness of the long-term use of chenodeoxycholic acid, whose ability to dissolve cholesterol gallstones I had reported to you earlier. If this new medical procedure indeed proves both safe and effective, gallbladder surgery can be considerably reduced, and we shall be able to bring about a marked reduction in the thousands of gallbladder surgery-related deaths which occur each year.

NIAMDD is responsible for a large portion of the nutrition research supported by the National Institutes of Health and of the medically oriented

nutrition studies supported by the Federal Government. Our program activities cover the full spectrum, from obesity research and basic metabolic and physiologic studies to projects designed to determine how best to alleviate and prevent malnutrition and to control specific nutritional deficiencies. In recent research, one of our grant-supported investigators detected essential fatty acid deficiency in patients who are maintained for long periods of time with the aid of total parenteral nutrition, and has used an intravenously administered fat solution to correct this deficiency state. In studying the nutritional status of alcoholics, another grantee has found that enlargement of the liver, a common manifestation of alcoholic liver disease, results from accumulation of protein as well as fat in the liver; this accumulation occurs as a result of that organ's inability to release into the blood certain proteins which are synthesized in liver cells.

Kidney Disease, Urology and Hematology

Urologic and kidney diseases are of prime importance, inasmuch as the latter group of disorders, including the various forms of glomerulonephritis (Bright's disease) and nephrosis, kills an estimated 48,000 Americans each year. We are concentrating on studies on the nature and cause of the many different kidney diseases and urologic disorders and on means of treating them more effectively as the best means of preventing chronic, irreversible kidney failure. At the same time we are seeking to make possible the use of kidney transplantation as an improved and relatively permanent therapeutic measure against irreversible loss of kidney function. Concurrently, the work of our Artificial Kidney-Chronic Uremia Program will continue to emphasize studies on the pathophysiology of uremia and a search for novel therapeutic approaches. With a greater understanding of the aberrations of end-stage kidney diseases, it will be possible to improve dialysis methods, to shorten dialysis time, to make this therapy less expensive, and to improve the quality of life obtained with it. In the meanwhile, an alternative to con-

ventional dialysis, peritoneal dialysis, which has advantages for specific groups of patients has now been successfully developed into an effective and practical routine maintenance treatment.

As the result of Senate action on the 1977 Appropriations Bill, this Institute is beginning a new program of Specialized Centers of Research (SCORs) in the field of kidney disease. The first such centers will concentrate on research on urinary tract stones, with the realization that this is a widespread disabling disorder in which there has been little research progress. New understanding about what causes the formation and recurrence of stones is essential if we wish to achieve more rational treatment methods and, hopefully, prevention. In the future, if we can obtain the resources, we would expand this center program and our research grants program with emphasis on glomerulonephritis. Over half the patients with end-stage kidney disease who must be treated with costly dialysis or transplantation suffered originally from one of the various kinds of glomerulonephritis, the causes of which are still imperfectly understood and the treatment of which, with means currently at our disposal, is far from effective.

Hematology

Research on blood is an integral part of the Institute's program, not only as a basis toward control of blood diseases but in the use of blood as a biological tool to study other biomedical problems. The principal research goal of NIAMDD is enhanced basic understanding of the physiology and metabolism of blood and its components, particularly the red and white blood cells. Such knowledge is essential for a better understanding of the various blood disorders, the normal and abnormal mechanisms which cause them, and ultimately, for improved diagnosis and therapy in this field.

In research related to Cooley's anemia, our Institute is supporting by contracts an intensive search for new iron-chelating, or binding, agents which could prevent the ultimately fatal buildup of iron in the tissues and

organs of patients who must be kept alive with the aid of repeated blood transfusions. Scientists now consider that such an agent could be developed with present technology, and this pursuit will remain a goal of Institute-supported researchers.

Dermatologic Disorders

As you know, our Institute is responsible for research on disorders of the skin, such as the disfiguring and incapacitating disease, psoriasis. In addition to our support of studies to determine the cause of the rapid turnover of skin cells that characterizes psoriasis, we are initiating support for the clinical evaluation of photochemical treatment of the disease, which involves use of the drug 8-methoxypsoralen and subsequent exposure to ultraviolet light of a special long wave length. Other serious, disabling, and disfiguring skin diseases currently subject to Institute-supported research include atopic dermatitis, pemphigus, and discoid lupus erythematosus.

Finally, I am also pleased to remind you that, for his work which started in our Bethesda laboratories, with the "Australia antigen" and its role in hepatitis, a former staff investigator at our Institute, Dr. Baruch S. Blumberg, shared the 1976 Nobel Prize in Physiology or Medicine.

In conclusion, Mr. Chairman, the budget request for the Institute for 1978 is $216,961,000. I shall be happy to try to answer any questions the Committee may have.

BUDGET REDUCTION FOR NEW AND COMPETING RESEARCH GRANTS

Dr. WHEDON. Mr. Chairman, would it be possible for me to make a brief opening oral statement? What is your wish?

Mr. FLOOD. We have your statement. It is just a question of timing. But you will be able to develop your answers in whichever way you see fit.

Now in your 1978 budget for the Institute here, you call for an increase of $7.9 million. That is over the level that was appropriated for 1977. But you are proposing to reduce new and competing research grants. What is the impact of that reduction?

Dr. WHEDON. Well, the basis for it is that we have more money tied up in noncompeting grants, grants that we have made in previous years. The impact, to follow your question, is that we will have less money available to fund those individuals who have been funded in the past and who are now coming in for competition in renewal and to those individuals submitting new applications.

In terms of percentage of study section approvals that can be funded, last year the average percentage was 45 percent for our Institute. In 1977 it will be 27 percent in all programs except diabetes. So we take a real drop in 1977 over 1976.

Now for 1978, the average situation will be about 33 percent. This is with the exception of the diabetes program where the situation is uncertain. In 1977, this current year, we don't know what the situation will be either, but we had a sizable increase in that program thanks to this committee.

Mr. FLOOD. Are you talking about competing research grants?

Dr. WHEDON. I am talking about competing—new grants and renewals, As a result of the considerable increase which this committee was instrumental in providing to us for research in diabetes, we have issued a broad Request for Applications. I understand there are 250 to 300 applications for work in this field in our hands to date.

BUDGET REDUCTION FOR DIABETES, ENDOCRINOLOGY AND METABOLISM

Mr. FLOOD. Look at page 148 of your budget justifications there. That is where I see that reduction in diabetes and endocrinology and metabolism, all of those activities.

Dr. WHEDON. That is right.

Mr. FLOOD. But there is also an increase in all the other areas you have there. Why would you be reducing this particular area of your Institute?

Dr. WHEDON. The reason for that, Mr. Chairman, is that through the action of this committee and of the Senate on the 1977 budget, there was an increase in funds for diabetes of 2½ times, in other words the amount of money available in 1977 for diabetes research is 2½ times what it was in 1976.

Mr. FLOOD. But which of these areas are you going to cut the most of the areas I mentioned, diabetes, metabolism, endocrinology, which will be cut the most?

Dr. WHEDON. The reduction shown here is almost entirely in the diabetes program.

Mr. FLOOD. That seems mighty strange in view of the congressional interest expressed in research in that disease.

Dr. WHEDON. May I explain?

Mr. FLOOD. Sure, that is a leading question.

Dr. WHEDON. From 1976 to 1977, as I was saying, diabetes was more than doubled. As a result of the action on our budget, all of the other programs were held to the 1976 level with very minor exceptions. There was an increase of $2½ million for the beginning of an arthritis centers program and there was a modest amount put in for research in digestive diseases and nutrition. But in all other programs we were held at about the 1976 level in total amount. As I just pointed out a moment ago, the percentage study section approvals that we could fund were considerably reduced for these other programs. So when we came to consider the situation for 1978 in the President's budget, we felt that the only way that we could bring some measure of restoration of this rather sharp imbalance between the relative wealth of the diabetes program and the other programs was to provide small increases for these other programs.

Now the diabetes program, even though it is going to be reduced by about $1.7 million, will still be able to handle all of the commitments that will have been made in this fiscal year.

Mr. FLOOD. Do you see why I asked that question, though, because as I have said on other occasions, when this bill goes on the floor you will be sitting up in that balcony. Mr. Natcher, Mr. Early, Mr. O'Brien and I will be down in the well of that House. Hence the questions. That was the purpose, among other things. So if you feel you would like to develop that for the record, don't hesitate to do so, out of an abundance of caution if nothing else.

Dr. WHEDON. We will be happy to do that. We can describe the course of events.

[The information follows:]

DIABETES BUDGET FOR 1978

The total assigned to the diabetes program for 1978 (exclusive of $3.7 million "diabetes-related" in other programs) is $34 million; within this figure funding for diabetes centers will be increased from $8.7 million to $9.5 million and training from $1.6 to $2.4 million, but research grants will be reduced from $21.9 million to $18.5 million. This step was taken thoughtfully in an effort, within the 3 percent overall increase provided to NIAMDD, to correct partially the extreme imbalance between diabetes and other programs in the 1977 budget. First, diabetes had received a 2½-fold increase in total funding from 1976 to 1977 of which about $15 million was for new and competing research grants. Compared with just over $3 million for new and competing grants in 1976, which provided support for 55 percent of study section approved applications, this additional $12 million represented a very large increase for new and competing renewal research grants for diabetes in 1977. To accommodate further increases in subsequent years, it is necessary to increase the manpower pool for diabetes research; hence, the funding for diabetes training was substantially increased in 1978. Finally, the funds provided in 1978 for research grants will enable all 1977 commitments to be honored.

Second, at the same time that the diabetes budget was increased by the Congress in 1977, most of the other programs were neglected or received increases for special programs other than regular research grants. As a result, the research grants budgets of these other programs (orthopedics, dermatology, metabolism, endocrinology, digestive diseases, nutrition, kidney, hematology and arthritis)

remained at about the 1977 President's Budget level; this resulted in a severe reduction in award of new and competing renewal research grants to levels averaging about 26 percent of study section approved applications, as compared to an average in 1976 of 45 percent. In consideration of these severe reductions in the other programs in contrast to extraordinary program growth in diabetes, it was decided that the 1978 budget should provide some restoration of vitality to these other important areas of research. In summary, since this was the first opportunity in two years to provide budgetary relief for the other nine programs of the Institute, the 1978 budget request represents the best, fully considered professional judgment of the needs and priorities of all of the various programs within the total funding level permitted.

DIABETES STUDY AMONG THE PIMA INDIANS

Mr. FLOOD. On the subject of diabetes, I recall we talked in the past about your experience with the Pima Indians. You told us that this group has a prevalence of diabetes 10 to 15 times the national average. You were talking about studies. What have your studies revealed to date on that? Is there some relationship between lifestyle and this disease we are talking about? In other words, do they have a diet that is high in calories and fats? Are they overweight or what?

Dr. WHEDON. We did a very extensive dietary study there about 8 years ago. The only difference that we could find in essential nutrients in their diet and that of other Americans was that there were more calories.

Mr. FLOOD. Is there any link between the lifestyle and the onset of diabetes?

Dr. WHEDON. Not that we can exactly put our finger on. They are distinctly more obese, however, than the average American. That has some impact, we are certain of that. But that doesn't account for all of it.

NO TEST FOR FUTURE DIABETICS

Mr. FLOOD. Do you have any way of testing an individual early in life to predict that he is going to develop diabetes in the future?

Dr. WHEDON. There have been studies directed at that very point over the last few years whereby a piece of tissue was taken from muscle to see what the thickness is of the so-called basement membrane, that is the thin membrane which runs around the inside of the smallest blood vessels.

Mr. FLOOD. You are speaking of humans?

Dr. WHEDON. Yes. We find in diabetes that this basement membrane is thickened, and it is more or less increased in thickness in direct relationship to duration of the disease. There were some suggestions from the work of some individuals who could be labeled as prediabetic, that is, both their parents had diabetes so that the offspring would be suspected to have it, might have thicker basement membranes than normal. But it is my understanding that now this is not certain. It doesn't look that way. So the answer to your question is no.

Mr. FLOOD. Is the test expensive to administer? In other words, is it something you would recommend to individuals whose families have a history of diabetes?

Dr. WHEDON. Since the answer to your question is really no, there is no method by which you can pick up future diabetes, it is not relevant In any case, what was used was a muscle biopsy. You would not want to do that on large numbers of people.

ANIMAL MODELS FOR DIABETES RESEARCH

Mr. FLOOD. I understand that one of the reasons that we know so little about the causes of diabetes is that currently there is no animal model which develops the complications of diabetes the same way that people do, of course. Is that correct?

Dr. WHEDON. That is not entirely correct. Various animal models have been developed, most of them by the administration of some chemical which would affect the insulin-producing cells of the islets of the pancreas in these animals. So these animals are rendered diabetic in an experimental fashion. Just recently a colony of guinea pigs have been found who apparently develop diabetes spontaneously. These animals have diabetes in a relatively mild form so they can be kept alive for a long period of time.

Mr. FLOOD. What is the likelihood that you will develop such an animal model for diabetes research; even money or what?

Dr. WHEDON. This has just been developed. The difficulty, of course, is that there are not that many of these animals. It is an unusual colony and it will take some time and funding support to expand this resource.

Mr. FLOOD. We are concerned about that because when you have this indication in the Congress where they are disposed to appropriate large sums of money for this program, would there be some limitations on your ability to do research in diabetes? That brings up the question again on your animal models.

Dr. WHEDON. It would certainly help, of course, to have more of these animals. In all of this research it will be useful to have very solid support.

TRAINING INCREASE

Mr. FLOOD. Your budget proposes here to increase the training activity at a little over $2 million. In what specific fields are you going to train these individuals and how do you determine now what particular field is going to need what additional manpower?

Dr. WHEDON. Let me open by saying that I feel that we have a need for research manpower in all of our fields. We are responsible for a very wide variety of categorical disease problems. Each of them has the necessity for greater effort.

I would say in general we would like to provide increases in training in proportion to the amount of money we are putting into research in that field. Theoretically there ought to be a sizable increase in the amount of training we can provide to diabetes in view of the considerable impetus we have given there. Unfortunately, we are rather limited in the amount of funds we can put into training. As a result, we have more or less spread the training funds through our various programs. Diabetes and digestive disease programs have been given the largest proportion.

Mr. FLOOD. Mr. Natcher?

DIABETES BUDGET INCREASE IN 1977

Mr. NATCHER. Doctor, in your opening statement you say you have formulated and distributed a request for applications to support research on a wide variety of aspects of diabetes. Do you expect to receive a sufficient number of high quality grant applications to utilize the sizable increase that Congress appropriated for this research?

Dr. WHEDON. Yes, we do, Mr. Natcher. As I mentioned a moment ago, up to this point the Division of Research Grants tells us that they have received 250 to 300 applications. I haven't taken time to price that out to see what that will amount to, but I really am quite confident that there will be enough valid meritorious applications in that set of applications that we will be able to utilize very sensibly the funding that we have been awarded.

Mr. NATCHER. What percentage of your approved grant applications for diabetes do you expect to fund in 1977?

Dr. WHEDON. That is hard to predict, but I expect that with the considerable funding we receive, that it will be quite high. It might well be 75 or 80 percent, which would be the highest percentage, I think, that we have been able to award in any program in a long time.

DIABETES PROGRAM FOR 1978

Mr. NATCHER. Doctor, assuming our committee recommended to the full committee and on into the House that as far as diabetes research is concerned that we have a sizable increase in the appropriation, same as we had last year, 1977, could you effectively use this money,

or would you find yourself in a position that you would have to start funding marginal projects in order to utilize the money?

Dr. WHEDON. I hesitate to be definitive, Mr. Natcher, but I really suspect that we certainly could. The National Diabetes Commission has recommended from their view that the field could deal with a considerable increase in funding. They recommended, for example, that in 1978, that as much as $64 million could be profitably spent for a whole variety of activities in diabetes, not just research grants, but centers and training, and so on. So I think that with the intensified awareness of the importance of diabetes, the great interest of investigators which has been stirred up, that a substantial increase could be applied in 1978 in this area.

ARTHRITIS

Mr. NATCHER. Doctor, do I understand from your statement that arthritis can be inherited? Is that the interpretation that we have?

Dr. WHEDON. I could not say that specifically. There is some tendency for arthritis to run in families, but the genetic pattern with respect to arthritis is not established, and it certainly could not be specifically labeled as an inherited disease.

Mr. NATCHER. What progress are you making in developing some sort of a mechanism to detect the early onset of arthritis? Where are we, Doctor?

Dr. WHEDON. This situation, I think, has not changed a great deal recently. The clinical signs of early arthritis are usually some defect in the comfortable operation of joints; morning stiffness, for example, was a classical early sign of arthritis. Now the specialists in this field tell me that is not as reliable as they once thought it was. Hence, one has to think about various blood tests.

Now in the period some 5 to 10 years ago, in fact a little earlier than that, actually, there were many tests developed for various abnormalities in protein complexes in the blood. The bentonite flocculation test is one of these that is used quite commonly as an early diagnostic test for rheumatoid arthritis. I am sure you realize, when we speak of arthritis, we are speaking of perhaps 100 different kinds of involvement of the joints, but the rather classically referred-to type which everyone is aware of, the most devastating as far as limitation of motion and deformity are concerned is rheumatoid arthritis, and that is the one we are trying to detect early.

PREVENTION OF DEFORMITIES

Mr. NATCHER. Doctor, are there currently any effective preventive measures for arthritis?

Dr. WHEDON. In a truly preventive way, with respect to the disease itself, no. But, if we think of prevention in arthritis in terms of prevention of deformity, that is, once the disease is developed with pain in the joints and limitation in motion often accompanied by fever, then the greatest efforts are applied to reduce the imflammation and prevent the development of inability to use the joints properly over a period of years.

Here, careful utilization of therapy with a variety of drugs—there are various drugs that can be used—and also of physical therapy, keeping the joints active and moving through their full range and carrying weight, and so on, is the most effective way of doing this.

MULTIPURPOSE ARTHRITIS CENTERS

Mr. NATCHER. Doctor, how many arthritis centers will you fund in 1977 and in 1978, and, if you would, tell me as to whether or not these centers will work with, and are working with, the local physicians? We get letters, Doctor, from time to time, from doctors, indicating that maybe in these centers there is no communication at all. You hear complaints along that line.

What about this matter, Doctor?

Dr. WHEDON. Your question comes in two parts. The first part with regard to the number of awards that we expect to make: $2.5 million has been set aside for this new program, and we would estimate that we would make 8 to 10 center awards in this fiscal year.

Now, the guidelines for these centers, consistent with the recommendations of the National Arthritis Commission, are that these centers be used for increased efforts in research and in training, not only of professionals but of allied health professionals, for educational activities for patients and the public, and also for what are called community programs. It is in this latter area that we would approach the second part of your question. The effort intended obviously is to develop systems of education, in quotation marks, for the practicing physicians in those areas. The intent of the recommendations of the Commission for these centers is that there be a truly integrated effort between the university medical center at the hub and the community practicing physicians and allied health personnel and nurses, and so on, around this focal center.

Mr. NATCHER. Thank you, Doctor.

Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Early?

Mr. EARLY. Thank you, Mr. Chairman.

U.S.-U.S.S.R. COOPERATIVE MEDICAL PROGRAM

Doctor, this arthritis co-op program with the Russians, how is that working?

Dr. WHEDON. We are making some very definite progress there. There have been a number of visits of our people to the U.S.S.R. and vice versa. At the present time, there are two main projects taking place. The principal one is for a study in each country of the effectiveness of a compound known as d-penicillamine on rheumatoid arthritis. On the last meeting of the Russian and American investigators, which was in Russia about 3 months ago, the protocol for this joint study was hammered out in great detail, patients are being accepted into this study, and I think that it will progress very well.

The other project is one that is of particular interest to the Russians, and that is for greater definition and understanding of juvenile rheumatoid arthritis.

Whether this will develop into a firm research investigation of this disease in terms of testing of treatment, I am uncertain. I think the first phase is what we are going through now, and that is an effort in defining terms, trying to find out if there are different characteristics in arthritis as it is found among the Russian children in their many populations, and as it is found in our country.

BENEFITS FOR BOTH COUNTRIES

Mr. EARLY. At the startup of this program, was either country well advanced on the other? Was there an exchange of ideas that benefited Russia more than us, or us more than Russia?

Dr. WHEDON. The situation at the start of this program was that there had been relatively little exchange among the doctors in both countries. There is an International League against Rheumatism which holds an international congress ever 3 to 4 years, and the Russians have attended those meetings. Of course, we have been very strong participants in those meetings.

In very recent years and particularly since this U.S.-U.S.S.R. program has started, there is much more involvement of the Russians, not only with us, but with other countries. They are meeting more frequently now with other doctors in European nations.

Mr. EARLY. This d-penicillamine, was that at the same stage held by both the United States and the U.S.S.R.?

Dr. WHEDON. Actually, this compound had been first developed by us, but not used very much because we were, I think, at that time principally concerned about its toxic side effects. Interestingly, British rheumatologists picked this drug up and used it to a much greater degree than we did and produced results that compelled everyone else to take notice of it. The Russians also took notice of it and began to use it, but not in a carefully controlled way. So it was a combination of a realization of Russian interest and realization of the results developed by the British that has led us to get into this study.

There is an important new feature to this, and that is that the dosage level of the compound is going to be considerably less than was originally recommended, and we hope in this way that we will find a dosage that will be effective, on the one hand, and relatively nontoxic on the other.

Mr. EARLY. I get the impression that this co-op plan with Russia is going to be productive?

Dr. WHEDON. We think it will. We are impressed with the reasonably good quality of training of the Russians, particularly the Russian leaders, and they are very interested in sharing their information that they learn with us.

CYSTIC FIBROSIS STUDY

Mr. EARLY. Doctor, in your statement you say you are going to conduct a comprehensive national study of the state of cystic fibrosis, and you suggested you will have a report within a year. How many people are going to be involved in this study?

Dr. WHEDON. This is not a research study. We awarded a contract to the National Cystic Fibrosis Foundation really to conduct a review or analysis of the state of the art with respect to cystic fibrosis. This has progressed to the point of establishing 12 subcommittees, the chairmen of these subcommittees have been selected. What will happen is that there will be a series of meetings of these subcommittees, and a comprehensive report will be formulated. But it is not per se a research study that is going on.

Mr. EARLY. But your statement suggests that we will get a report within a year.

Dr. WHEDON. This was the direction of this committee, but we are simply not going to be able to do that fully in 1977. The advice we have received from consultants of all sorts is that in order to do a really careful and meaningful analysis of this situation, we ought to take at least a year, and this is the feeling, also, of the Cystic Fibrosis Foundation. I would hope that by this time next year we definitely would have some information to provide.

IMPLEMENTATION OF NEW DRUGS

Mr. EARLY. Are you satisfied that the newly developed drugs are being tested and made available as quickly as they should be?

Dr. WHEDON. This is a perennial question, and I feel certain that there are some drugs that are not picked up as readily as they ought to be. Part of the answer, of course, is that the systems of getting the information out to practicing physicians are not as good as they ought to be in spite of the general effectiveness of the published scientific medical literature. On the other hand, there is a question of safety of these compounds, and I think one has to be very careful in the introduction of any new medication——

Mr. EARLY. You can be overcareful, too, as far as the trial and error process. You can go on eternally with this.

Dr. WHEDON. I think quite as many errors have been made on the side of jumping on the bandwagon with some new fad of therapy as with the reverse process.

Mr. EARLY Thank you, Mr. Chairman.

Mr. FLOOD. Mr. O'Brien.

COOPERATIVE PROGRAMS WITH THE U.S.S.R.

Mr. O'BRIEN. Doctor, sometime ago, we had an experience with a joint operation of the space shot with the Russians. It was my conclusion that they learned a lot; we picked up very little.

Do you have any impressions of that with reference to your arthritic cooperative program?

Dr. WHEDON. Well, I know something about the joint space flight with the Russians since I have been a consultant to NASA for some years. To be truthful about it, there was relatively very, very little of a scientific nature involved in that joint venture, and I think the principal matter that was accomplished was the demonstration that two different systems of launching vehicles into space could be compatible, that the individuals could meet, could exchange information

and data because they not only spoke to one another, they had data handling systems in their spacecraft.

It was a technical success, and I think both sides learned something from the other in that respect, but there was really nothing of any degree learned of a medical value.

Dr. FREDRICKSON. Mr. O'Brien, could I make one comment since you broadened it beyond arthritis? We have had a joint U.S.-U.S.S.R. biomedical arrangement now for approximately 4 or 5 years. The oldest program area is arteriosclerosis, and it is interesting that, while I think there is a good deal of transfer of technology from the United States to the Soviet side, it has been possible to arrange with them a study whereby we are now receiving, at our computer center in North Carolina, data on what will be a total of 10,000 Russian males. The Russians have agreed to complete compliance with an American-designed protocol which we have already worked out here for some twenty or more thousand males. We are going to get, in this unusual experiment, precise comparisons for a number of variables that relate to coronary artery disease between Russian males in Moscow and Leningrad and Americans in many centers. There are parts of this program, particularly the older parts, that do actually reflect true scientific interchange and some collaborative experimentation.

Mr. O'BRIEN. Do they have a national institute of health as we do?

Dr. FREDRICKSON. They have a ministry of health broken into a number of institutes such as for therapy, or for cancer research or cardiovascular research. They are highly discipline-oriented, and I guess they have more institutes than we have if you count all their subdivisions.

MORALE OF PATIENTS ON KIDNEY DIALYSIS

Mr. O'BRIEN. One more matter. With regard to the artificial kidney program, I went through one of those dialysis clinics back home, and that is an enervating experience, sort of dehumanizing. It is very difficult to keep your morale up. I notice from your report you describe the hypertension and the hyperlipidemia in that particular process. Are we a long way off from making something that someone can really live with very long?

Dr. WHEDON. There is really quite a lot I can say about that. The technology of artificial kidney treatments or hemodialysis has been steadily improved. I think interestingly one of the things that has happened just recently along the lines you are interested in is the development of a so-called mobile artificial kidney. That is, say, you have a businessman who has end-stage kidney disease and has to receive dialysis, but the requirements of his work compel him to travel from one city to another. Well, they have developed the means of putting an artificial kidney in a suitcase, and he can carry that plus another bag that carries other equipment with him, and a dozen or so individuals of this sort have thus far used this in going to other cities, and even abroad. They go to their hotel room, and they have the paraphernalia to hook up the artificial kidney to the faucets in the bathroom and can carry out their own dialysis for the several hours required and then pack it up and come back home again when their business is completed.

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The other development that I think will facilitate the quality of life, make an individual less tied down to the machine, is the rejuvenation of peritoneal dialysis. This is the system whereby machinery can be hooked up to a plug in the body cavity of the abdomen, and the toxins created by the body can be washed out by washing out the body cavity in this way by hookup to the abdomen. And, rather than going about it for 10 or 12 hours at one long sitting, the idea now is for a man to come home from work, or a women when she has finished her daily housework or job, or whatever, after supper hook up to the peritoneal dialysis machine for 2 or 3 hours until bedtime and then disconnect it. It is possible to do that every night as a routine while they watch television or read, or whatever, during the course of it.

But we are also very concerned about the quality of life. As a matter of fact, just in January of this year, 2 months ago, we had a symposium here in Bethesda in which a number of experts looked into this whole matter of the psychological aspects of chronic dialysis.

Mr. O'BRIEN. Thank you, Doctor. Thank you, Mr. Chairman.

RECOMMENDATIONS OF THE NATIONAL COMMISSION ON ARTHRITIS

Mr. FLOOD. To what extent does your 1978 budget reflect the recommendations of the Arthritis Commission?

Dr. WHEDON. The Arthritis Commission recommended that in fiscal year 1978, $72 million ought to be spent for arthritis activities. We actually will have available $29.8 million.

PRIORITIES IN ARTHRITIS PROGRAM

Mr. FLOOD. There are many areas discussed there. Of the many areas recommended for Federal support by the Arthritis Commission, which areas are of the highest priorities in your mind?

I ask you that question because there are so many constraints on the Federal budget, as you know, and if this committee has to pick and choose between the areas, and we have to do a lot of that, then we would like to know from a professional where would you set your arthritis priorities?

Dr. WHEDON. I think it is quite easy to make such a decision, Mr. Chairman. We believe that the regular research grant program is first in line to be bolstered. We are able in 1978 to increase that by less than a million dollars, about $800,000 only. I think next in line, I would put training, and we have raised our training over 1977, but only by $500,000. The next major area, I think, has to do with the multipurpose centers. This is a new venture, and we are not really anxious to put tremendous sums into this effort yet without having tried them out, but I do think significant increases ought to be allowed, if it is possible, in the new centers program.

JOINT REPLACEMENT

Mr. FLOOD. What progress are you making to develop the prosthesis, replacement of diseased joints? You started to talk about that once. What is the future in that area?

Dr. WHEDON. The future is quite good. Everyone knows about the artificial hip operation, and that has been quite successful. There are,

unfortunately, some recurrences, some breakdowns of the appliances that are put into the joints, so there is much work to be done along those lines in terms of developing biocompatible materials and the glues that hold the metal in the bone, and so on. But we have progressed now to artificial knees; they are quite in good shape. On the frontier, we have artificial elbows and wrists and fingers. These are in the course of development, and I think we will eventually get to many others. In mentioning those five different kinds of joints, we have mentioned the major joints that are involved in arthritis that may require replacements.

OSTEOPOROSIS

Mr. FLOOD. Osteoporosis is the underlying cause of the fractures largely of the hips and the wrists of older people. How much are you spending on research in this area, and do you plan to work with and collaborate with the Aging Institute to expand and support research on these problems?

Dr. WHEDON. I would have to look up the figure for our research on osteoporosis, but I think it is probably of the order of $1 million.

Mr. FLOOD. Working with the institute?

Dr. WHEDON. With funds from our own institute, and we, of course, are the main supporter of work on this area. Now when I speak of that level of support, I am just speaking of osteoporosis alone. We have other bone-related research.

Mr. FLOOD. Just speak of that and your cooperation with the Aging Institutes.

Dr. WHEDON. I have talked to Dr. Butler about this, and he is very much interested in it. We expected to share our plans in this respect, particularly in terms of workshops or conferences of that sort. We will, of course, be the lead institute because we have the main responsibility for bone and orthopedic research.

DIABETES RESEARCH AND TRAINING CENTERS

Mr. FLOOD. I think you were going to mention a minute ago how many diabetes research and training centers you will support in 1977 and 1978.

Dr. WHEDON. With the amount of money available to us in 1977, we will expect to fund five or six of these new centers.

Mr. FLOOD. Are they going to be geographically distributed or in clusters in certain places in the country?

Dr. WHEDON. I think that with five or six, they will be distributed around the country.

Mr. FLOOD. How are these diabetes centers going to work with the practicing physician in the community? You have to do the evaluation; how are you going to evaluate how well these centers and that cooperation are improving health care for the diabetic?

Dr. WHEDON. I would give much the same answer that I did a moment ago with respect to the arthritis centers. In other words, the recommendations of the National Diabetes Commission were that there be a combination of research training and education and community programs in those centers. There is a bit of a difference as reflected

in the anticipated cost of the research component which would be greater for diabetes, in that the Diabetes Commission was much more interested in emphasizing the importance of research in these centers than the Arthritis Commission was.

In both types of centers the intention of the Commissions was that there be maximal catalyzation of the work of the research and academic people in the center with that of the community practicing physicians.

DIGESTIVE DISEASES

Mr. FLOOD. Recently, it was brought to our attention that the digestive diseases, so the series of articles stated, are very little understood and considerably underfunded.

What percentage of your budget are you going to spend on digestive disease research?

Dr. WHEDON. In a total budget for 1978 of $217 million, the figure for the digestive diseases program is about $28.1 million, and the associated nutrition program is about $10.3 million.

Mr. FLOOD. Why is there so little known about these diseases?

Dr. WHEDON. As is the case in so many——

Mr. FLOOD. Digestive diseases, why is so little known about it?

Dr. WHEDON. Actually, I think quite a good deal is known, but progress has been slow with respect to dealing with the many different problems in digestive diseases. I think the most outstanding ones are ulcer and gallbladder disease, and we are putting special efforts into these areas. We have a superb ulcer research center at UCLA. I might say that support of the UCLA center is a cooperative venture with the Veterans' Administration. As you are quite aware, we have made a special effort with respect to gallstone disease in the last few years.

Mr. FLOOD. Is the research community, itself, expressing interest in doing more work in this area? Are there promising avenues available for the researchers to explore if they wish?

Dr. WHEDON. Yes; there is intense interest in more effort in this area, and this has been expressed in a legislative manner in the establishment of the Digestive Diseases National Commission by virtue of the legislation passed in October just past. This commission will hold its first meeting early in April and when organized, I am sure will try to develop recommendations in a very systematic way for the efforts that they think we and others should make in advancing work against the digestive diseases.

NUTRITION PROGRAM

Mr. FLOOD. Your budget proposes to spend $9.6 million for nutrition research.

We were talking to the cancer people, and we take a look at the Cancer Institute, and we see they plan to spend $7 million for nutrition.

How do these two programs differ, and how do you coordinate this work in the area of nutrition?

Dr. WHEDON. The efforts of the Cancer Institute are, I think, very highly focused on the special nutritional problems of the cancer patient, most obviously with respect to the maximal maintenance of good

health in the patient who is burdened with tumors, but also in investigation of the extent to which the nutritional status or intake may make an individual susceptible to the development of cancer. Our efforts are not in that direction at all. The major emphasis in our programs as recommended to us recently by an advisory group which met just 2 months ago are and should be in obesity, nutritional anemia, nutritional role of trace elements, dietary fiber and supportive nutrition. The latter has to do with the means of providing best nutrition in all kinds of other diseases including anemia. We shall get more into the trace elements problem and a new and very interesting area is that of the effects of dietary fiber. Fiber is certainly in all of the television commercials nowadays, all of the ads with regard to cereals and breads and to overstate the situation, fiber seems to be the answer to protection of the intestinal tract from everything.

Obviously that is not true, but it is a very important element in the diet and its usefulness in preventing disease, particularly of the lower intestine and, in fact, in protection from or possible prevention of cancer of the colon, is to be investigated.

COORDINATION OF BLOOD RESEARCH ACTIVITIES

Mr. FLOOD. You are asking for approximately $11 million for research on blood disorders. As you know, the Heart, Lung, and Blood Institutes were just here, and they are requesting $55 million for blood research. Maybe Dr. Fredrickson, you could tell us why more than one institute on blood research?

Dr. FREDRICKSON. I would be glad to answer that, Mr. Chairman. I have to ride the fences all the time.

This is but one example of many in which the territory of the Institutes seem to overlap, and I think that it is both good and inevitable that they do. The progress of biology is eroding the boundaries between all the Institutes and trying to keep them trim, in an effective and functional way, is a very important managerial problem. But it is also very important that more than one Institute fund a categorical area, because there is, for example an important difference between the Heart, Lung, and Blood Institutes emphasis on a certain number of specific diseases and on blood products and the emphasis of the Arthritis Institute which is much more concerned about the biology of the bone marrow and the production of blood.

Mr. FLOOD. You are the director. How do you coordinate these blood research activities?

Dr. FREDRICKSON. I meet with the Institutes one after the other, and I say, "What are you doing?" and I watch the areas carefully and try to make sure that we nurture a good relationship between them. They also talk to each other, particularly with reference to the dual assignments of research grants, to insure that each is doing its share to maintain a particular area. I think this maintains a very healthy system. This is only one of many areas where we have this problem—and its a good problem at NIH because it is important that this overlap always be there.

Mr. FLOOD. I asked the right person.

Dr. FREDRICKSON. I think you did in that case, Mr. Chairman.

Dr. WHEDON. I would just footnote that there is an actual, in-being, NIH coordinating committee on nutrition with membership from many institutes

PREVENTION AND TREATMENT OF KIDNEY DISEASES

Mr. FLOOD. You talked in the past about the escalating cost of treating kidney disease, and this year we understand that in the medicare trust fund there will be about $600 million spent for dialysis treatment. Are you making any progress or understanding on the causes of kidney disease?

Dr. WHEDON. Yes, Mr. Chairman, but not nearly as rapidly as we wish.

Mr. FLOOD. You talked about escalating; you are going to escalate the treatment?

Dr. WHEDON. I was talking a little bit ago about some of the accomplishments in the artificial kidney-chronic uremia program, but, of course, the ultimate answer to this situation of chronic kidney disease is in getting at the causes and preventing the disorder, treating the illness early so that people don't wind up with end-stage chronic kidney disease. Thus, we are emphasizing now as much as we can, study of glomerulonephritis, the inflammation which affects the filtering system in the kidney, and we also have a particular interest in kidney stones because ultimately stones, if untreated, may lead to obstruction, and with that to chronic kidney disease.

Mr. FLOOD. Are you talking about dissolving the stones?

Dr. WHEDON. That is to be seen. Attempts made in the past to dissolve kidney stones have been largely fruitless, but time have changed, and we have learned more, I would hope; the direction now is more toward prevention, especially of recurrences. In the new program which we are just organizing this year, specialized centers of research in kidney disease, the first group will be on urolithiasis or kidney stones.

LENGTH AND FREQUENCY OF DIALYSIS TREATMENT

Mr. FLOOD. Last year, you told us you were looking at the effectiveness of a shorter dialysis time. What have you learned so far about this, and will it also result in lower treatment cost?

Dr. WHEDON. In order to get the answer to that question about 6 months ago we launched, through contract support, a cooperative study involving many different centers, ultimately 10 to 12, to analyze this very situation. The response of patients treated in various centers with differing systems, particularly with regard to lengths of dialysis and frequency of dialysis will be compared in an effort to determine at the current stage of our knowledge what the best kind of treatment is.

Mr. FLOOD. We are talking about shortening the time and keeping the cost down.

Dr. WHEDON. Exactly, so obviously we are going to look particularly at the results with regard to protection of the patients and maintenance of well-being and health in those centers that have the shortest treatment time and thus keep the cost down.

Mr. FLOOD. How much will you spend on kidney research in 1977 and 1978?

Dr. WHEDON. In 1977, the total funding for the kidney urology program was $23 million, and in 1978 it will be $24.3 million.

COORDINATION OF KIDNEY RESEARCH WITH THE VETERANS' ADMINISTRATION

Mr. FLOOD. We understand that the Veterans' Administration is spending $4 million to $5 million annually on kidney research. How do you coordinate your activities with that agency?

Dr. WHEDON. We are in very close coordination with the Veterans' Administration, particularly in the area of hemodialysis, artificial kidney treatment, because they have a very large network of artificial kidney programs. Dr. Burton is in charge of our artificial kidney program and may have a word to say about coordination with VA.

Mr. FLOOD. Then, for the record, we want a brief description of the research that you support in kidney disease and a description of the kidney disease research supported by the Veterans' Administration, a statement of how they do this and how these different activities will complement each other.

[The information follows:]

KIDNEY DISEASE RESEARCH SPONSORED BY THE VETERANS' ADMINISTRATION

During fiscal year 1976, the Veterans' Administration supported approximately 600 projects in the area of kidney and urinary tract disease research. The VA research funds expended for these projects were approximately $6.4 million with an additional $2.5 million received from other than VA sources. In many instances, funding for a project was shared between VA and the NIH or nongovernmental sources.

Both formal as well as informal liaison between the VA and the National Institute of Arthritis, Metabolism and Digestive Diseases occur on all research receiving combined support. One such example is the artificial kidney program's support of the nutritional and metabolic aspects of a VA cooperative study combining hemodialysis and peritoneal dialysis.

KIDNEY AND URINARY TRACT DISEASES, RESEARCH SPONSORED BY THE VETERANS ADMINISTRATION—FISCAL YEAR 1976

Category	VA funds	Percent of total	Number of projects: Receiving VA research funds	Number of projects: Not receiving VA research funds	Number of projects receiving other research funds
Normal structure and function—kidney	$2,183,609	33.9	96	52	20
Renal disorders	1,446,970	22.5	70	62	18
Transplantation	1,071,087	16.6	38	24	15
Renal failure and dialysis	814,467	12.7	47	62	17
Urinary tract disorders and infections	530,779	8.2	35	47	9
Urolithiasis	150,734	2.3	6	5	
Neoplasms	245,475	3.8	18	35	11
Totals	6,442,969	100.0	310	287	[1] 90

[1] Total funds approximately $2,500,000 in fiscal year 1976.

COLLABORATIVE EFFORTS WITH THE VETERANS' ADMINISTRATION

Dr. BURTON. Mr. Chairman, we have liaison members who go to the Veterans' Administration when they plan one of the large new studies on end-stage kidney disease treatment and vice versa, and, in fact, we have sometimes collaborated, so the same center that is funded by them

for one type of research will pick up different data we need for another type of research and we save cost in this particular way.

Dr. Whedon mentioned before the rejuvenation and renaissance of peritoneal dialysis. We got together with the Veterans' Administration the moment we heard they were interested in it. They are funding a large study on peritoneal dialysis that covers more than 12 centers, and we have plugged in studies of our own on nutrition and metabolic aspects in two centers in order to make these parallel interests more effective at a fraction of the ordinary cost. Dr. Whedon mentioned the national cooperative clinical trial on shortening dialysis time and decreasing cost to be able to treat patients in 3 or 3½ hours rather than the usual 5½ or 6. The VA will have units in that collaborative study.

1978 TRAVEL INCREASE

Mr. FLOOD. For a change this sounds very good. Don't miss the opportunity to develop that one.

Here is something, Doctor; we went at some length last year, and we complimented you on holding down your travel costs. When we look at your travel budget for 1978, 25-percent increase, why such a large increase? Didn't you like the compliments we were giving you, or what was the reason for that?

Dr. WHEDON. I would say at the outset that I think we have always been extremely conservative in our travel costs.

Mr. FLOOD. We said that.

Dr. WHEDON. All right; repetition is good sometimes.

Mr. FLOOD. Sometimes.

Dr. WHEDON. But on that base, we are faced this year with considerable increases in program. We have a substantial increase in the research budget for the diabetes program, and we have two new centers programs in arthritis and in diabetes. This has resulted in a tremendous number of applications that have come in. These have to be reviewed. We have to cover the travel of our consultants; we have to cover the travel of our staff, individuals who actively participate in onsite visits for the review of these applications. The actual increase is $100,000, and as my administrative people price this out, they tell me that this is a rather minimal figure that we need in order to give appropriate review to the expansion on these programs.

Also, I am reminded of the new kidney centers program, which I mentioned a moment ago, and in conjunction with the diabetes and arthritis centers programs there are various workshops and symposia that have been recommended to us by the National Commissions that we ought to undertake. All of these activities require travel, and if we are to expand over that conservative figure we had before in our activities, we have to have money to do it.

Mr. FLOOD. Good question; I hope it is a good answer. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

GRANT APPLICATIONS IN DIABETES

Mr. PATTEN. In your prepared statement you mentioned the request for applications for support of diabetes research on aspects such as viral etiology, genetic factors, and vascular and neurologic areas. Does not this RFA infringe on the jurisdictions of fellow Institutes such as NIAID, NIGMS, NHLBI, and NINCDS? Does the NIAMDD have the expertise to evaluate these requests which touch on those specialties of the other Institutes?

Answer. In implementing the directive for greater effort in diabetes research through the funds added for the purpose in the budgets of several institutes, it was decided that it would be more efficient to put out the call for applications in a single notice rather than in several separate ones. Let me assure you that this request for applications for support of research on a wide variety of aspects of diabetes does not infringe on the rights and jurisdictions of our fellow Institutes. They are familiar with this RFA and they also know that certain of the applications which result from this solicitation will end up in their portfolio of approved grants to support. This was simply a more rational way to handle this matter, in a central, uniform fashion, especially since the majority of the funding will be underwritten by this Institute.

Apropos the second portion of your question, let me emphasize that the scientific evaluation of the resulting applications, as is the case in any research application to the NIH, will not be in the hands of individual Institutes. The primary review for scientific merit will be carried out by so-called study sections—groups of non-Federal experts in the relevant scientific disciplines who act as consultants for the NIH specifically for review of the scientific merit, feasibility, and promise of grant applications in particular specialized fields of research. The study sections are operated by the Division of Research Grants, NIH, to promote primary review by discipline, for all of the various Institutes.

VITILIGO RESEARCH

Mr. STOKES. What has the National Institutes of Health done so far in research of vitiligo?

Answer. A recent analysis of current research activity related to vitiligo shows that fundamental studies in photobiology, skin pigmentation, and pharmacology are being supported in an effort to increase our knowledge in these areas which may later be clinically applied to patients with vitiligo and other serious dermatologic diseases. Six projects were so identified at the National Institutes of Health by our analysis. Also, we organized a workshop on vitiligo which was held on March 3 and 4, 1977, at the NIH, and was attended by scientists from various disciplines and by representatives of the National Frontiers Vitiligo Foundation, Inc., to focus on those aspects of the vitiligo problem that hold the most promise for future research progress.

Mr. STOKES. Why has so little research taken place?

Answer. Although the number of projects being supported may seem small, there are many more projects being supported in areas not specifically labelled vitiligo that are concerned with pigment-hormone relationships and with dermatology in general and which are expected to have considerable impact on solving the problem of vitiligo by serving to increase our understanding of fundamental processes in the skin. This, in turn, can provide the rational basis on which to design truly effective treatment for vitiligo. In addition, stimulation of new ideas and directions in vitiligo research has been needed and we hope to have provided some of this by giving the opportunity for researchers from various different scientific disciplines and clinical areas to come together at our March workshop and to exchange new ideas and approaches to be introduced into research in vitiligo.

Mr. STOKES. Do you intend to initiate research in this field?

Answer. In line with the recommendations that have come out of the workshop, the institute does indeed plan to encourage research applications in vitiligo and related areas of dermatology research.

Mr. PATTERN. If so, how much money would be necessary to conduct significant research?

Answer. We believe that significant research is being conducted in dermatology from which will come the answers to the vitiligo problem. Designating specific sums for a particular disease about which much of the fundamental processes are unknown might actually hinder the basic studies so vitally needed to lay the foundation for understanding many skin disorders including vitiligo. Our total budget for fiscal year 1977 for skin disease research is $5.4 million.

Mr. STOKES. Can this research be funded by reallocating existing funds or would it require an increased appropriation?

Answer. The kind of research effort that is really needed—long-term, sustained fundamental studies in dermatology—requires sequentially increased appropriations for dermatologic research and training.

PRIORITY OF FUNDING

Mr. MICHEL. Your Institute covers a wide variety of diseases, and we perhaps get more lobbying on behalf of the diseases covered here than for any other Institute. What is your personal opinion on the priority of funding within NIH? Do you feel that perhaps too much attention and funding are given to such areas as cancer, and are thus hurting the efforts of your Institute?

Answer. Let me put it this way: I definitely feel that the diseases for which the NIAMDD bears responsibility represent important national health problems and that they should receive appropriate research attention and funding; moreover, we do not believe that they receive enough of the wherewithal to follow up on all of the current promising research leads that should be explored promptly and adequately. Needless to say, I cannot argue with the importance of a category of terrible diseases like cancer; it should not be said or assumed that too much attention and funding are given to cancer. It is possible at the same time to take a view that if specific diseases that are in the limelight are given a large share of the funds for research at NIH, since the overall funds that can be allocated to the NIH are limited, then the remaining diseases which are just as important to the patients afflicted with them, and to their families, may not be funded adequately.

Mr. MICHEL. When the Congress starts directing that certain diseases be given priority, as has been done with diabetes, arthritis and certain others in your Institute, it tends to upset your game plan and reduce funding for other disease areas, does it not?

Answer. The Congress already has the authority to express what it perceives as a reflection of public desires when it singles out a particular disease for add-on funds special treatment. We would prefer, of course, to apply emphases as our own professional judgment and that of our advisers, particularly our National Advisory Council, indicate is best for improvement in health for the greatest number of people. Incidentally, in 1977 diabetes was the only NIAMDD program to receive a major increase; arthritis received only a minor increase and that was to initiate the new multipurpose arthritis centers program.

EARMARKING OF FUNDS

Mr. MICHEL. What do you think of this business of Congress singling out certain diseases for favorable treatment?

Answer. Most of these disease areas are very important national health problems. Singling out specific diseases for favorable treatment, however, may indirectly cause other diseases to have insufficient resources for us to cope with their problems optimally and to capitalize on scientific opportunities when they become available. The case for general increases in funding versus specific earmarking is based on the interrelationship of bioscience across and through many disease areas. In many diseases true breakthroughs may well come when new knowledge is created in other fundamental disciplines which interact in the basic underlying processes involved in the various disorders. Thus, for instance, the problem of diabetes may well not be fully solved until we have attained much more, necessary knowledge in basic endocrinology and metabolism which is inextricably built into the matrix of this disorder. In other words, an overall major gain in fundamental biomedical knowledge across many disciplines is actually likely to be more important for ultimate solution of a specific disease than a moon-shot" type, heavily focused effort.

UNRENEWED PROJECTS

Mr. MICHEL. During the current fiscal year, and not taking into account any increases which may be provided in the supplemental, how many ongoing projects or grants will not be renewed because of a shortage of funds due perhaps in part to the siphoning off into other areas?

Answer. No ongoing (noncompeting) grant commitments will fail to be continued in 1977. The situation is simply that a smaller proportion than normal of competing new and renewal applications will be funded in the areas without special attention.

Mr. MICHEL. Are we losing a significant body of research by not funding these renewals, or is it only a minor loss?

Answer. As I mentioned, the yearly continuations of existing noncompeting research grants are being paid by us until the grant expires; competing renewals (applications from studies whose support has expired) and new applications will have greater competiton for fewer funds.

PERCENTAGE OF FUNDING

Mr. MICHEL. Of the grant applications in the fields covered by your Institute which have been received this year, what percentage will receive funding? In turn, what percentage of those approved by the study sections will receive funding?

Answer. Customarily about one-half to two-third of applications receive study section approval; in 1977 in the nine programs other than diabetes only 27 percent, as an average, of study section approvals will be funded.

ARTHRITIS RESEARCH

Mr. MICHEL. How much will you be allocating for arthritis research. And how does this compare with the current year?

Answer. In 1978, $25,761,000 has been allocated for arthritis research. In 1977 the comparable figure was $22,389,000.

ARTHRITIS CENTERS

Mr. MICHEL. How much is being allocated for the arthritis centers? And how many will be established?

Answer. In fiscal year 1977 we have been directed by the Congress to spend $2.5 million for multipuruose arthritis centers. We estimate that 8 to 10 centers will be awarded. In 1978, $4.2 million is provided in the President's budget for this purpose.

Mr. MICHEL. Have locations for these centers been picked as yet? And if so, where?

Answer. We have received 68 applications for the funding of arthritis multipurpose centers in fiscal year 1977 and these are now being reviewed. These applications will be reviewed carefully and thoroughly for merit and for consistency with the guidelines established for these centers. The review process will be completed in August and the awards made in early September.

U.S.-U.S.S.R. COOPERATIVE MEDICAL PROGRAM

Mr. MICHEL. What is the nature of this cooperative trial in the field of arthritis you are undertaking with the Soviet Union? Can you describe the mechanics of it?

Answer. About 1970 the United States first entered into an agreement with the U.S.S.R. for the purpose of cooperative medical studies in three areas, cancer, heart disease, and environmental health. In 1973 the agreement was extended to include arthritis. After meetings of rheumatology scientists of the two countries held both in the United States and in Russia, three principal problem areas were selected for joint efforts: evaluation of therapeutic modalities, microbiology and immunology, and orthopedic treatment including surgery. The most evident progress has been made in the first two categories and to keep my comment brief, I shall mention only some highlights.

A detailed protocol has been adopted for parallel studies in the two countries of two dose levels of a drug called d-pencillamine in treatment of rheumatoid arthritis, and patients in New York nad Moscow are being entered into the study. A second study to compare the characteristics of juvenile rheumatoid arthritis in the two countries has begun using mutually agreed on forms devised specifically for computer analysis in both countries.

Finally, a colony of mice, such as those which have been available in this country for several years and which spontaneously develop a disease similar to lupus erythematosus in man, has become available in Moscow. This development will enable a joint project for the testing of drugs newly developed in both countries and has significant potential for benefit to the treatment of lupus in human beings.

SYSTEMIC LUPUS ERYTHEMATOSIS

Mr. MICHEL. Can you tell us how much your Institute and others are spending, both directly and indirectly, on systemic lupus erythematosus (SLE)?

Answer. In 1976 our institute, the National Institute of Arthritis, Metabolism, and Digestive Diseases, spent approximately $1.1 million on research directly related to SLE. The National Institute of Allergy and Infectious Diseases, the other institute with major direct support, spent about $900,000. In addition, there are numerous other research projects supported by nearly all of the institutes at the National Institutes of Health which are indirectly related to SLE or in which only part of the program is related to SLE. The amounts are not significant.

Mr. MICHEL. I understand that in addition to the SLE research being conducted at your own facilities, some 100 other studies are being funded. Are there certain institutions where most of this research is being done that you can list for us?

Answer. Major centers of research on SLE include:

University of California at San Francisco, University of Connecticut at Farmington, Cornell University Hospital of Special Surgery in New York City, New England Medical Center in Boston, Robert Breck Brigham Hospital in Boston, Rockefeller University in New York City, Scripps Clinic and Research Foundation in La Jolla, Calif., University of Texas Southwestern Medical School in Dallas, and University of Virginia in Charlottesville.

Mr. MICHEL. Are we making any headway in finding solutions to this disease?

Answer. We are making some headway, but much more needs to be learned about SLE. We are fortunate in having experimental models of this disease in certain inbred strains of New Zealand mice and pedigrees of dogs. Certain viruses stimulate the emergence of this disease, but this is by no means the whole answer. Recent incidence indicates that there are genetic forces at work with some tendency for lupus to occur in certain families; one of our grantees has found an increased incidence of certain tissue types (HLA antigens) in SLE. Since 90 percent of lupus occurs in females, increasing attention is being paid to sexual hormones; androgens (male hormones) have been shown by one of our grantees to impede the development of SLE in the mouse model of SLE. Much research on SLE concerns immune abnormalities and there are promising leads, with therapeutic possibilities, from those investigations. Overall, therapeutic management of lupus has improved considerably, mainly through more judicious use of corticosteroids, in recent years so that the prognosis, the outlook for lupus patients has considerably improved.

Mr. MICHEL. Do you know how much in the way of nongovernmental funding is being spent for SLE research?

Answer. There is no precise way of knowing but I would say that such funding is of a relatively low order of magnitude.

DIABETES

Mr. MICHEL. How much is in your budget for diabetes research?

Answer. In fiscal year 1976, we spent $14.5 million in our diabetes program. The estimated expenditure for this program in other programs and in closely related research in fiscal year 1977 is $35.7 million—roughly a 2½-fold increase. In 1978 within the President's budget the allocation will be $34.0 million. For diabetes and closely related research the amounts will be: 1977, $39.7 million and 1978, $37.9 million.

Mr. MICHEL. As you indicate in your statement, there has been a 2½-fold increase in diabetes research grants due to increased funding. Are sufficient grant applications coming in to make use of these funds?

Answer. We have broadcast widely a request for applications (RFA) for supportive research on a wide variety of aspects of diabetes, including its possible viral etiology, genetic factors, normal and abnormal hormonal actions and metabolic regulation, the relationship of diabetes to nutrition and obesity, the vascular, neurologic, and renal complications of the disease, and potential, future new treatment methodologies, such as transplantation of insulin-producing cells and automatic blood glucose regulating assist-devices. We have thus far received nearly 300 grant applications in response to this RFA. In addition, I should add that we always receive a large number of applications every year in diabetes as in our other disease areas, even without resorting to a special widely published request for grant applications.

Mr. MICHEL. Are you funding lower priority applications than in other areas, due to the substantial increase in funds?

Answer. This is a very astute question. Since we have such greatly increased sums available in 1977 to fund research grant applications in diabetes, we can well anticipate that we shall fund not only the absolute highest priority approved applications—such as is the case in our other disease areas where our funds are limited—but that in diabetes a number of grants with somewhat lower priorities than other diseases will also be funded this year.

Mr. MICHEL. Do you think the diabetes funds have been increased too rapidly and that perhaps they are not being used as effectively as possible because of this?

Answer. Although this is a possibility to be considered whenever a new program is started or an on-going program expanded, I do not think that this will be so in this case. The National Diabetes Commission made its recommendations for funding of research, training, and related activities from careful deliberations involving many experts in diabetes and related fields called in to discuss this matter with the Commission. The funds thus far provided by the Congress are well within the Commission's recommendations.

DIABETES CENTERS

Mr. MICHEL. How much are you allocating for diabetes centers, and how many centers will be funded?

Answer. We have just started the review process for the applications for funding of multipurpose diabetes centers. The amount provided in the 1977 budget is $6 million for these centers. The careful and thorough review process of 14 applications is just beginning. We estimate that five or six centers awards will be made by early September. In 1978 within the President's budget, funds available for this purpose will not permit an expansion of this new program.

BLOOD RESEARCH

Mr. MICHEL. How does your research on blood differ from that conducted by the Heart, Lung, and Blood Institute?

Answer. The NIAMDD mission to alleviate or cure specific chronic diseases requires fundamental research into metabolic, immunologic and other blood aspects of resulting secondary blood disorders such as the anemias of chronic renal failure, arthritis, and nutritional deficiencies, and of hereditary blood disorders. Also, the accessible blood cells provide models for numerous biological processes. The NHLBI blood research program emphasizes investigation of certain specific blood diseases, such as sicklecell anemia, and of the various disorders of blood coagulation, plus development or improvement of various blood products for transfusion in treatment of many diseases.

ARTIFICIAL KIDNEYS

Mr. MICHEL. Where do we stand at present regarding the development and use of artificial kidneys?

Answer. As you know, we have a special program, the artificial kidney-chronic uremia program, in our Institute for this purpose. In the past, it has been instrumental for sponsoring and stimulating most of the developments in this area. These are some of the recent developments during the past year:

Patients treated by maintenance hemodialysis are limited in mobility and rehabilitation by the need to conform to a treatment schedule developed by their dialysis centers. Although the introduction of home hemodialysis has permitted great flexibility in scheduling daily activities, the patient cannot be separated

from a dialyzer for more than 2 or 3 days. To permit dialysis patients to travel in connection with work or vacations, Dr. Eli Friedman and associates at the SUNY Downstate Medical Center in Brooklyn developed a "suitcase artificial kidney," a portable compact dialysis system which is fully contained in a small aluminum suitcase and flight bag (the latter used for carrying accessories). During this last year, 12 patients used these suitcase artificial kidneys during travels both in the United States and abroad, dialyzing themselves in various locations in their hotel/motel rooms. In multiple dialyses for as long as 6 weeks on the road, patients fared as well as they did previously in center or home dialysis. Patient acceptance of this new development which promises to improve the quality of life on dialysis, has been uniformly good.

In another area, the Institute has placed considerable emphasis on further research and development in the field of peritoneal dialysis, an alternate mode of dialysis which has been known for many years but which has not been used frequently in the past because of its high cost and time requirements. This situation has now changed completely. Research sponsored by the Institute has resulted in the development of a permanent access device to the peritoneal (abdominal) cavity (the implantable Tenckhoff catheter) which permits relatively simple and repeated access for purposes of peritoneal dialysis. Subsequently, fully automated, closed-cycle peritoneal dialysis machines were developed which can be used in a center setting or in a patient's home for maintenance peritoneal dialysis at a considerably lower cost than before.

During the last year, while some investigators have demonstrated the feasibility and relatively low cost of home peritoneal dialysis, others, to avoid the long 10-hour treatment sessions, have demonstrated the feasibility and efficacy of daily peritoneal dialysis in the evening, with and without automated dialysate delivery systems. Using today's techniques, the rate of peritonitis due to microbial contamination has been reduced considerably and has been reported to be as low as 0.2 percent in daily self-dialysis. Also, in peritoneal dialysis, access is simpler, less critical and, in home dialysis, in case of a mishap, less fraught with serious risk. One should also mention that peritoneal dialysis invaluable for special groups such as patients with serious blood access problems, or with severe cardiovascular disease, for those of advanced age, and for diabetic patients in whom it does not appear to induce as rapid a loss of vision. Moreover, because it is simpler to learn and perform than is home hemodialysis, it may be used by patients who live alone who are otherwise not eligible for home dialysis.

In closing, I would like to mention a new type of artificial kidney treatment with importance for the future. Several years ago the artificial kidney program pioneered a completely new concept of blood purification for uremic patients based on a man-made imitation of the function of the natural filtration apparatus (glomerulus) of the kidney. This new technique—hemofiltration—has now reached the point where over a hundred patients have been on routine treatment for up to 1 year. The majority of these patients have been treated abroad where special circumstances facilitate a more rapid introduction of new machinery and clinical methods as well as government reimbursement of the treatment method in experimental patients. The clinical results of hemofiltration appear to be superior to those obtained with conventional hemodialysis (the patients are uniformly less uremic, their blood pressure—even in the most recalcitrant cases—is easily and effectively controlled, and they emphasize a true feeling of well being), and the artificial kidney-chronic uremia program has started intense efforts for extensive and larger scale clinical trials in the United States.

Mr. CONTE. In the 1977 appropriations bill, we provided for a $28.2 million increase over the previous year for your institute. I understand, however, that after congressionally mandated diseases were taken care of, a very small amount remained for so-called nonmandated disease research. We will be providing an increase in that area in our supplemental bill, but I wonder if you would care to comment on the problems you may have had and especially the need for increased funding outside of the specifically mandated areas?

Answer. There is indeed a great need for additional funds in all the other important disease areas of the institute which did not receive specific congressional mandates and, correspondingly did not receive specifically earmarked increases in fiscal year 1977. All of the programs other than diabetes received no increases to speak of while at the same time the funds available for them have lost purchasing power corresponding to the inflationary erosion of the

dollar and the increasing cost of doing sophisticated biomedical research. In 1976 these programs were able to fund, on the average, 45 percent of study section-approved, competing research grant applications; this percentage has dropped to 27 percent in fiscal year 1977. This means that some very excellent competing research grant proposals from some of the better, if not best, research workers in these fields simply cannot be funded.

Mr. CONTE. You mentioned that you have prepared special reports in a number of major fields. Will those reports be printed or summarized in the hearing record. If not, would you see that my office receives copies?

Answer. We have prepared annual reports for the Congress in the following fields: arthritis, diabetes, digestive diseases, kidney disease, nutrition, cystic fibrosis, and Cooley's anemia. We have delivered copies to the committee and have been assured that they will be included in the hearing record.

Mr. CONTE. You raised the possibility of an inherited susceptibility to infectious agents as a cause of arthritic diseases. Are you suggesting that arthritis may be contagious? What sorts of infectious agents are you looking at?

Answer. At the moment it is still too early and our state of knowledge is still incomplete so that I cannot give a hard and fast reply. Preliminary evidence, however, suggests that certain cases of rheumatoid arthritis are related to an infectious agent. For instance, in the new type of arthritis, which appeared in Connecticut and which was termed "Lyme arthritis" for the town around which the cases have been found, the disease picture indeed appears to be of infectious origin, and it is believed that the infectious agent was spread by an insect. Of course, we have always had infectious types of acute arthritis, such as joint infections and joint damage caused by the organism responsible for gonorrhea; similarly other types of septic arthritis were at one time not uncommon, but most of them can be managed nowadays with the aid of proper antibiotic therapy. I did mention in previous testimony an apparently significant correlation between inherent tissue antigen types (peculiar blood proteins) and the incidence of special types of arthritis such as rheumatoid spondylitis or Reiter's disease; here some investigators postulate that an underlying susceptibility is inherited and that an as yet unknown infectious agent, possibly a virus, is involved in triggering the arthritis proper.

Mr. CONTE. If you can identify risk-prone individuals, what sorts of preventive measures can be taken to ward off arthritis?

ANSWER. In general, in our present imperfect state of knowledge there are no specific measures that can be advocated today to prevent, in the strict sense of the word, some of the most important types of arthritis such as osteoarthritis or rheumatoid arthritis. What we can do in these forms of arthritis is to attempt to prevent deformity and disability. With judicious use of physical therapy and a variety of drugs, deformity can often be delayed and sometimes prevented. The picture is quite different in another type of arthritis, namely, gouty arthritis. Here our research of the last 15 years has given us the means to manage well the patient who suffers from the inherited metabolic disorder which underlies gouty arthritis. Here, once the patient has been identified, the painful attacks of gouty arthritis can now be treated and in fact prevented, and further progression of the disease can be prevented with proper drug therapy.

Mr. CONTE. Could you provide more information about the origin and investigation that has been undertaken of "Lyme arthritis"?

ANSWER. As I was describing a moment ago, "Lyme arthritis" has received this name because all the cases of this type of arthritis known today have appeared in or around the town of Lyme in Connecticut. The cases of the disease have appeared in clusters which seem to indicate that they have been spread locally possibly by an insect vector. A team of investigators from Yale University School of Medicine, including grantees of our institute, has characterized this disorder by a painful swelling of the large joints which often follows a skin rash or skin lesion resembling insect-borne infections. Not all the patients with a skin lesion developed arthritis symptoms, but the ones who did, all had the special types of antibodies in their blood which are peculiar for a viral infection. This, the researchers said, supports the hypothesis that the arthritic manifestations of this disorder are caused by a virus spread by an insect vector, but the virus has not yet been identified.

Mr. CONTE. Could you provide a breakdown showing the percent of funded new and competing regular research grants in the various disease categories under your Institute's jurisdiction for this year and last year? And can you include some sort of projection under your budget request?

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES, REGULAR RESEARCH GRANT FUNDING ESTIMATES

[Dollar amounts in thousands]

Disease category	1976				1977 estimate [1]				1978 estimate [1]			
	Noncompeting grants	Competing grants			Noncompeting grants	Competing grants			Noncompeting grants	Competing grants		
		Applications	Funded	Percent		Applications	Funded	Percent		Applications	Funded	Percent
Arthritis	$10,598	$7,328	$3,151	43	$10,597	$8,583	$2,304	[2] 27	$8,840	$11,683	$5,413	[2] 46
Orthopedics	6,048	4,900	1,617	33	5,348	6,368	1,494	[2] 23	3,605	8,931	4,266	[2] 47
Skin	3,000	2,289	1,007	44	3,315	2,350	512	22	2,396	3,655	627	17
Diabetes	6,505	5,625	3,094	55	6,923	([3])	14,458	([3])	([3])	([3])	([3])	([3])
Endocrinology	12,703	10,389	3,948	38	11,103	13,750	3,788	28	11,048	15,545	3,233	21
Metabolism	17,140	11,052	4,863	44	16,201	14,000	4,300	31	13,887	18,428	6,163	33
Digestive diseases	13,113	10,645	5,003	47	12,150	13,200	3,715	28	12,809	14,316	3,312	23
Nutrition	6,052	4,504	2,522	56	5,508	5,600	2,617	46	6,048	5,837	2,573	44
Kidney, Urology	11,241	9,784	4,403	45	11,344	11,250	2,986	27	10,540	13,635	4,435	33
Hematology	7,931	4,157	2,037	49	6,405	6,450	2,550	40	7,638	6,117	1,838	30

[1] The 1977 and 1978 estimates represent more current estimates of the grant funding than those shown in the justification.

[2] Maximum estimates—no consideration of increased applications as a result of Commission report.

[3] Because not all of the applications have been received from a special request for applications in diabetes, the number of applications and percent funded cannot be reliably estimated for 1977 and no estimates can be made for 1978.

Mr. CONTE. You mentioned the issue of a request for applications to deal with the two and one-half-fold increase in diabetes research grants provided by congressional action. Do you foresee any problems in coming up with sufficient numbers of top-quality applications to use all of the funds which have been provided? Do you have adequate numbers of administrative personnel and research review panels to screen these numbers of grants and effectively administer them?

ANSWER. We do not have adequate numbers of scientific staff and administrative personnel to handle the extraordinary increase in diabetes research grant applications which we now see coming into our Institute as a result of the large increase in funds for diabetes research in fiscal year 1977 over fiscal year 1975 and fiscal year 1976. Moreover, our research review panels of outside consultants will have difficulty in reviewing this increased number of applications in the usual time period available for such action. Our Institute has not been allocated even a minimum of the number of necessary positions to provide for the additional staff needed to handle all the new activities in diabetes and arthritis mandated by congressional action. With respect to the question concerning sufficient numbers of high-quality applications needed to use up all of the new funds which have been provided for diabetes research: no doubt we will receive a large number of topflight applications; I am told that so far we have received nearly 300 altogether.

Mr. CONTE. In your statement you mentioned the appearance of diabetes in a colony of guinea pigs that seemed to be contagious. Are you suggesting that human diabetes may also be contagious?

ANSWER. I have mentioned the "spontaneous" appearance of diabetes in a colony of guinea pigs because there it appeared most likely that the lesion was of infectious origin; this was proven further when newly diabetic animals from this colony were housed with normal animals and the disorder spread to the new animals as well. This demonstrates the possibility that in animals a diabetes-like disease can cause the destruction of insulin-producing cells. This, in turn, justifiies similar suspicions in regard to diabetes-like disorders in man as well. We are not at all sure that "diabetes" is one monolithic disease and in theory it is possible that more than one specific factor may be at the root of the impairment or destruction of insulin-producing cells in the islet tissue in the human pancreas, resulting in the end in a final common picture of "diabetes." There have been advocates of this hypothesis who have pointed at strange epidemiologic clustering of new cases of juvenile diabetes in young children right after major outbreaks of viral disease in the same communities and locations.

Mr. CONTE. I was pleased to note that you have activated your contract-supported project for a comprehensive study of work being done in the field of cystic fibrosis. Can you tell me when that report will be complete? And what is the actual scope of the study?

Answer. Our staff and that of the Cystic Fibrosis Foundation, which is carrying out this study under a contract from us, estimate that this project would require between 12 and 18 months for its completion. The purpose of the study is to develop information which will accurately define the current state of the art in cystic fibrosis research and in the entire range of cystic fibrosis-related activities and to use this information to plan for future directions in research and improved patient management. The study will focus on cystic fibrosis and its complications. Its findings, however, may also have medical and scientific implications for numerous diseases including other pediatric pulmonary diseases (e.g., bronchial asthma, bronchiectasis, bronchitis) and disorders of the gastrointestitinal (e.g., celiac disease) as well as for a variety of genetic syndromes.

Mr. CONTE. Why are there so many gallbladder surgery-related deaths each year? What can be done to reduce that number?

Answer. About 300,000 surgical removals of the gallbladder and gallstones are carried out each year. This is usually indicated when the patient suffers from acute or chronic symptoms caused by the presence of gallstones in his biliary tract. The symptoms may be brought about by the chronic infection of the gallbladder which is conditioned by the presence of gallstones there or by an acute and painful crisis brought about when a stone moves from the gallbladder into the common bile duct and impacts there, obstructing the normal flow of bile to the small intestine. Normally the type of surgery involved does not involve a great mortality risk. However, some patients represent poor surgical risks be-

cause of other concurrently existing conditions such as highly advanced age or poor cardiac status, and especially when such patients are subject to emergency surgery because of an acute gallbladder attack, and there is little choice but to operate, the surgical mortality is higher than desirable. As a result there are about 6,000 deaths each year associated with cholecystectomies. As you know, our institute is sponsoring a large-scale study to demonstrate the feasibility and safety of the dissolution of cholesterol gallstones by the daily oral administration of a bile salt (chenodeoxycholic acid). We have already demonstrated the feasibility of such action and we are now trying to establish long-term safety of this procedure. In the long run we hope to demonstrate that it is possible to prevent the formation of new gallstones in gallstone-prone patients. Needless to say, this new medical treatment or possible prevention of cholesterol gallstones embodies a significant potential to decrease the annual rate of gallbladder surgery and the mortality connected with it.

Mr. CONTE. Can you tell me more about peritoneal dialysis? What advantages does it offer over conventional dialysis? How widely is it being used?

Answer. Our institute through its special artificial kidney-chronic uremia program, has placed considerable emphasis on further research and development in the field of peritoneal dialysis, an alternate mode of dialysis which has been known for many years but which has not been used frequently in the past because of its high cost and time requirements. This situation has now changed considerably. Research sponsored by the Institute has resulted in the development of a permanent access device to the peritoneal (abdominal) cavity (the implantable Tenckoff catheter). This device permits relatively simple and repeated access for purposes of flushing the abdominal cavity with a special solution. The flushing process carries out of the body the uremic impurities which tend to accumulate in patients who have lost their natural kidney function. This type of lavage is referred to as "peritoneal dialysis." Subsequently, fully automated, closed-cycle peritoneal dialysis machines were developed which can be used in a center setting or in a patient's home for maintainence peritoneal dialysis at a considerably lower cost than before.

During the past year, while some investigators have demonstrated the feasibility and relatively low cost of home peritoneal dialysis, others, to avoid the long 10-hour treatment sessions, have demonstrated the feasibility and efficacy of brief daily peritoneal dialysis in the evening, with and without automated dialysate delivery systems. Using today's techniques, the rate of peritonitis due to microbial contamination has been reduced considerably and has been reported to be as low as 0.2 percent in daily self-dialysis. Also, in peritoneal dialysis, the handling of dialysis access is simpler, less critical and, in home dialysis, in case of a mishap, less fraught with serious risk. One should also mention that peritoneal dialysis is invaluable for special groups, such as patients with serious blood access problems, or with severe cardiovascular disease, for those of advanced age, and for diabetic patients in whom, with peritoneal dialysis, a loss of vision seems to occur less rapidly. Moreover, because it is simpler to learn and perform than is home hemodialysis, peritoneal dialysis may be used by patients who live alone and are not eligible for home hemodialysis. I am pleased to say that whereas peritoneal dialysis has been used in the past primarily in cases of acute renal failure, there are now close to 1,000 patients with permanent kidney failure who are being maintained alive with the aid of maintenance peritoneal dialysis in the United States and Canada, and we think this figure will grow further.

Mr. CONTE. What are you doing to find new iron-chelating agents? Why does iron build up from repeated transfusions? Does this occur with all transfusions, or only those associated with particular disorders?

Answer. I would like to answer these questions in reverse order. Ordinarily when a patient receives one or two transfusions, it is to counteract some blood loss usually of acute nature, such as during surgery or as a result of a traumatic accident. In this particular case the matched blood which has been infused into the patient takes the place of the blood that has been lost and brings the total blood volume of the patient back to normal (or near normal) so that the patient's circulation can function effectively in supporting the body's internal activities.

When a person suffers from most types of anemia, he has an insufficient amount of total hemoglobin in his blood—the specialized substance in red blood cells which binds oxygen in the lungs and carries it to the various tissues where it is needed. Ordinarily the physician prescribes whatever is found to be the lacking

substance which prevents the patient's blood from carrying the full complement of hemoglobin; this may be iron, a very important component of hemoglobin, or vitamin B_{12} or folic acid—two vitamins which are essential for the production of heroglobin and the maturation of new red blood cells in the bone marrow.

In the case of Cooley's anemia, such therapy does not work; there is an underlying inherited defect which results in the production of an abnormal hemoglobin and very brief survival of the red blood cells which carry it. Thus far, only periodically spaced multiple blood transfusions can supply the patient with enough red blood cells to provide him with adequate hemoglobin. Unfortunately, the periodically transfused cells break down and release their iron which cannot be excreted easily. The extra iron accumulates in vital organs such as the spleen, liver or heart muscle. In the latter, it may cause cardiac dysfunction and ultimately heart failure. The physician is therefore confronted with having to walk a tightrope between prescribing for the patient an adequate number of blood transfusions so that he can function normally and holding down the number of these transfusions to stave off a serious degree of potentially fatal iron overload.

Our institute has organized a contract-supported research program to find effective and safe iron "chelating" or binding agents which would selectively bind excess iron so that it would not become deposited in vital organs but would be excreted together with the chelating agent through the bile into the intestine and carried out from the body via the feces. Obviously the ideal iron chelating agent must not only be effective in iron binding, but must be innocuous with respect to the rest of the body tissues since it would become part of the long-term maintenance treatment of Cooley's anemia and thus should not have cumulative toxic effects. The chelating agent conventionally used (desferrioxamine) lacks the desired effectiveness and causes pain when administered. Our research program has put 61 new compounds through initial screening thus far. Five have exhibited some degree of efficacy in removing iron and they will now be studied extensively for signs of toxicity in experimental animals.

Mr. CONTE. Of course the National Heart, Lung, and Blood Institute is also working on Cooley's anemia. Is there any difference in your Institute's approach to this disease as opposed to the Heart Institute's? Do you engage in any pooling of resources with the other institutes, or jointly fund research projects? How do you coordinate your efforts in something like Cooley's anemia?

Answer. In addition to developing and testing new, safe and effective chelating compounds, our own institute maintains a research grant program of fundamental and clinical research related to Cooley's anemia and to its early detection. Intramural research related to Cooley's anemia has traditionally been carried out in the laboratory of a renowned expert in the field, Dr. French Anderson, in the NHLBI. In addition, the NHLBI also has a sizable research grants program concerning blood and blood diseases and supports other aspects of mostly clinical research which are of importance directly or indirectly to our search for better knowledge in Cooley's anemia. We are in constant touch with the NHLBI and both institutes communicate effectively and freely in this area. Moreover, all of the institutes at the NIH who are engaged in some aspect of blood-related research are pooling their knowledge and communicating with each other and coordinating their activities with the aid of a very active NIH Coordinating Committee on Blood Diseases, including Cooley's anemia.

Mr. CONTE. Are there any other diseases which your institute conducts research on which are also partially covered by other institutes? Could you provide a compilation of those diseases?

ANSWER. It would be very hard indeed to find a major disease research area at the NIH in which at least some aspects are not also supported by another institute in addition to the obvious and designated lead institute for the particular disease. In the case of our own institute, the National Institute of Arthritis, Metabolism, and Digestive Diseases is the lead institute for diabetes, but many other institutes support diabetes-related research. For instance, diabetic eye disease is being investigated under the aegis of the National Eye Institute, and diabetic neuropathy under the aegis of the National Institute of Neurological and Communicative Disorders and Stroke. The list of diseases or research areas which also receive research support from other NIH institutes, but for which the NIAMDD has lead responsibility, includes the following: diabetes, arthritis, blood diseases like Cooley's anemia and others, kidney disease, digestive diseases, metabolic diseases and metabolism, diseases of the skin and the fields of nutrition and endocrinology.

Mr. CONTE. What sort of research do you have ongoing in ileitis and colitis? Do you foresee any major accomplishments in this area in the near future?

ANSWER. In the important area of digestive diseases ileitis and colitis, specifically regional enteritis or Crohn's disease, and ulcerative colitis are both grave disorders of the intestine of a chronic nature, the specific causes of which have not yet been elucidated. In either case our research is multipronged and ranges from the most fundamental aspects which could give us clues concerning the specific causative factors to the most practical and immediate aspects of finding improved methods of management. Thus, for instance, we pursue on one hand clinical trials of various modes of therapy for Crohn's disease to select the type of therapy which is the most effective and less fraught with side effects for the patient. Simultaneously we must pursue all fundamental aspects of these diseases so as to evolve rational approaches to therapy based on the precise causative factor in contrast to our current, fairly empirical approaches to treatment. In the case of ulcerative colitis, allergic reactions and autoimmunity, viral and bacterial infection, and psychosomatic factors, have all been implicated at one time or another as the basic causes of this condition, and truly effective treatment hopefully prevention, will only evolve once our fundamental state of knowledge concerning this disease has improved and the true causation been found. In the short run, we hope to improve present day treatment methods through clinical studies but major true breakthroughs leading to a true cure or even prevention are not anticipated in the immediate future.

Mr. CONTE. Your budget reflects significant decreases in competing renewals. Why? Will that change after approval of the supplemental appropriation?

ANSWER. As I mentioned in my answer to an earlier question, in fiscal year 1977 new funds for our budget were provided only through specific earmarks most of which were limited to congressionally mandated programs. Thus all the other areas either had to continue on the level of the previous year and in a few cases there were even decreases in research grants when funds were used for increased training efforts, for instance. Moreover, because of the constantly increasing cost of pursuing biomedical research and because of the yearly erosion of the purchasing power of the dollar, the same number of dollars in fiscal year 1977 buys, in fact, less research than in the previous year. Finally, when the total amount of funds in a program is the same as in the preceding year, a greater proportion must usually be assigned to noncompeting commitments. All of these factors led to a sharp reduction in funds available for approved competing renewals.

At this point the Congress has not yet finished its action on a supplemental appropriation for our Institute, therefore, I cannot tell you specifically to what extent this situation will be changed during the balance of fiscal year 1977. In general, however, I can state that any additions to our fiscal year 1977 budget would permit us to pay additional competing renewals. If these supplemental funds are earmarked for specific disease fields, this improvement will, however, only be limited to those fields.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Amounts Available for Obligation

	1977 Appropriation	1978 Estimate
Appropriation.....	$209,000,000	$216,961,000

National Institute of Arthritis, Metabolism, and Digestive Diseases

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	Number	FTE 1/	Amount	Number	FTE 1/	Amount
Research Grants:						
Regular program:						
Noncompeting projects	1,554		$102,476,000	1,547		$110,192,000
Competing renewals	272		16,497,000	174		10,545,000
New	180		10,998,000	115		7,030,000
Supplemental	(95)		1,200,000	(95)		1,200,000
Subtotal	2,006		131,171,000	1,836		128,967,000
Special programs:						
Multipurpose Arthritis centers			2,500,000			4,200,000
Diabetes Research and Training centers			6,000,000			6,480,000
Kidney Special Centers of Research			1,500,000			1,620,000
Multidisciplinary centers			5,437,000			6,318,000
Research career programs	148		4,090,000	180		5,257,000
Subtotal			19,527,000			23,875,000
Total Grants			150,698,000			152,842,000
Training Programs:						
Individual awards						
Noncompeting	115	115	1,725,000	47	47	706,000
New	48	48	687,000	158	158	2,300,000
Institutional awards						
Noncompeting	86	286	5,727,000	114	438	8,771,000
New	28	76	1,507,000	---	---	---
Total Training Programs	277	525	9,646,000	319	643	11,777,000
Research and Development Contracts	110		10,162,000	115		11,578,000
Intramural Research			30,483,000			32,634,000
Direct Operations			7,130,000			7,271,000
Program Management			881,000			859,000
Total			209,000,000			216,961,000

1/ Full-time equivalents.

DHEW - National Institutes of Health

Crosswalk - 1977 Column 1978 Justification

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

(Amounts in Thousands)

PROGRAM ACTIVITY	MECHANISM										
	Research Grants				Training Programs		Intramural Research	Direct Operations	Research and Development Contracts	Program Management	Program Total
	Regular Program		Specials								
	Noncompeting	Competing	Centers	Other	Individual	Institutional					
1. Arthritis, Bone and Skin Diseases.....	$20,219	$5,120	$2,500	$646	$523	$1,567			$1,070		$31,645
2. Diabetes, Endocrinology and Metabolism.....	40,003	17,628	8,736	1,842	749	2,245			917		72,120
3. Digestive Diseases and Nutrition.....	21,305	3,710	2,701	1,116	534	1,603			2,575		33,544
4. Kidney Disease, Urology and Hematology.	20,949	2,237	1,500	486	606	1,819			5,600		33,197
5. Intramural Research.....							$30,483				30,483
6. Direct Operations.....								$7,130			7,130
7. Program Management.....										$881	881
Total Obligations....	102,476	28,695	15,437	4,090	2,412	7,234	30,483	7,130	10,162	881	209,000

DHEW - National Institutes of Health

Crosswalk - 1978 Column 1978 Justification

NATIONAL INSTITUTE OF ARTHRITIS, METABOLISM, AND DIGESTIVE DISEASES

(Amounts in Thousands)

PROGRAM ACTIVITY	MECHANISM										
	Research Grants										
	Regular Program		Specials		Training Programs		Intramural Research	Direct Operations	Research and Development Contracts	Program Management	Program Total
	Noncompeting	Competing	Centers	Other	Individual	Institutional					
1. Arthritis, Bone and Skin Diseases.....	$20,970	$5,446	$4,200	$1,364	$688	$2,007			$1,930		$36,605
2. Diabetes, Endocrinology and Metabolism.....	47,939	5,419	9,518	2,047	930	2,726			1,276		69,855
3. Digestive Diseases and Nutrition.....	21,581	3,161	3,280	1,252	677	1,968			2,612		34,531
4. Kidney Disease, Urology and Hematology.....	19,702	4,749	1,620	594	711	2,070			5,760		35,206
5. Intramural Research.....							$32,634				32,634
6. Direct Operations.....								$7,271			7,271
7. Program Management.....										$859	859
Total Obligations....	110,192	18,775	18,618	5,257	3,006	8,771	32,634	7,271	11,578	859	216,961

Summary of Changes

1977 Estimated Obligations	$209,000,000
1978 Estimated Obligations	216,961,000
Net change	+7,961,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	---	$260,000	---	+$234,000
2. Incentive pay for additional medical officers	---	404,000	---	+106,000
3. Federal Employee Compensation Fund rate increase	---	13,000	---	+26,000
4. Federal Telecommunications System rate increases	---	26,000	---	+2,000
5. Payment for centrally furnished services	---	12,814,000	---	+709,000
(Standard Level User Charge)	---	(369,000)	---	(+45,000)
6. Increased assessment for primary review of research grants	---	496,000	---	+54,000
Subtotal	---	---	---	+1,131,000
B. Program:				
1. Net increase for noncompeting continuation grants awarded in prior years	---	112,476,000	---	+9,336,000
2. Support of 289 new and competing grants in 1978	---	27,495,000	---	+17,575,000
3. Three additional Multipurpose Arthritis Centers	---	2,500,000	---	+1,500,000
4. Thirty-two additional research career program awards	---	4,090,000	---	+1,167,000
5. Support of 118 additional individual awards	---	9,646,000	---	+2,131,000
6. Incremental cost of intramural research supplies, materials and services	---	9,921,000	---	+1,178,000
7. Increased travel for intramural research and grant and contract management	---	404,000	---	+100,000
8. Support of 5 additional research and development contracts	---	10,162,000	---	+1,416,000
Subtotal	---	---	---	+34,403,000
Total increases	---	---	---	+35,534,000

Summary of Changes--continued

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Built-in:				
1. One less day of pay in 1978....	509	$10,589,600	---	-$39,000
Subtotal.....	---	---	---	-39,000
B. Program:				
1. Completion or conversion to noncompeting status of 452 new and renewal research grants awarded in 1977.....	---	27,495,000	---	-27,495,000
2. Reduction of positions.....	36	881,000	-2	-39,000
Subtotal.....	---	---	---	-27,534,000
Total decreases.....	---	---	-2	-27,573,000
Total net change....	---	---	-2	+7,961,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
156	Arthritis, Bone and Skin Diseases.....	---	$31,645,000	---	$36,605,000	---	+$4,960,000
159	Diabetes, Endocrinology and Metabolism.....	---	72,120,000	---	69,855,000	---	-2,265,000
163	Digestive Diseases and Nutrition.....	---	33,544,000	---	34,531,000	---	+987,000
166	Kidney Disease, Urology and Hematology.....	---	33,197,000	---	35,206,000	---	+2,009,000
169	Intramural Research.....	463	30,483,000	463	32,634,000	---	+2,151,000
	(Standard Level User Charge).....		(298,000)		(328,000)		(+30,000)
172	Direct Operations.....	89	7,130,000	89	7,271,000	---	+141,000
	(Standard Level User Charge).....		(71,000)		(86,000)		(+15,000)
173	Program Management.....	36	881,000	34	859,000	-2	-22,000
	Total Obligations....	588	209,000,000	586	216,961,000	-2	+7,961,000
	(Standard Level User Charge)..		(369,000)		(414,000)		(+45,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	588	586	-2
Full-time equivalent of all other positions	63	68	+5
Average number of all employees	666	676	+10
Personnel compensation:			
Permanent positions	$12,325,000	$12,496,000	+$171,000
Positions other than permanent	895,000	1,001,000	+106,000
Other personnel compensation	296,000	298,000	+2,000
Subtotal, personnel compensation	13,516,000	13,795,000	+279,000
Personnel benefits	1,839,000	1,862,000	+23,000
Travel and transportation of persons	404,000	504,000	+100,000
Transportation of things	72,000	75,000	+3,000
Rent, communications and utilities	640,000	750,000	+110,000
Printing and reproduction	375,000	425,000	+50,000
Other services	4,918,000	5,703,000	+785,000
Payment for centrally furnished services	12,814,000	13,523,000	+709,000
Project contracts	10,162,000	11,578,000	+1,416,000
Supplies and materials	2,940,000	3,260,000	+320,000
Equipment	976,000	867,000	-109,000
Grants, subsidies and contributions	160,344,000	164,619,000	+4,275,000
Total obligations by object	209,000,000	216,961,000	+7,961,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1977 House Report	
1. "The Committee...therefore directs that a study be undertaken and completed within the next year on what is being done in research and patient care in cystic fibrosis and allied diseases." Page #32	1. A contract is being negotiated to conduct this study.
1977 Senate Report	
1. "...and the Committee recommend the establishment of multipurpose arthritis centers...." "The centers should be funded separately from other activities...to give them a maximum amount of visibility." Page #50	1. This program is being established in 1977 at a level of $2,500,000 and will be expanded to $4,200,000 in 1978.
2. "The Committee is interested in establishing SCOR centers for kidney and genitourinary diseases...." Page #51	2. Kidney Special Centers of Research are being established at a level of $1,500,000 in 1977.
3. "The Committee...directs the NIAMDD to do an analysis of the needs and priorities for dermatological research." Page #51	3. A group of experts in dermatology has been convened to make a study of the current state of the art and to identify research needs and research initiatives for the future.
4. "The Committee encourages the NIAMDD to develop a Task Force or Special Advisory Committee (on psoriasis)..." Page #51	4. A group of experts in psoriasis has been convened to conduct an evaluation study and a scientific workshop will be held.

Authorizing Legislation

Legislation	1978 Authorized	1978 Appropriation requested
Public Health Service Act		
Section 301--Research and Investigation, in general	Indefinite	$205,184,000
Title IV, Part D--National Institute on Arthritis, Metabolism, and Digestive Diseases	Indefinite	
Title IV, Part D--Diabetes Research and Training Centers	$12,000,000	
National Diabetes Advisory Board	300,000	
Title IV, Part D--Arthritis		
Demonstration Projects	3,000,000	
Arthritis Data Systems	1,000,000	
Multipurpose Arthritis Centers	18,700,000	
National Arthritis Advisory Board	300,000	
Arthritis, Diabetes, and Digestive Disease Amendments of 1976		
Section 301--National Commission on Digestive Diseases	1,500,000	
Title IV, Part I--National Research Service Awards Act	Pending	11,777,000 1/

1/ Authorization expires September 30, 1977; extension legislation is pending.

National Institute of Arthritis, Metabolism, and Digestive Diseases

Year	Budget Estimate to Congress	Comparable House Allowance	Comparable Senate Allowance	Appropriation
1968	144,239,000	144,239,000	147,489,000	144,239,000
1969	152,003,000	141,572,000	147,572,000	144,173,000
1970	137,953,000	137,953,000	155,285,000	132,046,000
1971	132,437,000	138,624,000	140,624,000	138,624,000
1972	135,879,000	148,650,000	164,075,000	153,449,000
1973	132,142,000	158,592,000	173,276,000	158,592,000 1/
1974	134,003,000	156,289,000	163,395,000	153,956,000 2/
1975	153,181,000	162,427,000 3/	178,220,000	173,265,000
1976	148,694,000	174,257,000 4/	177,257,000 4/	179,801,000 5/
1977	180,837,000	202,837,000	230,837,000	209,000,000
1978	216,961,000			

NOTES:

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by PL 93-192.

3/ Excludes amount for contracts not considered by the House due to lacking authorization.

4/ Excludes Fellowship and Training Grants--Not considered due to pending legislation ($4,344,000).

5/ Includes $4,344,000 for training programs authorized under continuing resolution.

The figures presented in this Table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

National Institute of Arthritis, Metabolism, and Digestive Diseases

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Actual Appropriation
1968	143,954,000	143,954,000	147,204,000	143,954,000
1969	146,489,000	141,287,000	147,287,000	143,888,000
1970	137,668,000	137,668,000	155,000,000	131,761,000
1971	132,152,000	138,339,000	140,339,000	137,986,000
1972	135,433,000	148,204,000	163,629,000	153,337,000
1973	159,089,000	167,316,000	182,000,000	167,316,000 1/
1974	133,608,000	155,894,000	163,000,000	153,561,000 2/
1975	152,961,000	162,207,000 3/	178,000,000	173,121,000
1976	148,409,000	173,972,000 4/	176,972,000 4/	179,516,000 5/
1977	180,837,000	202,837,000	230,837,000	209,000,000
1978	216,961,000			

NOTES:

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by PL 93-192.

3/ Excludes amount for contracts not considered by House due to lacking authorization.

4/ Excludes Fellowship and Training Grants--Not considered due to pending legislation ($4,344,000).

5/ Includes $4,344,000 for training programs authorized under continuing resolution.

Justification

National Institute of Arthritis, Metabolism, and Digestive Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Arthritis, Bone and Skin Diseases..	---	$31,645,000	---	$36,605,000	---	+$4,960,000
Diabetes, Endocrinology and Metabolism.....	---	72,120,000	---	69,855,000	---	-2,265,000
Digestive Diseases and Nutrition.....	---	33,544,000	---	34,531,000	---	+987,000
Kidney Disease, Urology and Hematology.....	---	33,197,000	---	35,206,000	---	+2,009,000
Intramural Research..	463	30,483,000	463	32,634,000	---	+2,151,000
Direct Operations....	89	7,130,000	89	7,271,000	---	+141,000
Program Management...	36	881,000	34	859,000	-2	-22,000
Total.....	588	209,000,000	586	216,961,000	-2	+7,961,000

General Statement

The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters, and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases and disorders within its purview. Research and training projects are supported in over 400 non-Federal institutions through the use of grants and contracts, the vast majority of which are awarded to universities and medical schools. Approximately 93% of the funds in these program categories are used for grants and 7% are used for contracts. In addition, the Institute conducts intramural research and clinical research projects at facilities at the National Institutes of Health in Bethesda, Maryland and at field stations in Phoenix, Arizona.

Research grant applications, initiated by the investigator, are reviewed on scientific merit and within the available funds, compete on this basis with other applicants in the same program area. Approximately 452 applicants in 1977 and 289 in 1978 will receive awards from current year funds and will be promised support for an average of two additional years. When these awards are combined with those awards made in prior years which are continuing as a result of a commitment for future support, the Institute will be supporting approximately 2,006 individual research projects in 1977 and estimates it will support a total of 1,836 projects in 1978.

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Research and development contracts are also awarded as the result of competition based on scientific merit. Proposals, in this case, however, are solicited in response to specific, well defined objectives developed by the Institute to meet special needs in the development of program objectives.

When the need becomes evident for new development, such as new, more efficient, less costly artificial kidney machines or coordinated clinical evaluation of the efficacy of various regimens in the treatment of regional ileitis, it is usually impractical and inefficient to reassign intramural scientists who have specialized and are engaged in a productive research program. It is likewise seldom that competent outside scientists will volunteer to drop their ongoing studies in favor of a new problem which has become a special programmatic interest to the Institute. In attempting to meet special needs, direct collaboration is sought with special scientific talent or resources, usually already engaged and competent in closely related efforts and techniques, through the use of research and development contracts.

In addition to universities and medical schools, both non-profit and commercial research organizations may be awarded contracts. In 1977 approximately 110 contracts will be awarded for a one year period, although future support may be planned. In 1978 approximately 115 contracts will be supported.

Previously supported programs for research training have been phased out and in their place a new program was initiated to provide for post-doctoral training in specific shortage areas in biomedical and health-related sciences only. The program is directed toward the training of individuals for full-time careers in research and/or teaching. Upon completion of their training, recipients are expected to pursue this objective for a period at least as great as the period of training and individuals who go into clinical medicine or non-health related research may be required to reimburse the Government for the cost of the training.

Under this new program, the Institute expects to support 525 fellows in 1977 and 643 in 1978.

The mission of the intramural research area of the Institute is to obtain information and knowledge for the understanding of the fundamental biological processes underlying the major diseases within the Institute's purview. Over 260 research projects including various combinations of laboratory, clinical, epidemiological and biometric investigations are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms, to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH Institutes, other government agencies and outside investigators ensure a minimum of duplication and a maximum exchange of research findings.

Arthritis, Bone and Skin Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Arthritis	---	$18,569,000	---	$21,672,000	---	+$3,103,000
Bone Diseases	---	7,728,000	---	8,930,000	---	+1,202,000
Skin Diseases	---	5,348,000	---	6,003,000	---	+655,000
Total	---	31,645,000	---	36,605,000	---	+4,960,000
Budget Mechanism:						
Research Grants						
Regular:						
Noncompeting	306	20,219,000	294	20,970,000	-12	+751,000
Competing	81	5,120,000	84	5,446,000	+3	+326,000
Subtotal	387	25,339,000	378	26,416,000	-9	+1,077,000
Arthritis Multipurpose Centers	---	2,500,000	---	4,200,000	---	+1,700,000
Research career programs	23	646,000	47	1,364,000	+24	+718,000
Subtotal	23	3,146,000	47	5,564,000	+24	+2,418,000
Training Programs 1/						
Individual	35	523,000	47	688,000	+12	+165,000
Institutional	78	1,567,000	100	2,007,000	+22	+440,000
Subtotal	113	2,090,000	147	2,695,000	+34	+605,000
Research & Development Contracts	6	1,070,000	7	1,930,000	+1	+860,000
Total		31,645,000		36,605,000		+4,960,000

1/ Numbers are full-time equivalents.

Arthritis and Related Diseases

While it is apparent that much can be done to benefit individuals with one of the many rheumatic diseases by the application of available knowledge, the ultimate causes of most types of rheumatic diseases remain unknown. The available knowledge, impressive as it is, is not complete enough to have produced specific cures, or practical methods of prevention, with rare exceptions. Symptomatic, and often effective, treatment is available for most patients with certain forms of rheumatic disease but this treatment may cause serious side effects.

The research effort of the Arthritis Program is concentrated in two major areas. The first is the support of research in the various components of connective tissue, such as collagen, and in the immunological mechanisms that play a major role in causing the inflammation associated with many forms of arthritis. The second category is related to specific research initiatives against systemic lupus erythematosus, rheumatoid arthritis, and degenerative joint disease. The remainder of the program is concerned with support for research in several other rheumatic diseases.

A program of systematic multicentered studies was instituted for clinical research in several important areas. Studies supported are those that cannot be performed by individual investigators or single research groups. Opportunities are provided to obtain new knowledge about the natural history of selected rheumatic diseases, environmental and pathogenetic factors, and to establish criteria for infrequent, but important disorders.

The Institute will, within constraints, carry out as many as possible of the recommendations of the National Commission on Arthritis and Related Musculoskeletal Diseases. Consistent with these recommendations, the Institute has announced its intent to establish a number of Multi-Purpose Arthritis Centers to develop new knowledge about arthritis, to demonstrate effective application of arthritis treatment, and to serve as educational focal points within communities.

The Institute will also continue joint US-USSR programs in collaboration with Soviet rheumatologists in arthritis research. The first cooperative trial in this field was launched in recent weeks by the dispatch of D-penicillamine to the Soviet Union. The drug will also be used in American patients participating in the trials.

Bone Diseases

The replacement of diseased joints by prostheses is a major success story in the area of orthopedics. Artificial hips are the most highly perfected of the artificial joints: implants of hip prostheses are often very successful and are widely used. Artificial knees are being inserted frequently but their longevity is at present uncertain. Developments of prosthetic elbows, ankles, shoulders, and fingers are in progress. However, there is need to develop prosthetic materials with longer life and wearability, and increased biocompatibility. It is important that more bioengineers be trained to work closely with orthopedic surgeons and researchers to develop the best possible prostheses.

Since the healing of fractures can cause the loss of productivity and work days for weeks or months at a time, any means of shortening the healing process would be a welcome discovery. The stimulation of fracture healing by electrical current has shown some promising results in animals. Several difficult non-unions in humans have also been successfully healed by mild stimulation of the bone by electrical current. This is an exciting area with potential for success.

Osteoporosis, a condition characterized by the reduction in total amount and strength of bone in the skeleton, is the underlying cause of many fractures of hips and wrists in older persons. It is estimated that 15 million persons in the United States have osteoporosis detectable by X-ray. Even though research into the factors influencing the formation and resorption of bone is being supported, present treatment does not provide much help for victims of osteoporosis. Added research into the prevention, cause, and treatment of this important disease, prevalent in older individuals, is sorely needed.

Skin Diseases

The NIAMDD has primary responsibility for supporting research into the major dermatologic diseases which include psoriasis, eczema, and allergic contact dermatoses, acne, fungal and bacterial infections, blistering diseases of the skin, vitiligo, phototoxicity and photo-allergy, collagen diseases, and genetically determined cutaneous disorders.

Psoriasis is a continuing scaline disorder of the skin that affects approximately 2% of the population. Its cause has not yet been determined, but Institute-supported research has resulted in better understanding of the morphologic, biochemical and vascular components of the disease process. It appears to be influenced by hereditary factors, but external factors are also important in the precipitation, remission, and regression of the disease. The Institute is currently supporting studies to determine whether systemic chemotherapeutic agents can be safely and efficiently utilized for control of psoriasis. A new method of management, known as photochemotherapy, which includes oral doses of a photo-active drug, methoxsalen, followed by exposure to long-wave ultraviolet light, is currently undergoing clinical investigation. The NIAMDD will support a five-year follow-up of 1,500 patients who have undergone this new treatment in order to determine the efficacy and safety of photochemotherapy. The NIAMDD plans also to support a large survey to determine the social and economic impact of psoriasis in this country.

Eczema and allergic contact dermatoses are responsible for a significant number of lost wages in this country. Following a broad-based review of immune mechanisms in dermatologic disorders by an NIAID-NIAMDD jointly sponsored workshop last year, it is the intent of the Dermatology Program to focus efforts into stimulating more research in atopic dermatitis and contact allergy.

NIAMDD-sponsored research has narrowed down the search for the pathogenesis of acne to a relationship between circulating male hormone and its effect on receptor surfaces of sebaceous glands. The technology for in vitro studies of the isolated sebaceous glands is being developed through NIAMDD-support, and it is anticipated that this area of investigation will have greater potential for advancement in the years ahead.

Bullous or blistering diseases of the skin such as pemphigus remain a threat to life, either from the disease itself or from the drugs required over long periods of time to suppress the disease. Immunologic advances within the field of dermatology will require additional support in order to understand such diseases.

Vitiligo is a genetically determined patterned loss of melanin pigment that follows the destruction of melanocytes. The bizarre patchy loss of skin color is emotionally devastating. Little research is being conducted on vitiligo. Following an NIH Workshop on Vitiligo in March 1977, the Dermatology Program will attempt to establish small regional centers for the development of more effective research and therapy for this disease.

There is ample evidence that the effects of repeated exposure of human skin to sunlight are cumulative and eventually lead to serious alterations resulting in premature aging, cancer, and a variety of light-induced diseases. Additional funding for the study of light-sensitive diseases will be required.

Diabetes, Endocrinology and Metabolism

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Diabetes	---	$32,843,000	---	$30,925,000	---	-$1,918,000
Endocrinology	---	17,147,000	---	16,891,000	---	-256,000
Metabolism	---	22,130,000	---	22,039,000	---	-91,000
Total	---	72,120,000	---	69,855,000	---	-2,265,000
Budget Mechanism:						
Research Grants						
Regular:						
Noncompeting	607	40,003,000	673	47,939,000	+66	+7,936,000
Competing	278	17,628,000	83	5,419,000	-195	-12,209,000
Subtotal	885	57,631,000	756	53,358,000	-129	-4,273,000
Diabetes Research and Training Centers	---	6,000,000	---	6,480,000	---	+480,000
Multidisciplinary Centers	---	2,736,000	---	3,038,000	---	+302,000
Research career programs	67	1,842,000	70	2,047,000	+3	+205,000
Subtotal	67	10,578,000	70	11,565,000	+3	+987,000
Training Programs 1/						
Individual	51	749,000	63	930,000	+12	+181,000
Institutional	113	2,245,000	136	2,726,000	+23	+481,000
Subtotal	164	2,994,000	199	3,656,000	+35	+662,000
Research & Development Contracts	8	917,000	12	1,276,000	+4	+359,000
Total		72,120,000		69,855,000		-2,265,000

1/ Numbers are full-time equivalents.

Diabetes Mellitus

Diabetes mellitus is one of the major public health problems of our nation today. It is common -- the National Commission on Diabetes estimates that as many as 10 million Americans suffer from this disease and that this number is steadily increasing -- and it is one of the leading causes of morbidity and mortality. Diabetics are, for example, 25 times more prone to blindness, 17 times more prone to kidney disease, 5 times more prone to gangrene and twice as prone to heart disease than are individuals without diabetes. Life expectancy among people with diabetes is approximately one-third less than that of the general population. In 1974 38,000 deaths were directly attributed to diabetes and in several times that number diabetes was primary factor contributing to death due to heart attack, stroke, and kidney failure. It is perhaps more than revealing that the direct and indirect impact of diabetes on the national economy is estimated to be more than five billion dollars per year, even without considering the cost of its complications.

Although basic and clinical research in diabetes has, over the years, significantly advanced our understanding of this disease and new knowledge is being increasingly applied in the treatment of diabetic patients, the fundamental basis of this disease remains unknown and efforts to prevent or cure it have failed to keep it from increasing in frequency and severity. There is, then, an urgent need for a major research effort into the cause, prevention, and cure of diabetes, and for the development of new and improved methods of treatment.

The impetus for this effort was provided through the National Diabetes Act of 1974 and the subsequent authorization by the Congress in October 1976 of new funds for diabetes research according to the recommendations of the National Commission on Diabetes in its Long-Range Plan to Combat Diabetes.

NIAMDD, the lead NIH Institute for diabetes research, has already begun to implement this plan, and is preparing to further expand existing, and to initiate new, programs in diabetes research in 1978 according to the specific recommendations of the Commission.

For example, NIAMDD will substantially increase its support of research into the cause of diabetes; studies by several researchers strongly suggest that there may be more than one cause of this disease. Support of research into the role of heredity, immunological factors and viruses in the etiology of diabetes will expand, as will support of studies of the relationship between diabetes, diet, and obesity.

Recent studies make it clear that diabetes is a disease not only of a deficiency of the hormone insulin, but one in which the interplay of several other hormones such as glucagon and growth hormone are of great importance. The Institute plans, therefore, to significantly expand its support of research into the character of secretion and mechanism of action of these hormones as they relate to diabetes. The discovery of a new hormone, somatostatin, and its identification as an important factor regulating the secretion of these hormones and the level of blood glucose, has provided a new tool for research in this area.

Transplantation of pancreatic islets and of the whole pancreas is of great interest as a new and potentially effective mode of treatment for diabetes. The Institute plans to increase research on pancreatic transplantation and the development of artificial devices for controlling blood glucose concentration in an effort to achieve better control of the diabetic state. At the same time, a clinical trial will be undertaken to determine whether or not the major complications of this disease are correlated with the level of glucose in the blood.

In an effort to provide a broader and more balanced attack on diabetes, and to achieve proper integration of the many planned research studies, NIAMDD has this year initiated a new program, the multipurpose Diabetes Research and Training Centers. These new centers are devoted to achieving an optimal mix of research, training, educational activities and their translation into improved health care for the diabetic. It is anticipated that five centers will be established in FY 1977, and an additional five to six centers are planned for FY 1978.

In order to insure that a national pool of high quality biomedical researchers will be available in sufficient numbers to meet the changing and increasing needs in diabetes, the Institute plan to increase its research manpower training programs.

NIAMDD intends to establish a National Diabetes Information and Education Clearinghouse as a means of addressing the need for a central resource for educational materials and information, as well as a National Diabetes Data Group for the purpose of fostering the collection, analysis, and dissemination of diabetes data related to public health policy.

Through these as well as other expanded efforts and new initiatives NIAMDD is confident that the goal of understanding and therefore combating diabetes can be approached.

Endocrinology and Endocrine Disorders

Endocrinology concerns itself with the study of the endocrine glands and their secretions the hormones, and with the effects of these hormones as regulators of the growth, metabolism, and reproduction of man. Several diseases of the endocrine system, such as goiter and other thyroid dysfunctions, Addison's disease, and other afflictions of the adrenal gland, tetany and hyperparathyroidism, and pituitary dwarfism, are not only serious but common. Thus, research in the field of endocrinology is considered one of the most important areas of Institute concern.

Since the hormones control the function of all tissues throughout the body, and these diseases are the direct result of alterations in their production or action, it is essential to understand the factors that regulate the normal production and secretion of hormones from glands, the precise mechanism by which they act to control cell function, and how these normal processes are altered in these and other disease states. NIAMDD supported researchers have begun to make considerable progress in some of these areas.

For example recent studies have greatly increased our understanding of hypothalamic control of endocrine function, providing not only new and useful knowledge about fundamental processes of physicological control and function, but also new insights into the nature and treatment of various endocrinologic diseases. One of the recent major advances achieved in this area has been the discovery, isolation and identification of a new hypothalamic hormone, somatostatin. This substance controls the release of the hormone which plays a key role in the growth and development of the body - growth hormone - and the secretion of the pancreatic hormones glucagon and insulin which are prime regulators of the body's metabolism.

There has also been significant advancement with respect to the way in which hormones control cellular function. Thus, it is now possible to measure and examine hormone binding to various cells and their constituents. Such advances not only provide new insights into the mechanisms by which hormones regulate cell function, but also improve our understanding of a variety of endocrinologic disorders.

The Institute plans to expand its support of both basic and clinical studies of hormone secretion and action in an effort to determine the factors that regulate the production and secretion of these substances and the mechanism by which they influence cellular function in health and disease.

Metabolism and Metabolic Diseases

Many pathologic states are considered to be the result of alterations in metabolic processes; diabetes, atherosclerosis, cystic fibrosis, the glycogen storage diseases, and gout are but a few examples. These diseases are the result of alterations in the complex chemical process which take place in the body cells, tissues and organs, and which represent the biochemical basis for all life processes. Continued progress in NIAMDD supported metabolic research has provided new and useful insights into these metabolic processes and diseases. Among the major research achievements are those that have demonstrated that the cyclic nucleotides are key factors in the regulation of cellular function. The impact of this new knowledge is relfected in increasing investigations into the

possible role of these substances in disease states as seemingly diverse as cancer, immunologic deficiencies, hypoparathyroidism, and diabetes mellitus. The Institute plans to continue its support of basic and clinical research in these areas of metabolism, and to initiate new programs aimed at increasing the understanding of the physical and chemical processed by which substances are produced, processes, and maintained by the living organism, especially as these impact upon the understanding of human disease. Specific areas of this expanded effort will include: 1) research into mechanisms of metabolic control of diverse cellular functions; 2) studies of the role of cyclic nucleotides in normal and disordered metabolic regulation; and 3) studies of the biochemical basis and clinical character of specific metabolic diseases such as cystic fibrosis. The Institute plans to undertake a careful and extensive evaluation of the needs for research into this disease.

Digestive Diseases and Nutrition

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Digestive Diseases	---	$24,613,000	---	$24,876,000	---	+$263,000
Nutrition	---	8,931,000	---	9,655,000	---	+724,000
Total	---	33,544,000	---	34,531,000	---	+987,000
Budget Mechanism:						
Research Grants						
Regular:						
Noncompeting	323	21,305,000	303	21,581,000	-20	+276,000
Competing	58	3,710,000	49	3,161,000	-9	-549,000
Subtotal	381	25,015,000	352	24,742,000	-29	-273,000
Multidisciplinary Centers	---	2,701,000	---	3,280,000	---	+579,000
Research career programs	40	1,116,000	43	1,252,000	+3	+136,000
Subtotal	40	3,817,000	43	4,532,000	+3	+715,000
Training Programs 1/						
Individual	36	534,000	46	677,000	+10	+143,000
Institutional	80	1,603,000	98	1,968,000	+18	+365,000
Subtotal	116	2,137,000	144	2,645,000	+28	+508,000
Research & Development Contracts	16	2,575,000	16	2,612,000	0	+37,000
Total		33,544,000		34,531,000		+987,000

1/ Numbers are full-time equivalents.

Digestive Diseases

The digestive diseases program encompasses research of organ systems associated with the gastrointestinal tract, including salivary glands, esophagus, stomach, pancreas, liver, gallbladder, and small and large intestines. Research activity is concerned with basic aspects of the anatomy, histology, physiology, endocrinology, and biochemistry of the digestive tract in health, and of their aberrations in different disease states. Efforts include studies of the cause, prevention, diagnosis and treatment of specific diseases such as esophagitis, peptic ulcer, pancreatitis, inflammatory bowel disease states such as ulcerative colitis and regional ileitis (Crohn's disease), malabsorption syndrome, gallstones, and cirrhosis, among others.

Although diseases of the gastrointestinal tract are among the most common illnesses in the country, second only to diseases of the heart and circulation in the number of physician office visits or house calls they require, many of these ailments are poorly understood and hence treatment is often less than optimal. Diseases of the stomach and intestines may afflict persons of any age, but most often affect those in the middle-aged group at the peak of their more vigorous and productive periods, often causing prolonged and expensive hospitalization and

outpatient treatment, and countless social and emotional problems. Some diseases such as Crohn's disease are of a chronic nature. Many patients are afflicted for years and may have to undergo extensive and repeated treatments and surgery at great cost economically and in terms of human suffering.

Among the many research studies which will continue to be supported during the next fiscal year are investigations on the dissolution of gallstones, through oral administration of a specific bile salt, to obviate the need for surgery. Ten treatment centers are involved in studies of 1,000 patients with gallstones to evaluate the safety and efficacy of using chenodeoxycholic acid in the management of gallstones.

Another of the Institute's main goals is to lessen the toll that peptic ulcers now exact in chronic sickness, deaths and dollars. About 10 million Americans are estimated to have ulcer symptoms on an intermittent basis and each year about 10,000 Americans die of complications of peptic ulcer.

Through interdisciplinary studies at increasing levels of organization from cells, tissues, animals, man and finally entire populations, researchers expect to gain new insights into the causes and natural history of peptic ulcer, and to apply this knowledge to preventing ulcers or their recurrence and to achieving improvements in their diagnosis and medical and surgical treatment. One study which will be supported concerns a synthetic analogue of prostaglandin E_2, a naturally occuring substance in the body, which has been found to inhibit gastric acid secretion in patients with duodenal ulcers. Also, the acid-suppressing activity and clinical effectiveness of cimetidine, an anti-histamine analogue, will be further substantiated. At this point, in ongoing clinical studies, the FDA has been supplied with an increasing body of evidence concerning the clinical effectiveness of this new drug (which is already approved for the treatment of peptic ulcer abroad) so that one may look forward to its ultimate use in the United States.

As part of the Institute's efforts to intensify program efforts in the area of digestive diseases, an ongoing collaborative research project, the National Cooperative Crohn's Disease Study, will continue. This study is designed to examine the efficacy of several commonly used regimens in the treatment of regional ileitis (an inflammatory disease of the bowel), which has devastating effects on its patients, young adults in particular, causing prolonged periods of hospitalization and frequently leading to abdominal operations involving resection or removal of portions of the intestine.

Nutrition

The Institute's nutrition program will continue to focus on those aspects of basic and clinical nutritional science which have particular relevance to improvement of human health and longevity. In the main, these are concerned with advancement of knowledge concerning the nutritional role of vitamins, trace minerals and elements, proteins and amino acids, fats, fatty acids and carbohydrates, and their relationships to normal and disordered states of metabolism. In certain of these areas, encouraging and important advances have been made during the past fiscal year by investigators whose research has been supported in large part by Institute funds.

Research in abnormal nutrition involves discovery and definition of deficiency states, nutrient toxicity, obesity, malabsorption of specific nutrients, and investigation of the relationship of diet to specific disease entities, such as celiac disease. Other research relates to nutrition in specific diseases or stress states, such as in diabetes, bone and joint disease, endocrine and immune disorders, gastrointestinal and infectious diseases, inborn errors of metabolism, liver and kidney disease, anemia, skin disorders, and stress (including surgery, trauma, wound healing and environmental extremes).

Among nutrition research studies during Fiscal Year 1978 will be those regarding the effect on the level andavailability of water-soluble vitamins contained in food when large doses of vitamin C are administered (such as is advocated in some quarters for prevention and treatment of the common cold). Research to facilitate prevention and control of obesity will continue to be strongly supported by the Institute. Overweight and obesity to a degree that interferes with optimal health and longevity affects more than 20 percent of adults in the United States, and constitutes a public health problem of major concern to the lay public and physicians. Attention will be given to morphogenesis of adipose tissue cells, multiple aspects of lipids and lipid metabolism, effects of fasting and periodicity of eating, neural and other factors influencing appetite, endocrine dysfunctions and hereditary factors. Of timely importance will be studies related to the surgical treatment of severe obesity by creation of intestinal shortcuts ("by-pass surgery") and elucidation of the long-term safety and effectiveness of such procedures, the use of which has increased in recent years.

Kidney Diseases, Urology and Hematology

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Kidney Disease and Urology.....	---	$22,963,000	---	$24,232,000	---	+$1,269,000
Hematology.....	---	10,234,000	---	10,974,000	---	+740,000
Total.....	---	33,197,000	---	35,206,000	---	+2,009,000
Budget Mechanism:						
Research Grants						
Regular:						
Noncompeting.....	318	20,949,000	277	19,702,000	-41	-1,247,000
Competing.....	35	2,237,000	73	4,749,000	+38	+2,512,000
Subtotal.....	353	23,186,000	350	24,451,000	-3	+1,265,000
Kidney Special Centers of Research.....	---	1,500,000	---	1,620,000	---	+120,000
Research career programs.....	18	486,000	20	594,000	+2	+108,000
Subtotal.....	18	1,986,000	20	2,214,000	+2	+228,000
Training Programs 1/						
Individual.....	41	606,000	49	711,000	+8	+105,000
Institutional....	91	1,819,000	104	2,070,000	+13	+251,000
Subtotal.....	132	2,425,000	153	2,781,000	+21	+356,000
Research & Development Contracts.....	80	5,600,000	80	5,760,000	0	+160,000
Total.....		33,197,000		35,206,000		+2,009,000

1/ Numbers are full-time equivalents.

Kidney Disease and Urology

The magnitude of the human and economic costs of chronic renal failure is reflected in the Federal expenditures in 1977 for end stage renal disease: over $597 million dollars are being spent for dialysis and/or kidney transplantation for 33,000 patients. Minimal estimates by the Social Security Administration are that over 50 thousand patients will require these treatments at a cost of $1.2 billion by 1981. These treatments are "half-way technologies" which enable patients to lead reasonable lives but do not provide the normal existence that would be possible if a "high technology" were developed that would allow arrest or prevention of the causative disorder. Between one and two-thirds of these patients have a type of glomerulonephropathy caused by immunologic mechanisms. The sequelae of obstructive and neuromuscular disorders of the urinary tract are responsible for another twenty percent. Hereditary and congenital disorders are also major causes.

Significant morbidity resulting in hospitalizations, work loss, physical discomfort, and economic strictures is associated with disorders such as urolithiasis (kidney and urinary tract stones), benign prostatic hyperplasia,

urinary tract infections, and the hypertension associated with kidney disease. Although accurate data are not available for these maladies, it was estimated in 1972 that over one percent of Americans were hospitalized for episodes of kidney stone annually at a cost of well over 50 million dollars (an additional large number of patients are treated for stones without hospitalization), benign prostatic hyperplasia will affect over 55% of men by age 55 and over 80% of men by age 80. At least 10% of these men will require surgical intervention for relief of its symptoms. Urinary tract infections are among the top three bacterial infections encountered in clinical medicine and are a major cause of work loss among women.

Considering that an understanding of the basic mechanisms responsible for the kidney and urinary tract disorders that result in chronic renal failure would aid in development of rational treatment or prevention, a major portion of the kidney/urology program's grants address this area. Paralleling these, there is sizeable support for studies in dialysis, transplantation, and into many aspects of chronic renal failure (uremia: a composite common pathway resulting from many different kidney diseases). Research into congenital disorders of the kidney and urinary tract, benign prostatic hyperplasia, obstructive and neuromuscular disorders, and into structure and function of the kidney in health and disease comprises a fair proportion of the remaining grants. A small number of Specialized Centers of Research into urolithiasis, basic and clinical mechanisms are being initiated during 1977 to bring a cross-disciplinary approach to this complex disorder. Initial efforts to improve epidemiologic and statistical data about kidney and urinary tract disorders include a retrospective analysis of their denominator population by the Kaiser Foundation in the San Francisco-Oakland area; in cooperation with Walter Reed Army Institute of Research, a retrospective study of hospitalizations in the three military services; inclusion of appropriate parameters by the National Center for Health Statistics in the current Ambulatory Health and Nutrition Survey. The study, Evaluation Study of Research Needs in Nephrology and Urology, conducted under the aegis of this Institute, with participation of over 100 urologists and nephrologists, is nearing completion. This study provides a resource of expert advice about feasible research and needed areas for future research that includes considerations of cost/benefit in relation to incidence, prevalence and the human and economic costs of disease.

During 1978, studies into basic mechanism of kidney and urinary tract disorders will continue as well as the large number devoted to problems of chronic renal failure. Increased research efforts will be addressed toward glomerulonephropathies to increase understanding of immune mechanisms and indicator systems so that better clinical management and prophylaxies may be possible. Studies of host factors predisposing individuals to development of immunologic injury to the kidney and a cooperative study of the natural history of glomerulonephritis are considered of high priority. Expansion of the Special Centers of Research program to include glomerulonephritis and benign prostatic hyperplasia as well as more studies of urolithiasis is projected. Further efforts to acquire valid data about epidemiology and costs to the economy are planned. As feasible, those recommendations of the Evaluation Study of Research Needs in Nephrology and Urology will be implemented with consideration of priorities in relation to human and economic costs, incidence and prevalence of kidney and urinary tract diseases and potential for research to add knowledge necessary to provide more rational treatment and/or prevention.

Artificial Kidney Program

The Artificial Kidney Program, a collaborative research and development program, seeks to develop simpler, more efficient and less costly artificial kidneys and improved methods of treatment for patients with permanent loss of kidney function.

In Fiscal Year 1978, priority will be assigned to studies related to the pathophysiology of uremia. Emphasis will be on the complications of long-term

dialysis - the anemia of uremia, peripheral neuropathy, the hypertension and hyperlipidemia characteristic of long-term dialysis which is implicated in the heart and vascular disease deaths (the predominant cause of death in long-term dialysis patients). Emphasis will also be placed on development of new methodology which will permit reduction of the total number of hours devoted weekly to dialysis and on determination of what constitutes adequate dialysis treatment. There will be a determined effort for improvement of clinical dialysis methodology, with emphasis on "custom-tailored" individualized treatment schedules, prevention of the rather common clinical complications, thus -- more effective cost control.

Hematology

In order to design therapeutic methods or cure for the many disabling and fatal blood disorders and anemias afflicting Americans, hematologic research is directed toward development of a fundamental understanding of blood and blood-related systems. The number of individuals affected is large; for example, the anemia of chronic renal failure is a major complication in all of the nearly 50,000 patients with end stage renal disease; nutritional anemias, of which iron deficiency anemia is one of the commonest, occurs in over 10% of adults; nearly 60% of patients with systemic lupus erythematosus have anemia as a complication; sickle cell anemia occurs in 160 per 100,000 births in American blacks, and beta-thalassemia (Cooley's anemia) occurs in 40 per 100,000 births among Americans of Mediterranean origin.

Current hematologic research focusses on these and other important disorders of blood. In chronic renal failure, there is a marked reduction in synthesis of the hormone erythropoietin by the kidney, resulting in a loss of red blood cell production and anemia. Five percent of the program's funds are directed toward the study of this condition. Understanding of erythropoietin synthesis and action may lead to therapeutic techniques of stimulating blood cell production. Nutritional anemias can be alleviated by developing methods of providing essential nutrients, such as iron, in a more readily available form. The study of metabolism and transport of nutrients related to blood cell formation is emphasized. Other continuing research efforts include the study of genetic disorders of hemoglobin and its production, such as sickle cell anemia and Cooley's anemia; the enzymatic and other metabolic defects of blood cells; porphyrias, in which hemoglobin degradation products produce painful and disfiguring symptoms as well as abnormal behavior; disorders of white blood cell production and metabolism; and immune reactions related to humoral and white blood cell factors. This research will also have implications for cure and treatment of other diseases of concern to this Institute, including arthritis, diabetes, and kidney diseases.

Several specific lines of research will be sponsored in FY 1978. The repeated blood transfusions used to treat Cooley's anemia result in fatal iron deposition in vital organs such as the heart. Development of a safe, effective agent to remove excess iron is now feasible and will be pursued. Emphasis will be placed on development of techniques leading to isolation, synthesis and administration of erythropoietin for therapeutic use in the anemia of chronic renal failure. Research will be pursued on immune rejection of organ and tissue transplants. Key factors in rejection are the genetically determined antigens of white blood cells, antigens also associated in some little understood manner with resistance to many diseases and infections.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Research.. .	463	$30,483,000	463	$32,634,000	---	+$2,151,000

Intramural activities of NIAMDD are devoted to the support of research in fundamental sciences that are the foundation of knowledge pertinent to the Institute disease categories: chemistry, biochemistry, enzymology, molecular biology, anatomy, histology, pathology, physiology, medicinal chemistry, pharmacology, toxicology and genetics. Branches for clinical investigations include arthritis and rheumatism, diabetes and other metabolic diseases, digestive diseases, clinical endocrinology, pediatric metabolism, and clinical hematology.

The mission of the intramural research area of the Institute is to obtain information and knowledge for understanding the fundamental biological processes underlying the major diseases within the Institute's purview, and to pursue studies on diagnosis, treatment, and prevention in specific diseases. Over 260 research projects, including various combinations of laboratory, clinical, epidemiological and biometric investigations, are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH Institutes, other government agencies, and outside investigators ensure a minimum of duplication and a maximum exchange of research findings. Indicative of the caliber of Institute scientists is Dr. Baruch S. Blumberg, who shared the 1976 Nobel Prize in Physiology or Medicine. Dr. Blumberg, now with the Fox Chase Cancer Center in Philadelphia, won the award for research performed while at the Institute, where he discovered the so-called Australian Antigen which he determined was part of the virus that causes the most severe form of hepatitis.

Arthritis and Rheumatism

Like their colleagues across the nation, Institute scientists are studying the possibility that rheumatoid arthritis is the result of chronic inflammation probably triggered by an abnormal immune reaction. In Fiscal Year 1978 Institute scientists will also be evaluating methods to remove rheumatoid granulation tissue (pannus) from affected joint areas in selected patients. Preliminary research has indicated that surgical removal of this tissue will prevent the progressive destruction of cartilage, bone, and periarticular supporting structures that is characteristic of rheumatoid arthritis.

Systemic lupus erythematosus (SLE) is another connective tissue disorder similar to rheumatoid arthritis in certain respects. It develops in about 50,000 new patients each year, most often affecting people in the 20-40 year age group, particularly young women.

Although the cause of SLE is not known, much evidence points, as in the case of rheumatoid arthritis, to a disorder of the body's immune mechanism which may or may not be tied to a previous infectious process. The disease can appear as a result of hypersensitivity to certain drugs, and this phenomenon is among those being studied by Institute researchers at the NIH Clinical Center. Patients are

also under investigation there in a study involving the immunosuppressive drugs cyclophosphamide and azathioprine in the treatment of certain of the complications of SLE.

Chronic hepatitis, as a sequela of acute hepatitis, or appearing insidiously, resembles the autoimmune group of diseases. Not only may autoimmune antibodies appear, as in "lupoid" hepatitis, but the clinical manifestations may strikingly overlap rheumatoid arthritis or lupus erythematosus. The natural history of remission and exacerbation suggests a similar pathogenesis. Furthermore, patients with classical arthritis, lupus, Sjogren's syndrome, or other "autoimmune" diseases may develop transient or even chronic hepatitis. Of particular interest are patients with uncomplicated chronic hepatitis with or without other manifestations and patients with autoimmune diseases in whom hepatitis appears. Patients with these diseases, but without cirrhosis or a significant history of excessive alcohol intake, will be examined for the relationship of autoimmunity and hepatitis virus immunity to the natural history of their disease.

Diabetes and Other Metabolic Diseases

A primary goal in Institute diabetes research in the coming fiscal year will be to learn the basic impairment of insulin activity, a complete knowledge of which would uncover some of the riddles now surrounding diabetes. Research will focus on the physiology of insulin, and how this hormone exerts its influence on cell membranes and cellular metabolism. Institute scientists will study ways in which insulin acts upon individual body cells primarily by binding to specific receptor sites on cell membranes. Scientists will also examine how the multiple effects of insulin, e.g., increased glucose transport into the cell, decreased mobilization of fat, increased glycogen synthesis, depend upon one or more "second messengers" that act within the cell, such as spermine and spermidine (which have been found to mimic intracellularly some of the actions of insulin) or "cyclic AMP." Continuance of such fundamental studies is essential for elucidation of the mechanisms by which insulin exerts its multiple essential effects on cellular processes, and may permit development of rational and effective treatments for diabetic patients. Hypoglycemia, or low blood sugar, will also be investigated in the next fiscal year.

The Southwestern Field Studies Section will continue its epidemiological investigation of diabetes mellitus among Indians of the Southwestern United States, and in particular, the Pima Indians of Arizona, who have a diabetes incidence about ten times that of the rest of the population of the United States. Various factors, including hereditary, environmental, dietary, and anthropological aspects that may have a bearing on the frequency and severity of this disease, are and will continue to be investigated. Selected findings are being contrasted with similar studies performed on other populations with different characteristics and environments.

Among Institute intramural research projects planned for the next fiscal year, investigators will be studying parathyroid disorders and hormone-conditioned metabolic bone diseases. The recent development of a highly sensitive radioimmunoassay for parathyroid hormone is expected to improve diagnostic accuracy for hypo- or hyperparathyroid states, and allow measurement of rates of secretion of the hormone which exerts a regulatory influence on bone mineral metabolism. Patients with hypercalcemia, hypophosphatemia, nephrocalcinosis, nephrolithiasis, or other manifestations of hyperparathyroidism will be examined for the therapeutic effects of calcium or EDTA infusions or dietary phosphate on the secretion of parathyroid hormone.

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Digestive Diseases

Intramural digestive disease research will continue to cover clinical and laboratory investigations to determine abnormalities in structure and function of the esophagus, stomach, small and large intestines, pancreas and liver, and research on certain hereditary metabolic diseases. Work will be directed at an understanding of human digestive tract disease and its treatment in terms of underlying derangements in the body's metabolism and physiology.

The causes and manifestations of intestinal malabsorption are numerous and varied. In many instances such fundamental problems as the etiology, the nature of the pathological physiology, the optimum therapy, and the importance of hereditary factors still require extensive investigation. In Fiscal Year 1978 the Institute will study selected patients having proven malabsorption, and emphasis will be placed on evaluating those having celiac disease (gluten-sensitive enteropathy).

In addition, primary biliary cirrhosis and vinyl chloride associated liver disease will be investigated. The latter disorder involves individuals with evidence of liver disease having a history of occupational exposure to vinyl chloride.

Institute clinical research in blood disease this coming fiscal year will stress, among other studies, the biochemistry of blood coagulation with particular reference to the development of better forms of therapy for various congenital and acquired hemorrhagic diseases. Such disorders as hemophilia A or B, von Willebrand's disease, hemophiloid conditions such as Factor VII deficiency, circulating anticoagulants, afibrinogenemia, fibrinolysis, as well as obscure, undiagnosed bleeding disorders, will be studied. New approaches to therapy of acute and chronic idiopathic thrombocytopenic purpura (ITP) and the thrombocytopenia of lupus erythematosus (a generalized connective tissue disease) will also be evaluated.

Changes in this activity from the prior year include an increase for centrally furnished services, within-grade increases and other mandatory increases and an incremental increase to cover the rising cost of supplies, materials and services in order to maintain the current level of research effort.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations.....	89	$7,130,000	89	$7,271,000	-	+$141,000

Nearly two-thirds of the resources of this activity are devoted to review and approval of grants functions including 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 information relevant to all transactions.

The other major function under this activity is the review, management and negotiation of research and development contracts of the categorical program areas, the largest contract program being the Artificial Kidney/Chronic Uremia Program which is developing more effective, less costly methods of treatment of end-stage kidney disease.

The total increase of $141,000 requested for this activity is required for mandatory items primarily within-grade pay increases and this Institute's proportionate share of increased costs of centrally furnished services such as receipt and initial review of all grant applications, maintenance of buildings and grounds, custodial services, communications, and transportation.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.....	36	$881,000	34	$859,000	-2	-$22,000

This activity provides support for the immediate office of the Institute Director and for certain administrative and business management functions including financial management, personnel management, property control and travel audit and control, which are most efficiently performed as centralized functions. This staff, which continues to absorb new responsibilities and reporting functions such as required under the Freedom of Information Act and the manpower productivity measurement program, has remained at the same level over the past decade.

The change requested for this activity is an increase of $17,000 for mandatory items and a decrease of $39,000 related to the reduction of 2 positions.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Arthritis, Bone and Skin Diseases (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$31,645,000	Indefinite	---	$36,605,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments in 1977: In 1977, 387 research grants, 35 individual fellows, 78 fellows under institutional awards and 6 contracts were supported. Of the research grants awarded, 306 were noncompeting continuations of previous awards and 81 were new or competing continuations.

Objectives for 1978: The estimate for 1978 provides for support of 378 research grants, 47 individual fellows, 100 fellows under institutional awards and 7 research contracts. Of the research grants, 294 will be noncompeting continuations and 84 will be new or competing renewals. No new institutional awards will be made in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Diabetes, Endocrinology and Metabolism (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$72,120,000	Indefinite	---	$69,855,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments in 1977: In 1977, 885 research grants, 51 individual fellows, 113 fellows under institutional awards and 8 contracts were supported. Of the research grants awarded, 607 were noncompeting continuations of previous awards and 278 were new or competing continuations.

Objectives for 1978: The estimate for 1978 provides for support of 756 research grants, 63 individual fellows, 136 fellows under institutional awards and 12 research contracts. Of the research grants, 673 will be noncompeting continuations and 83 will be new or competing renewals. No new institutional awards will be made in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Digestive Diseases and Nutrition (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$33,544,000	Indefinite	---	$34,531,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments in 1977: In 1977, 381 research grants, 36 individual fellows, 80 fellows under institutional awards and 16 contracts were supported. Of the research grants awarded, 323 were noncompeting continuations of previous awards and 58 were new or competing continuations.

Objectives for 1978: The estimate for 1978 provides for support of 352 research grants, 46 individual fellows, 98 fellows under institutional awards and 16 research contracts. Of the research grants, 303 will be noncompeting continuations and 49 will be new or competing renewals. No new institutional awards will be made in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Kidney Disease, Urology and Hematology (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$33,197,000	Indefinite	---	$35,206,000

Purpose: The National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD) conducts, fosters and assists research and training directed toward preventing, diagnosing, treating and controlling the numerous diseases encompassed in this activity. Programs are carried out through the use of research grants (approximately 85% of the funding), research and development contracts, fellowships and training grants.

Accomplishments in 1977: In 1977, 353 research grants, 41 individual fellows, 91 fellows under institutional awards and 80 contracts were supported. Of the research grants awarded, 318 were noncompeting continuations of previous awards and 35 were new or competing continuations.

Objectives for 1978: The estimate for 1978 provides for support of 350 research grants, 49 individual fellows, 104 fellows under institutional awards and 80 research contracts. Of the research grants, 277 will be noncompeting continuations and 73 will be new or competing renewals. No new institutional awards will be made in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
463	$30,483,000	Indefinite	463	$32,634,000

Purpose: The mission of the intramural research area of the Institute is to obtain information and knowledge for the understanding of the fundamental biological processes underlying the major diseases within the Institute's purview. Over 260 research projects including various combinations of laboratory, clinical, epidemiological and biometric investigations are conducted in facilities in Bethesda, Maryland and Phoenix, Arizona. Medical, biological, physical and chemical investigations range from studies of fundamental mechanisms, to specific disease oriented laboratory research, to clinical evaluation and treatment programs. Close collaboration with scientists of other NIH Institutes, other government agencies and outside investigators ensure a minimum of duplication and a maximum exchange of research findings.

Objectives for 1978: Changes in this activity from the prior year include an increase for centrally furnished services, within-grade increases and other mandatory increases and an incremental increase to cover the rising cost of supplies, materials and services in order to maintain the current level of research effort.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
89	$7,130,000	Indefinite	89	$7,271,000

Purpose: Nearly two-thirds of the resources of this activity are devoted to review and approval of grants functions including 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 application 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 organization; continuous surveillance of scientific activities and progress; and recording and reporting of fiscal and scientific information relevant to all transactions.

The other major function under the activity is the review, management and negotiation of research and development contracts of the categorical program areas, the largest contract program being the Artificial Kidney/ Chronic Uremia Program which is developing more effective, less costly methods of treatment of end-stage kidney disease.

Objectives for 1978: Nearly all of the increase for this activity in the budget request is for mandatory items primarily including within-grade pay increases and an increase of this Institute's proportionate share of increased costs of centrally furnished services such as receipt and initial review of all grant applications, maintenance of building and grounds, custodial services, communications, and transportation.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis, Metabolism, and Digestive Diseases

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act Title IV Parts D and I)

1977 Appropriation			1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
36	$881,000	Indefinite	34	$859,000

Purpose: This activity provides support for the immediate office of the Institute Director and for certain administrative and business management functions including financial management, personnel management, property control and travel audit and control, which are most efficiently performed as centralized functions. This staff, which continues to absorb new responsibilities and reporting functions such as required under the Freedom of Information Act and the manpower productivity measurement program, has remained at the same level over the past decade.

Objectives for 1978: The total change requested for this activity includes an increase of $17,000 for mandatory items and a decrease of $39,000 related to the reduction of 2 positions.

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

WITNESSES

DR. DONALD B. TOWER, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. ELDON L. EAGLES, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE
DR. GEORGE C. MURRAY, DIRECTOR, PROGRAM PLANNING AND EVALUATION, NINCDS
ROBERT L. SITHENS, FINANCIAL MANAGEMENT OFFICER, NINCDS
H. RICHARD MILLER, ASSISTANT DIRECTOR, BUDGET, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. We will continue with the National Institutes of Health, the National Institute of Neurological and Communicative Disorders and Stroke. This presentation will be made by Dr. Donald B. Tower, the Director, and we have your biographical sketch, Doctor, which we will place in the record at this point.

[Dr. Tower's biographical sketch follows:]

BIOGRAPHICAL SKETCH

Name: Donald Bayley Tower.
Position: Director, NINCDS.
Birthplace and date: Orange, N.J., December 11, 1919.
Education: A.B., Harvard College, 1941; M.D., Harvard Medical School, 1944; M. Sc., McGill University, 1948; Ph. D., McGill University, 1951.

EXPERIENCE

Director, NINCDS, May 31, 1974 to present; Acting Director, NINDS, May 1, 1973 to May 30, 1974; Chief, Laboratory of Neurochemistry, IR, NINDS, May 1961 to May 1973; Head, Section on Amino Acid and Electrolyte Chemistry, LNC, IR, NINDS, May 1961–May 1974; Assistant Surgeon General, USPHS (active), 1975 to present; Acting Associate Director, EP, NINDB, July 1967–June 1968; Chief, Section on Clinical Neurochemistry, IR, NINDB, July 1953–May 1961.

Assistant professor of experimental neurology, McGill University, 1952–53; Associate neurochemist, Montreal Neurological Institute, 1951–53; Externe (neurology), National Hospital, Queen Square, London, 1951 (5 months); Research Fellow, Montreal Neurological Institute, 1947–51; Assistant resident (neurosurgery), Montreal Neurological Institute 1948–49; Medical officer, USNR, 1945–46 (active duty, Phillippine theatre); interne (surgery), University of Minnesota hopsitals, 1944–45.

ASSOCIATION MEMBERSHIPS

American Academy of Neurology, American Association for the Advancement of Science, American Chemical Society, American Neurological Association, American Society for Neurochemistry, American Society of Biological Chemists, Canadian Neurological Society, Canadian Physiological Society, International Research Organization (member, central committee), and International Society for Neurochemistry.

SPECIAL AWARDS CITATIONS, OR PUBLICATIONS

Alpha Omega Alpha, Sigma Xi, Markle Scholar 1951–53, Chief editor (Western Hemisphere), Journal of Neurochemistry. 1968–73, Chairman, neurochemistry delegation to U.S.S.R. under United States-Soviet exchange program, 1969, Lennex guest lecturer, American Epilepsy Society, 1970, Temporary advisor, World Health Organization, 1976–77, and Author of over 100 scientific papers and monographs.

Mr. FLOOD. Do you have some people with you that you want us to meet?

Dr. TOWER. Next to me is Mr. Sithens, our budget officer, and Dr. Eagles, Deputy Director, and Dr. Murray, Director of Program Planning and Evaluation.

Mr. FLOOD. We have your statement which we will place in the record at this point.

[Dr. Tower's statement follows:]

Department of Health, Education, and Welfare
National Institutes of Health

Statement of Director
National Institute of Neurological and Communicative Disorders and Stroke
on
"National Institute of Neurological and Communicative Disorders and Stroke"

Mr. Chairman and Members of the Committee:

I am most appreciative of the opportunity to summarize for you the accomplishments and current research programs of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS). Funds from NINCDS support the majority of research in this country on the nervous system and its disorders. In this endeavor NINCDS collaborates with other Federal agencies and a number of concerned voluntary professional and lay organizations, and depends on the dedicated cooperation of many patients and their families.

The challenge to all of us is awesome, when one contemplates the formidable array of disorders for which we still do not know the cause, lack specific diagnostic procedures, and await effective preventive or therapeutic measures. The challenge is also awesome, when one contemplates the forty-to-fifty million Americans disabled or dying from these many neurological and communicative disorders, and how thinly spread are our modest resources in manpower and money.

Like other NIH institutes, we are keenly aware of the importance of translating the results of research into better health care for our nation's citizens. I believe that the NINCDS record in this respect is responsive, as exemplified by such projects as: drug developments in epilepsy, Parkinson's disease and myasthenia gravis; clinical research centers and comprehensive programs in stroke, head injury , spinal cord injury and epilepsy; neural prostheses for the paraplegic and the deaf;and workshop-conferences in a variety of research and disease problem areas. The NINCDS

has in its Scientific Information Program Advisory Committee (SIPAC) a group of non-governmental experts charged with advising us on new and better means to discharge our information dissemination responsibilities. Current activities include our expanding monograph and bibliographic series and audio and video tape programs for professional audiences, as well as an expanding series of health information pamphlets for distribution directly or through some 25 voluntary health agencies to the general public. In addition the Institute is engaged on an experimental basis: in a regular service of program and research news items to neurological and communicative disorders journals; in distribution of health information pamphlets via distribution outlets in supermarkets and in Government Consumer Information Centers across the nation; and in development of additional index classifications to permit better access to the National Library of Medicine resources in the fields of neurological and communicative disorders.

Nevertheless, the principal thrust of NINCDS-supported research must still be at the fundamental level, focussed on the acquisition of new and better knowledge about the nervous system, if we are to succeed in our assault on the many remaining areas of clinical ignorance.

I am encouraged by several signs that indicate a growing appreciation and support for this viewpoint. Interest in neuroscience research is increasing rapidly. More and more mature investigators are being attracted from other fields, and the recently formed Society for Neuroscience is becoming a dominant force on the American research scene.

Moreover, the President's Biomedical Research Panel selected neurobiology as one of five research areas to be given special emphasis. The

Panel concluded its report by saying in part: "Perhaps the ultimate challenge to biomedical research, representing the very pinnacle of our understanding of the human organism, lies in neurobiology: how the brain and nervous system develop, how they function in health and disease, how thought occurs, how memory is stored, how we reason, how we are motivated, and how we interact with our physical and social environment.....This Panel commends neurobiology as a compelling long-range interest worthy of national attention."

Finally there is the more personal example in the selection of Dr. D. Carleton Gajdusek, chief of our Laboratory of Central Nervous System Studies, as 1976 Nobel Laureate in Medicine. The award to him of the Nobel Prize recognizes his remarkable discovery that degenerative and dementing disorders of the human nervous system can be caused by transmissible virus-like agents--a finding hitherto totally unsuspected. The Nobel award also recognizes his discovery that four such disorders are caused by transmissible agents which exhibit properties unlike those of any known bacteria or viruses and thus may well represent a completely new biological phenomenon. As Dr. Gajdusek has emphasized, what has been discovered may be only the tip of the iceberg, with many of the more common chronic and degenerative diseases of the nervous system as likely or potential candidates for similar slow or latent virus-caused disorders.

Let me turn to brief consideration of each of our major program areas.

For the FUNDAMENTAL NEUROSCIENCES Program, representing those projects in the basic research area not readily identifiable with any of the other NINCDS extramural program areas, the Institute is supporting 26 program project and other targeted research grants totalling $5.6 million, as well as 269 regular research grants, 36 fellowships, and 12 contracts.

From the many projects let me select a few highlights: New and important details of nerve cell structure and inter-connections have been revealed by the use of freeze-fracture and scanning electron-microscopic techniques. The study of viral infections and immune responses of host animals has been facilitated by the introduction of a new sensitive, inexpensive procedure called enzyme-linked immunosorbant assay (ELISA). The essentiality of calcium ions has been demonstrated in the release of chemical messengers, the transmitter agents at nerve-to-nerve or nerve-to-muscle connections. The nature and effects of defective interfering (DI) viral particles have been elucidated, so that we now know that they prevent normal replication and shedding of viruses from host cells and thus either prevent spread of acute infection or produce a chronic degenerative disorder. The neurotransmitter, dopamine, has been recognized as a major factor controlling release from the pituitary of prolactin and growth hormone. Important approaches to the mechanisms of viral and immunological diseases are the use of viral probes and DNA hybridization techniques and the study of the role of T-lymphocytes in cell-mediated immune responses in the nervous system.

A special feature of the Fundamental Neurosciences Program is the subprogram on neural prostheses, which provides examples of basic research developments that are now in practical use. If stroke patients are put on an electrostimulation exercise regime, normal or unaffected muscles, which would otherwise atrophy from disuse, can now be strengthened to permit better rehabilitation and fatigue resistance. To provide amputees with feedback control of force and position of an artificial prosthesis, a coiled-wire electrode, like a miniature version of the coiled telephone cord, has proved most suitable. It is gratifying to be able to exploit relatively quickly such newly acquired knowledge of nerve and muscle function by effective translation into the rehabilitation of disabled

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patients.

In the STROKE AND CENTRAL NERVOUS SYSTEM TRAUMA Program, a total of 62 program projects, clinical research centers and other targeted research grants are now being funded by NINCDS at a level of $13.6 million, as well as 103 regular research grants and 7 contracts.

For stroke, the blood vessels of the brain have been shown to be especially sensitive to hypertension but unlike heart vessels, they are not sensitive to elevated blood levels of cholesterol. Moreover, the effects of high blood pressure and the development of atherosclerosis in brain differ from those in the heart and general circulation. In the United States it is the large blood vessels at the base of the brain which are the principal sites for stroke involvement, whereas in Asian countries like Japan it is the smaller penetrating vessels that are involved. Currently we are seeing a shift in the emphasis of basic stroke research from earlier preoccupation with cerebral blood flow to investigations on perfusion (supply) and metabolism in brain tissue itself, with special attention to the effects of reduced oxygenation (hypoxia) or blood supply (ischemia). Clinically, increasing research attention is directed to the means for intensive care monitoring of the level or state of consciousness in the stroke patient. From such monitoring we may anticipate more precise predictors of clinical course and more appropriate indicators for specific therapies.

The CNS Trauma research program is today essentially where the stroke program was some years ago. We are in the process of building competent research teams and research programs where the many basic and clinical problems can be more effectively addressed. Last May at an international conference in Montreal, reports by participants indicated that the important problem of edema (excess fluid) in brain or spinal cord of trauma

patients is now being constructively pursued. Also last May we were finally successful in our efforts to bring Soviet experts in spinal cord injury to this country for conferences with American researchers. Clinical management and outcomes in the USSR appear not to differ significantly from those in this country. The Soviet studies purporting to demonstrate enzyme therapy-induced regeneration of cord function after experimental transection are provocative but clearly need independent replication before definitive conclusions may be drawn. Such studies are now being initiated in several U.S. laboratories. Research is active in the area of central regeneration and plasticity with increasing competition for available funds.

In stroke and CNS trauma, the NINCDS is embarking on comprehensive programs designed to deal with epidemiology, flow of facilities and organization of community resources. A comparable comprehensive program for epilepsy is already under way in five states. Such programs provide excellent opportunities for interfaces between research results and the delivery of health care. We believe that it is timely to identify and request separate funding for these programs.

For the NEUROLOGICAL DISORDERS Program, the NINCDS is supporting 42 program projects, clinical research centers and other targeted research grants totalling $11.0 million, plus 428 regular research grants, 290 fellowships, and 14 contracts.

Staff liaison and Institute resources are being provided by this program for the Congressionally-mandated commissions on Epilepsy and on Huntington's Disease, both of which are expected to complete their work and submit reports during FY 1977. Also staff support has been provided to two work groups set up by the NINCDS Advisory Council to advise on

the implementation of recommendations by the commissions on Multiple Sclerosis and on Diabetes and on programmatic priorities for funding relevant research. The reports of these work groups comprise our submissions on multiple sclerosis and diabetes to this Committee as requested last year.

In June of this year the Institute has planned a workshop-conference on Alzheimer's disease and other senile dementias, in collaboration with the National Institute of Aging and the National Institute of Mental Health. Current knowledge and recommended directions for future research will be emphasized.

For epilepsy, a highly successful symposium was held recently on the reliable quantification of blood levels of antiepileptic drugs by clinical laboratories. This is an area where the entire application of knowledge might have faltered if the NINCDS Neurological Disorders Program had not encouraged and collaborated with other voluntary and federal agencies to ensure this important application of knowledge. In two of the comprehensive epilepsy programs, units have been opened for intensive monitoring of intractable and problem cases of epilepsy.

Recent events re-emphasize our view that multiple sclerosis is one of the most complex neurological disorders confronting the researcher. A number of initially promising leads reported this year for diagnostic tests or causative viral agents have proved difficult to confirm in subsequent attempts at replication. Basic research studies on cell-mediated immunity and on slow or latent virus infections appear to hold more promise for solutions in both multiple sclerosis and amyotrophic lateral sclerosis.

There are promising new techniques for studying in culture the Schwann

cells which elaborate the fatty insulating sheath called myelin around peripheral nerves. With such techniques experimental models and factors in various disorders can be investigated. Diabetic neuropathy commands special priority in this respect but we also expect to intensify studies on the peripheral polyneuropathy called Guillain-Barré syndrome. A workshop on the latter problem will be organized later this year.

In developmental neurology, the fruits of the collaborative perinatal project initiated by NINCDS some 15 years ago are beginning to appear. Most of the principal monographs are in the publication process and will provide data and analyses on the 50,000 pregnancies and 7-year follow-ups on the offspring. Findings on febrile seizures, on toxemias during pregnancy, and on effects on the fetus of drugs taken during pregnancy are examples wherein significant improvements in preventive management have emerged. All the primary data and analyses from the project are available on tapes for appropriate research studies. At present four other institutes at NIH are utilizing portions of the tapes for a variety of studies. In retrospect, I think we can say that despite its cost and inevitable shortcomings, the NINCDS collaborative perinatal project stands as a unique endeavor which will continue to provide a wealth of data far beyond any expectations at its inception.

In the COMMUNICATIVE DISORDERS Program, a total of 40 program projects, clinical research centers and other targeted research grants are currently being funded by NINCDS at a level of $10.0 million, as well as 189 regular research grants, 57 fellowships and 7 contracts.

Evaluations have been completed of 13 profoundly deaf patients implanted with cochlear or inner ear prostheses, and a report will be published shortly in the Annals of Otolaryngology. The study was done under contract with

the University of Pittsburgh, with the cooperation of the patients and the two California clinics where the cochlear implants were performed.

The development of tissue cultures of embryonic otocysts will permit study of the factors contributing to congenital deafness. Special micropipettes to sample and recirculate cochlear fluids promise identification of the chemical transmitter agents that mediate the conversion of sound waves to nerve signals in the inner ear. One study in collaboration with the National Cancer Institute is examining the ototoxicity of a number of anti cancer drugs. In an experimental study other scientists are investigating the facilitatory or additive effects of noise and ototoxic drugs on hearing loss.

Better management of adult aphasia (linquistic confusion or deficits) following stroke is being achieved as a result of the recognition of memory deficits for verbal information and the resort to visual, non-verbal symbols for communication. By utilizing newly-designed measures of the degree of communicative independence in daily life, the efficacy of such rehabilitative treatment of aphasics can be evaluated.

Staff of the Communicative Disorders Program are currently engaged in creating a modest clinical facility in the NIH Clinical Center for evaluating auditory (hearing) and vestibular (balance) functions in patients and for testing speech and language disorders. At present most such studies on Clinical Center patients must be done elsewhere if the patient is moveable. The provision of on-site facilities seems to us long over due.

Space limitations preclude any extensive sampling of research contributions from the NINCDS laboratories at Bethesda. One major area, involving investigators in a number of our laboratories and branches, comprises a

variety of complementary studies on viral infections and immune responses of the central nervous system. Experimental studies with defective interfering (DI) viral particles demonstrate striking modifications of virally-induced disease in animals. In one case the expected acutely fatal viral encephalitis is converted by DI particles into a chronic paraplegia. The clinical pictures are so different that one would never suspect that they were caused by the same virus. Concurrently the immune responses as measured by antibody titers to the virus are vastly different in the two situations. In another study utilizing a multiple sclerosis-like animal model called experimental allergic encephalomyelitis (EAE), the disorder can be transferred to another animal or reactivated from the quiescent phase by the T-lymphocytes which are the mediators of cellular immunity. These various studies have particular relevance for multiple sclerosis, which is almost certainly an autoimmune disease. They may also be relevant for amyotrophic lateral sclerosis (ALS) for which there is circumstantial evidence for a viral association and for which recent studies at the NINCDS research facility on Guam demonstrate significant abnormalities of cell-mediated immunity in the majority of ALS patients tested.

Our Bethesda-based investigators owe many research advances to their access to highly specialized new instruments and techniques. One example is the newer generations of computerized axial tomographic (CT) brain and body scanners. At the four-fold better resolution available, CT scans of brain reveal details of anatomical structures and pathological changes (especially demyelination) hitherto available only on direct visual examination. For superior examinations of spinal cord, CT-assisted myelography or angiography combine the CT scan with the injection of radio-opaque materials into the spinal fluid around the cord or into cord blood vessels. Moreover, the computerized scans can be converted from the original axial or cross-sectional scans of the spinal cord into views in the longitudinal plane, so that the

extent of abnormalities and their relationship to other structures are clear.

A fascinating glimpse into the future is provided by the technique of tomochemistry, in which the CT scan is utilized to provide a sort of living "biopsy" of the brain By varying the energy of the scanning X-ray beam on successive scans, one can discriminate for intrinsic components like calcium or added substances like xenon (a blood flow indicator) in small tissue volumes. Many of these aspects of CT scanning of the nervous system were discussed at a recent NINCDS-sponsored conference.

For most neurological and communicative disorders data on prevalence and cost are approximate at best or lacking entirely. During the past two years our biometry and epidemiology unit has contracted for surveys based on national probability samples to obtain such data for brain tumors, head and spinal cord injuries, multiple sclerosis, and stroke. Epilepsy will be added this year. There is active collaboration with the National Center for Health Statistics (NCHS) especially looking toward development of a system for collection of chronic disease data for monitoring annual trends. Most other NIH institutes have expressed an interest in participating. In addition an epidemiological survey of major neurological disorders has been initiated in a defined population of whites and blacks in Mississippi. This is the first such study ever carried out on a black population in this country. Field work is being done by the Bureau of the Census, and the survey will provide a valuable testing instrument to the NCHS for larger-scale surveys. We anticipate that the results of such surveys together with program analyses by our planning and evaluation unit will materially improve our effectiveness as program managers.

In conclusion, Mr. Chairman, the budget request for the National Institute of Neurological and Communicative Disorders and Stroke for 1978 is $161,461,000. I shall be pleased to answer any questions and supply additional information as desired for the record. Thank you.

NONCOMPETING GRANTS

Mr. FLOOD. I want to ask you about the 1978 budget request which provides for an increase of $5.9 million over 1977, but then again we take another look at your research grant category, and we see a reduction of $6.5 million in noncompeting grants. Why is that?

Dr. TOWER. I think the explanation is the same as you probably had from the other institute directors. We have cycles of increases in commitment base or continuing grants from year to year, and then cycles in which these come up for renewal.

In 1978, a great many of those that have been ongoing came up for renewal and that accounts for the decrease in the noncompeting base.

Mr. FLOOD. Is it correct to say, then, that your 1977 budget provides enough money to meet all the costs of all the noncompeting grants?

Dr. TOWER. Just barely, Mr. Chairman. We have had a very large, relatively speaking, commitment base or amount of noncompeting grants in 1977, which has been somewhat at the expense of being able to fund competing grants, so that our funding of approved grants during this year will be probably less than 29 percent of all the approved competing grants.

Now next year, 1978, the situation will improve because we will have more money made available from the termination of those grants that have been ongoing, and as they come up for renewal with the new grants.

BUDGET INCREASE

Mr. FLOOD. Your budget shows an increase of about $8 million for the new and competing research grants.

What research area are you going to emphasize since you have this increase in funds?

Dr. TOWER. We are going to emphasize as many as we can, but I would like to particularly emphasize the area of fundamental research. This may not seem popular these days, but in our case it is important. A great many of the disorders that we deal with still lack precise knowledge of cause, precise diagnostic measures and precise preventive and treatment measures, and, therefore, we need the acquisition of new knowledge, in order to get at these problems, and that is the fundamental research we hope to support.

Mr. FLOOD. It is not unusual to have these problems anyplace in the campus out there.

Dr. TOWER. I think we have our share.

TRAINING AWARDS

Mr. FLOOD. Your budget proposes to reduce the individual training awards and increase institutional training grants. Why are you making that shift, and, by the way, how does that proposal that you intend to make comply with the clear intent of the National Research Service Act?

Dr. TOWER. Mr. Chairman, the increase in the institutional awards is actually very small and it represents particular areas where we have a special need. We have five or six areas where the number of experts in the country is very small and in order to provide adequate training

for these people, they must have a proper institutional environment, and that is why we are emphasizing in those cases institutional awards. These are the areas of neuroimmunology, neurovirology, neuro- and otopathology, neurobiology, developmental neurology, and sensory physiology and biophysics.

In addition, we have to be guided with regard to the individual fellowships by the recommendations that have been made by the National Academy of Sciences, and so there will have to be some reductions in some areas.

Mr. FLOOD. I still raise flatly the issue, of the intent of the National Research Service Act. Do you think you are flying in the face of the intention of that act, by that shift?

Dr. TOWER. No, sir; if you are referring to the proportion of individual to institutional grants, no, sir, because you will find if you look at the proportions between the two that we have maintained a dollar ratio of approximately 2 to 1 in favor of the individual awards, and we cannot start any new institutional awards until reauthorized by OMB.

COMMUNICATIVE DISORDERS

Mr. FLOOD. Last year, you told the committee that there was a shortage of trained researchers in the field of communicative disorders. Will the training part of your budget in 1978 begin to solve that problem? You made quite a thing out of that.

Dr. TOWER. We have begun to address that situation this year. We have made a substantial number of awards in that area already this year, so I think we are improving that situation considerably.

STROKE

Mr. FLOOD. We understand that although stroke is the third leading cause of death in the country, that the incidence of stroke is declining. How do you explain the decrease in the incidence of stroke?

Dr. TOWER. I don't know that we can prove it, but I would like to think——

Mr. FLOOD. Does it have anything to do with your efforts to screen and treat hypertension?

Dr. TOWER. This is shared with the Heart Institute, Mr. Chairman, and I think between our two institutes and the measures of the various voluntary groups on the outside, that we are beginning to make some inroads into getting understanding to the public and to the physicians about diet, about hypertension, about smoking and other things which we know are risk factors for both heart disease and stroke.

Mr. FLOOD. Can we expect this decrease to continue?

Dr. TOWER. I certainly hope so, sir. We are working very hard on it.

Mr. FLOOD. Are there any reliable preventive measures to lessen the chance of stroke?

Dr. TOWER. The ones that I have mentioned are the most important ones as far as we know.

COMPREHENSIVE STROKE CENTERS

Mr. FLOOD. Have you initiated your program of comprehensive stroke centers? If so, how many are there?

Dr. TOWER. We are in the feasibility stage, sir. I can't tell you how many there will be yet, because this is just at the very beginning. It will be about three or four months before we know how many good proposals for full comprehensive centers we will have resulting from the feasibility stage. This program is modeled to a large extent on our comprehensive epilepsy centers programs, of which we have five now, and we hope that this will engage the communities and the practicing physicians even more than has been possible in the past.

Mr. FLOOD. You are going to focus on the clinical findings to the community?

Dr. TOWER. Yes, sir.

Mr. FLOOD. How many did you say?

Dr. TOWER. We hope to start with three comprehensive stroke centers next year.

Mr. FLOOD. How much do you intend to spend on these comprehensive stroke centers in fiscal 1978?

Dr. TOWER. That depends on how quickly we can get the program going, but if it goes as we hope, we hope to fund three at approximately $1.5 million.

COLLABORATION WITH INSTITUTIONS

Mr. FLOOD. How are these centers going to work with the practicing physician in the community?

Dr. TOWER. We will provide a nucleus at a university hospital center, which will be a clinical research unit, and from this the coordinators of the program will mobilize the community resources, both at the local and at the regional and state levels, and we will provide special two-way flows of information between these research units and practicing physicians in the community by hot lines, by satellite and outreach programs and conferences, and this sort of thing.

Mr. FLOOD. That is going to improve his skills I suppose in detecting and treating the stroke patient?

Dr. TOWER. Yes, sir, that is correct.

EMERGENCY MEDICAL SERVICE

Mr. FLOOD. I believe you told us last year that you were considering collaborating with the research program of the Emergency Medical Service Agency. A big deal has been made out of that, in the last year especially. Are you collaborating and if so, how?

Dr. TOWER. As yet this has not come to pass.

Mr. FLOOD. What we had in mind was the business of the spinal cord injury being treated immediately and if you do that, you can minimize permanent damage. It is essential in those two programs that we have to work together.

Dr. TOWER. I agree with you, sir. It has not come to pass yet, but we are working on it and proposing to have comprehensive trauma centers to deal with head and spinal cord injuries, which must be in concert with the other emergency medical services available.

TRAUMA CENTERS

Mr. FLOOD. You say this is a new trauma center?

Dr. TOWER. These will supplement the head injury and spinal cord injury programs we have. In some cases they may participate and be amalgamated into this program.

Mr. FLOOD. How many are you going to have in fiscal 1978?

Dr. TOWER. We are hoping to have 3, but these are just entering the feasibility stage. I cannot guarantee these will come as quickly as we like.

Mr. FLOOD. What will those trauma centers do that is not being done by the trauma and burn centers that the Institute for General Medical Sciences set up?

Dr. TOWERS. Ours will deal with the problems of the nervous system. They will obviously be integrated and I should say intercoordinated. We will engage at the proper time in discussing this with Dr. Kirschstein and her staff in the National Institute of General Medical Sciences.

Mr. FLOOD. How will these trauma centers interface with the emergency medical service program?

Dr. TOWER. Well, this is the point at which we feel the most important interface should be made because it is essential to deal definitively with these patients as early as possible.

We know from past experience that we can salvage a great many more patients than we can now with the somewhat disconnected types of acute care that have gone on. So the closer we can bring together all the emergency medical services, the better I think we can do for these patients.

REGENERATION

Mr. FLOOD. People keep telling us that we are not investing enough money in research for the central nervous system regeneration. How much do you plan to spend in that area in 1977 and 1978?

Dr. TOWER. I think altogether we have in the spinal cord research approximately $6.5 million and about $2.2 million of that will be for regeneration. So that I believe that we are making a good beginning in that area.

One of our problems this year is that we have not been able to fund as many good proposals as we would like. So this program has been a little slower getting off the ground than we had hoped.

Mr. FLOOD. What are you going to spend in 1977 and in 1978?

Dr. TOWER. In 1977 it will be about $2.2 million. In 1978 we would hope to increase that to $2.3 million.

OTHER REGENERATION PROGRAMS

Mr. FLOOD. Are there any other Federal agencies which support research toward the regeneration of the central nervous system such as VA?

Dr. TOWER. VA's program has been rather small. Up until this year they were putting about $100,000 into research in addition to funds purely for service activities.

FUNDS FOR RESEARCH

Mr. FLOOD. Do you have a large number of very promising leads in this area that are not being pursued simply because you don't have the money? I ask that because we are told that the research on the central nervous system regeneration has been stopped at the University of Chicago, UCLA and Harvard, because of the lack of funds. What do you know about that?

Dr. TOWER. The funds are not as plentiful as we would like to have them, Mr. Chairman, but we have a lot of research going on. $2.2 million buys a lot of research. I think that some of the leads are very promising, but I think it would be a mistake to be too optimistic that we are going to have a breakthrough in so many months or just a year or two. This is a long-term proposition. We know that the central nervous system has potentiality for regenerating, but we don't yet know how functionally effective that is. That is the key question that needs to be answered now.

Mr. FLOOD. Do you have a number of promising leads?

Dr. TOWER. Yes, and we are working on as many of them as we can.

Mr. FLOOD. Mr. Natcher?

COMMISSIONS

Mr. NATCHER. Doctor, what effect have the commissions on multiple sclerosis, epilepsy, and Huntington's disease had upon the resources of your Institute?

Dr. TOWER. Research support for the multiple sclerosis commission is past history, that is a couple or 3 years ago. As far as the epilepsy and Huntington's disease commissions are concerned, when they are finished at the end of this year they will have cost the Institute in resource support approximately $1½ million and five positions.

Mr. FLOOD. What is your total as far as expenditure on commissions is concerned?

Dr. TOWER. Including the three commissions, in excess of $2 million.

Mr. FLOOD. Can you give us some idea as to how many research grants could have been funded if you had had the money available instead of having to spend it on the commissions?

Dr. TOWER. Approximately 22 research grants. In our Institute the average total cost for each grant is around $90,000 now including indirect costs.

Mr. NATCHER. Doctor, you would agree with me that your programs in your particular Institute are becoming more complex?

Dr. TOWER. Yes, sir, they are.

MANPOWER RESOURCES

Mr. NATCHER. Do you have adequate manpower to manage these increasingly complex programs that you have underway?

Dr. TOWER. We can manage with the manpower we have but it is getting spread mighty thin, Mr. Natcher.

BASIC RESEARCH

Mr. NATCHER. What is happening to basic research in relation to your total budget, as far as basic research is concerned?

Dr. TOWER. We have been struggling with support for basic research this year, Mr. Natcher, because various forces came together in terms of our programmatic reorganization, research commitments from previous years and so on, so that it has been difficult to fund what I consider an adequate amount of basic research applications this year.

We have actually transferred some funds from other program areas into the basic research area to try and keep them afloat. Next year their situation will improve slightly because they will have more money becoming available for new and renewal grants.

But I think that we still need to keep an adequate effort going in that area because this is where the new knowledge comes from that we can apply to the many disease problems that we are confronted with.

RESEARCH TEAMS

Mr. NATCHER. Doctor, in your statement you say you are in the process of building competent research teams and research programs. When you say a research team, what do you have in mind?

Dr. TOWER. Many of the research areas require experts from a great many different kinds of disciplines. We need good people in electron microscopy to look at the anatomy of the system. We need people knowledgeable in the sophisticated areas of recording the electrical activity that is manifested by the system. We need those competent to understand the reactions of the nervous system to virus invasions and the immune competence of the system.

These are the kind of teams I am talking about. It is very seldom possible for a single man to address such a problem anymore. He needs lots of help, either by working in a team or collaborating with people down the hall, or across the country. This is what we try to promote.

Mr. NATCHER. How do you get it altogether? You have the teams, the grants and the programs. How do you get it together to see where you are heading and what you have accomplished?

Dr. TOWER. One of the most effective means is to hold workshops inviting people around the country and also from other countries together to find out where we are, where the gaps are and what the problems are that need to be addressed and that we have not addressed and how we are doing.

We have done this in a great many areas. One of these workshops, which we are planning for this June 6, is a workshop on the dementias. We are doing this with the National Institute on Aging and the National Institute of Mental Health. We are going to address a problem which has been neglected for many, many decades. I think this will be a very exciting affair. I am looking forward to it.

COCHLEAR IMPLANTS

Mr. FLOOD. Doctor, for a number of years we have talked about our old friend cochlear implants. Last year you told us this technique was going to be evaluated. Have you completed your evaluation? What do you have to report?

Dr. TOWER. We have completed the evaluation. It will be published in the Annals of Otolaryngology next month. This study was done by an institution in your State, at the Eye and Ear Hospital in Pittsburgh by Dr. Robert Bilger and his colleagues. They had the opportunity to examine 13 out of the 20 patients who have had the cochlear implants and are still wearing them. Most of the patients had implants done in California. They were brought to Pittsburgh and examined by the team there over a week's time.

I think this a very extraordinary example of collaboration and cooperation among a great many people, patients mostly, physicians who did the implants out in California who were willing to turn their records and patients over to another institution for this purpose, and the funding that we were able to provide in order to have this evaluation done.

Mr. FLOOD. I certainly asked you the right question at the right time on that one.

Dr. TOWER. It is a very interesting study. I think that this is going to be a model for how this sort of thing ought to be done.

AUTISM

Mr. FLOOD. Doctor, I believe you recently called together a panel of international experts on the problem of autism. What did that group recommend and what research are you going to pursue in that area?

Dr. TOWER. The group on autism met about a year ago. I am a little embarrassed to tell you, Mr. Chairman, that the report is not yet out. It is nobody's fault. It is one of those unfortunate things in which the gentleman who was charged with working up the report passed away, I am sorry to say. We had to get a new person who then promptly fell ill, but the report is in press and it will be out shortly.

One of the biggest problems we ran into was getting some kind of consensus on a definition of autism. This is a disorder in which there are apparently a number of subgroups of children who have different aspects of disorder and some who don't have it at all.

There has been quite a problem in getting a consensus so we can go on with research which depends on being able to specify whether or not a child is autistic. I think we have made progress and as soon as the report comes out I expect research will pick up as other people have an opportunity to see what we have come up with and what the opportunities are.

MULTIPLE SCLEROSIS

Mr. FLOOD. We have seen a lot of publicity on this new blood test on the diagnosis of multiple sclerosis. Can you tell us about this test and what is it going to mean for the future? In other words, will we be able to detect this disease in its early stage and prevent it?

Dr. TOWER. Not very soon I am sorry to say. There are a number of new tests that have come out over the past year or so, both in this country and abroad. They look promising but every one of them, I think, can readily be characterized by pointing out that it is extremely difficult to carry out. It depends on having precisely the right conditions and every one of them has been extraordinarily difficult to repeat and validate in other people's hands.

A test that is going to be useful must be one that almost anybody can do. That is certainly not true of any of the ones that have come out so far. I think we have a number of suggestive leads but that is about as far as I could go with it at the moment.

Let me say one more thing about multiple sclerosis. It is turning out to be one of the most complex diseases of the nervous system we have to deal with.

Mr. FLOOD. It is getting more publicity?

Dr. TOWER. Yes, sir, it is getting more complicated all the time.

Mr. FLOOD. There is a lot of publicity that a persistent measles infection in the small intestine is causing multiple sclerosis. Has that been confirmed?

Dr. TOWER. I think that is carrying the evidence beyond what is warranted.

Mr. FLOOD. It is a good question.

Dr. TOWER. It is an interesting observation. It needs to be repeated. We are repeating it in our own laboratories in Bethesda, but the results have not yet come in.

There is no question but that there is a strong set of circumstantial evidence indicating measles as some part of the cause of multiple sclerosis. However, we have never been able to demonstrate any sort of reaction to measles virus directly in the nervous system of multiple sclerosis patients. This is a little discouraging because in all the other conditions known to be associated with the measles virus you can find some evidence that the measles is or has been there. We can't find that in multiple sclerosis.

Mr. FLOOD. How much will you spend in 1978?

Dr. TOWER. Something in the order of $11.5 million.

DIABETIC NEUROPATHY

Mr. FLOOD. You have a large current research program in diabetes neuropathy. What are your plans in that?

Dr. TOWER. In 1977 we are spending $1.86 million. We hope to go up to $2 million in 1978.

Mr. FLOOD. We heard recently that there is not a suitable animal model for diabetes research. How does that affect your whole research program in diabetic neuropathy if you don't have an animal model?

Dr. TOWER. I think we have a better animal for neuropathy than people have for other aspects of the diabetes problem because there is a counterpart of the multiple sclerosis situation in the central nervous system for the peripheral nervous systems using the proteins of the peripheral nerve to produce in the animal a reaction similar to diabetic neuropathy and with that we can evaluate the effects of changes in blood sugar and the like.

Mr. FLOOD. But no suitable animal model?

Dr. TOWER. Yes; we have for neuropathy specifically.

In addition, we have tissue culture models which are promising to do the same thing with the cells which nourish the nerves in the periphery of the body.

OTITIS MEDIA

Mr. FLOOD. What is the status of your clinical research on otitis media? Last year, you told us there was very little agreement, if any at all, among the scientists on how to deal with this problem. Do you have any agreement now?

Dr. TOWER. We are working up to another workshop in which the collaborators can get together and compare results. We have several projects being supported and we are going to have another look at that problem this year.

In addition, we also have ongoing a collaborative study of the tonsil and adenoid problem to see whether the numbers of tonsillectomy and adenoidectomy procedures now going on are sufficient or excessive.

Mr. FLOOD. That is a longstanding question.

Dr. TOWER. Yes, sir, and we are looking at it.

COMPREHENSIVE EPILEPSY CENTERS

Mr. FLOOD. Have you completed the assessment of your comprehensive epilepsy centers? What is the chance of these centers in the future?

Dr. TOWER. These five comprehensive centers will come up for review beginning the latter part of this calendar year so that the evaluation is not yet complete. I would not like to prejudge them; however, I think so far we can say we are very happy with what we see going on.

I had the opportunity to visit one of them out in the Midwest at the time when they dedicated one of their intensive care units. We know that they are beginning to activate their satellite or outreach programs. I think these are exciting a great deal of attention and effective operation at the community level.

We are happy with them so far. That is about as far as I would like to go until the review is over.

INTRAMURAL RESEARCH

Mr. FLOOD. Now, in your budget justification for your intramural research program, there you list an Office of Biometry and Epidemiology. Now, here is the problem: You state this group will support investigations using a contract mechanism. That seems to me if you contract for services, then you are no longer engaged in intramural research. We would like you to clear that up.

Are you going to do this work in-house or are you going to have the contractor do the work for you?

Dr. TOWER. Mr. Chairman, I think it is not quite correct to consider the biometry as part of our intramural research program. It is part of the Office of the Director of the Institute. So it is administratively a direct operation rather than extramural operation. What we are engaged in primarily in biometry and epidemiology is looking at the dimensions of chronic disease problems. We have very few solid data about incidence and prevalence, how many new cases occur, how many cases there are in a country at any given time, what they cost, and this sort of thing.

We are contracting out to concerns that have expertise in probability sampling techniques that are necessary for this to give us this type of information.

Mr. FLOOD. How much of that work is actually being performed by contractors, percentage and dollars both?

Dr. TOWER. I am not sure that I have premisely the figure, but I can get it for you.

Mr. FLOOD. We want that. That would follow through with the answer you are giving.

Dr. TOWER. I think you are going to find some of these types of information that we are collecting extremely interesting. For example, in preliminary data that we have on brain tumors, we find that over one-half of the brain tumors are secondary malignant tumors rather than primary tumors. I don't think most people out there realize that.

It is this sort of information which we think is very important.

Mr. FLOOD. Are these data-gathering activities coordinated with the National Center for Health Statistics?

Dr. TOWER. They most certainly are. We have very close collaboration and fund joint projects with the National Center for Health Statistics and also the Bureau of the Census in collecting the information. We hope that the National Center for Health Statistics will be able to take over the sampling techniques which we are pioneering and carry them on not only for our institute but for the whole of the medical scene.

DISTRIBUTION OF INTRAMURAL BUDGET

Mr. FLOOD. Would you prepare for the record at this point a true breakout of your intramural research budget showing the positions and dollars for fiscal 1977 and 1978? Don't forget, we want the contracted activities set aside and the intramural activities.

Dr. TOWER. Yes.

[The information follows:]

INTRAMURAL RESEARCH PROGRAM

The budget justification for intramural research includes the office of biometry and epidemiology because of the support relationship required for the laboratory and clinical programs of the Institute.

As the chart below indicates, this activity also includes contracts which are a specific activity in support of the intramural research of NINCDS.

The investigator-initiated research effort of our intramural program is still the predominant mechanism to create the new knowledge with which to achieve progress.

INTRAMURAL RESEARCH

[In thousands of dollars]

	1977		1978	
	Position	Amount	Position	Amount
1. Laboratory and clinical research in house	295	15,072	295	16,684
Laboratory and clinical research contracts		2,966		3,134
2. Office of Biometry, in house	29	1,037	29	1,098
Office of Biometry, contracts		524		541
3. NIH Management fund		7,815		8,562
Total, intramural research	324	27,414	324	30,019

PROGRAM EVALUATION FUNDS

Dr. TOWER. May I make you aware that some of the moneys for these studies are being supported through what is known as set-aside funds at NIH which are provided specifically for evaluation studies. So this is a contribution that each Institute makes to a central pool and about something in the order of $683,000 in our case has been used for this.

Mr. FLOOD. All right.

Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

Mr. MICHEL

FUNDING LEVELS

Mr. MICHEL. I get the impression from the statement you've submitted that you feel your Institute is underfunded. Is that an accurate impression?

ANSWER. The Institute in 1977 will not be able to fund 72 percent of approved competing grants. The dollar value of unfunded research grants in 1977 will be $29,952,000 and training programs will fall $2 million short of full funding of all worthy fellowships.

NIH FUNDING RATIOS

Mr. MICHEL. Are you concerned at all about the priorities in NIH where some areas such as Cancer receive substantial funding while others have to fight for the remainder? Would you suggest any different funding ratios?

ANSWER. Yes; we are concerned in terms of the difficulty of garnering research resources for some of the less publicized disease and disorder problems. These represent collectively, a significant portion of the health care costs of the Nation. It is estimated that each year the health care costs alone for nuerological and communicative disorders, including stroke, exceed $19 billion for some 46 million patients. Unfortunately, many of these disorders leave the patient disabled for many years contributing to a staggering health care burden and economic loss over a lifetime. We would hope that funding would reflect in part the severity of problems and their social and economic costs, as well as the research opportunities to attack and effectively address those problems. We are confident that the resulting increased research effort on treatment and prevention of these less publicized disorders will be well justified by future savings both in dollars for care and in reduced human suffering.

PERCENT OF GRANTS FUNDED

Mr. MICHEL. In the fields covered by your Institute, what percentage of the grant applications received this year will be funded, and second what percentage of the applications approved by the study sections will be funded?

ANSWER. It is estimated that approximately 14 percent of the grant applications received in fiscal year 1977 will be funded, and that 28 percent of competing applications approved by the study sections will be funded in fiscal year 1977.

EPIDEMIOLOGY STUDIES

Mr. MICHEL. I note in your statement a suggestion that there should be "separate funding" for programs designed to deal with epidemiology, flow of facilities and organization of community resources. What do you mean by separate funding in this case?

ANSWER. I intended to point out in my statement that the Institute supports at a significant dollar level programs designed to deal with epidemiology, flow of facilities, organization of community resources in a number of disease areas, including epilepsy, stroke and central nervous system trauma through the mechanism of comprehensive centers for these specific disorders. These centers repre-

sent a significant effort in the translation, transfer, and application of research results to community health care practice and to coordinate this with community resources necessary to rapidly capitalize on research advances in those areas. If the approach of these experimental comprehensive centers to the coupling of research to community practice and comprehensive care is successful, they will each require on a time-limited basis significant resources which we feel could, and probably should be, identified separately in the budget from the more traditional, clinical and fundamental biomedical research. I, therefore, suggest that it is timely to consider the appropriateness of such separate funding for these particular programs.

NOBEL AWARD

Mr. MICHEL. It was certainly a noteworthy accomplishment that Dr. Gajdusek received the Nobel Prize. Would you discuss for us some of the implications of his finding that degenerative nervous disorders can be caused by viruses?

ANSWER. As a result of the discoveries by Gajdusek and his colleagues, it is now firmly established that chronic degenerative neurological disorders of man can arise by the slow but relentless multiplication of infectious agents of the slow virus group which cause disease many years after the initial infection.

These discoveries have already been responsible, in large measure, for the recognition of a slow virus cause for two other degenerative disorders of the human nervous system: subacute sclerosing panencephalitis caused by a defective measles virus and progressive multifocal leukoencephalopathy caused by the JC and SV40 strains of papova virus.

By the late 1960's, four neurological disorders—scrapie and transmissible mink encephalopathy in animals and kuru and Creutzfeldt-Jakob disease in man—had been established as caused by an atypical slow viruslike agent or agents which produce closely similar, if not identical, diseases in a variety of primate, rodent and ungulate species. Such discoveries are viewed by many as having significant implications for the nature of multiple sclerosis, amyotrophic lateral sclerosis, Alzheimer's disease and other presenile or senile dementias. In fact, two cases of the familiar form of Alzheimer's diseases have been transmitted to subhuman primates, and the amyloid plaques typically seen in scrapie and kuru brains appear to be identical with the immunoglobulin-derived amyloid plaques characteristically present in the brains of patients with presenile dementias.

As Cedric Mims states, it seems probable that we have still not gathered the full harvest of the discoveries made by Gajdusek. As Gajdusek has pointed out, these unconventional, atypical viruslike agents represent an entirely new biological phenomenon. They are unlike any other known infectious agent—an extraordinary discovery in itself—and warrant special precautions by neurosurgeons and neuropathologists.

Yet the last word belongs to Carleton Gajdusek, who insists that the discoveries to date represent only the beginning. Our appreciation of the extent of neurological involvement and our understanding of the significance of the slow virus biological phenomenon are still to come.

Mr. MICHEL. What kind of followup work is being done in connection with that discovery?

ANSWER. Much of the followup work will, in the future, be conducted in the NINCDS facility nearly ready for occupancy at the Frederick Cancer Research Center, where close interactions with NCI investigators will be greatly facilitated.

STROKE

Mr. MICHEL. Your statement indicates that the source in the brain for stroke involvement differs for Asian countries compared with the United States. Why is that?

ANSWER. No one knows why there are differences among different peoples in the site of pathology, yet not the type of pathology. Cerebral infarction due to thrombo-embolus is clearly the major cause of stroke. Yet in some countries this occurs more frequently in the larger blood vessels at the base of the brain; in other countries, it occurs more often in the smaller penetrating arteries. Genetics, living style including diet, and the incidence of hypertension are obvious important factors; however, these do not adequately explain these differences. Institute epidemiological studies are focused on finding an improved explanation for these differences.

TRAINING AWARDS

Mr. MICHEL. Your budget shows a substantial decline in new training awards. Does that indicate that we have developed a sufficient supply of scientific manpower in the fields covered by your Institute?

ANSWER. No, sir, we have not developed a sufficient supply of scientific manpower in the fields of neurology. With regard to the individual fellowship we have to be guided by the recommendations of the National Academy of Sciences to determine the new awards for any given year. Also, there has been a moratorium on the award of new institutional NRSA's until a review of the program is completed.

CLINICAL TRIALS

Mr. MICHEL. How much of your funds are going to clinical trials?

ANSWER. A review of the Inventory of Clinical Trials indicates that 45 trials were supported by NINCDS in fiscal year 1976. The cost of these trials was approximately $2,280,000 for that year. This amounts to approximately 1.6 percent of the Institute's budget.

Mr. MICHEL. Would you list for the record the clinical trials being funded, their projected length, and the funding for each?

ANSWER. A list of the funded clinical trials, their projected duration and the fiscal year 1976 support follows.

NINCDS CLINICAL TRIALS

Title	Date started	Expected duration (years)	Fiscal 1976 fund
Effect of formal speech therapy on aphasia patients	November 1974	3	$18,750
Urokinase therapy in acute thromboembolic cerebrovascular disease.	December 1973	4	50,000
Clinical evaluation of a new anticonvulsant drug, dimethoxymethyl phenobarbital.	June 1974	4	60,000
Use of l-dopa in parkinsonism	January 1967	12	90,000
Treatment of acute spinal cord injuries	January 1974	5	100,000
Effect of l-dopa on intellectual deterioration in parkinsonism	January 1975	5	45,000
Effect of papaverine on dopa treatment of parkinsonism	January 1974	5	28,000
New pharmacological agents in treatment of basal ganglia disorders.	January 1971	10	60,000
Stereotoxic techniques in the management of intractable seizures	July 1971	7	182,000
Fluid restriction in acute subarachnoid hemorrhage	January 1975	3	268,350
Study of anticonvulsant properties of valproate and ethosuximide	June 1969	9	138,000
Investigation of posttraumatic epilepsy prophylaxis	June 1972	6	150,000
Study of treatment of complex partial seizures	June 1970	7	210,000
Development of a model for assessment of new antiepileptic drugs.	June 1968	9	100,000
Intravenous infusion of respective missing enzyme to patients with Fabry's disease and patients with Gaucher's disease.	February 1973	3	[1] 78,890
Acoustical and perceptual differentiation of 2 types of dysarthria	January 1975	2	[2] 17,150
Death and anxiety in Huntington's disease	April 1975	1	[2] 17,150
Effects of norepinephrine on dyskinesia and dystonia	January 1974	2	[2] 17,150
Turnover of monamine metabolites in CSF	November 1972	4	[2] 17,150
Effect of fenfluramine on anterior pituitary hormone release in man	October 1974	2	[2] 17,150
Bromocryptine treatment of neurologic disease	February 1975	3	[3] 34,300
Immune responses to rubeola and rubella vaccines	April 1974	3	[3] 34,300
Pilocarpine therapy of neurologic disorders	May 1975	2	[2] 17,150
Double blind crossover therapeutic trials of azathioprine and prednisone versus placebo and prednisone in polymyositis/dermatomyositis.	January 1975	2	[4] 8,575
Combined l-dopa and MK-486 therapy	January 1970	10	[3] 34,300
Fusaric acid treatment of parkinson's disease and related disorders.	January 1971	5	[5] 6,860
ET-495 treatment of neurologic disorders	January 1973	4	[2] 17,150
Lioresal therapy of neurologic disorders	January 1972	4	[5] 6,860
Imidazole acetic acid therapy of Huntington's chorea	May 1973	3	[2] 17,150
HA-966 therapy of neurologic disorders	do	3	[2] 17,150
Effect of clonidine treatment on neurologic disease	January 1973	3	[5] 6,860
Fenfluramine treatment of neurologic disorders	do	3	[3] 34,300
Effect of lithium treatment on hyperkinetic neurologic disorders	do	3	[5] 6,860
Melatonin treatment of Huntington's chorea and related disorders	January 1974	2	[2] 17,150
Effect of deanol in hyperkinetic disorders	do	2	[3] 34,300
Effect of depakine or extrapyramidal and seizure disorders	March 1974	3	[2] 17,150
Effect of GABA on extrapyramidal and seizure disorders	April 1974	3	[2] 17,150
Effect of caffeine on l-dopa or ET-495 induced changes in extrapyramidal function.	May 1974	3	[2] 17,150

See footnotes at end of table.

NINCDS CLINICAL TRIALS—Continued

Title	Date started	Expected duration (years)	Fiscal 1976 fund
High single dose alternate day prednisone treatment of myasthenia gravis.	January 1970	10	[2] 34, 300
Acetazolamide	January 1966	12	[5] 6, 860
High single does alternate day prednisone treatment of polyneuropathy.	January 1967	11	[2] 17, 150
High single dose alternate day prednisone treatment of dermatomyositis/polymyositis complex and treatment of prednisone failures with azathioprine.	January 1964	12	[2] 17, 150
Therapeutic trials in the treatment of mucopolysaccharidosis	1974	2	[6] 41, 160
Clinical and biochemical studies of epilepsy	1973	4	[7] 51, 450
Combined therapy of malignant gliomas	January 1973	6	[8] 102, 900
Total support			2, 280, 425

[1] 2.3 man-years.
[2] 0.5 man-year.
[3] 1 man-year.
[4] 0.25 man-year.
[5] 0.2 man-year.
[6] 1.2 man-years.
[7] 1.5 man-years.
[8] 3 man-years.

MULTIPLE SCLEROSIS

Mr. MICHEL. How much is in your budget for multiple sclerosis?

ANSWER. In 1978 the budget estimate contains an amount of $11,484,000 for research on multiple sclerosis.

Mr. MICHEL. Have you established as yet any separate division for multiple sclerosis with a full-time administrator?

ANSWER. We are actively recruiting a full-time neurologist to be a focus for demyelinating and sclerosis disorders within the neurological disorders program. The ad hoc work group of the NANCDS Council Report, submitted to this subcommittee, addresses the role to be played by this person in the program.

Mr. MICHEL. Are you fully carrying out the recommendations of the National Advisory Commission on Multiple Sclerosis, or are there some areas where you disagree?

ANSWER. A detailed analysis of the Multiple Sclerosis Commission report recommendations has been made by the ad hoc work group of the NANCDS Council. In general, we are in agreement with the recommendations of the Multiple Sclerosis Commission and where practicable have amply implemented the recommendations. We defer to the report of our Council work group as, submitted, for an independent assessment.

SPINAL CORD

Mr. MICHEL. How much in our budget is being allocated for spinal cord research?

ANSWER. The 1978 budget includes an estimated amount of $6,500,000 for spinal cord research.

SPINAL CORD

Mr. CONTE. What research are you supporting on spinal cord injury and other trauma to the nervous system? To what extent is your research in this area coordinated with programs involved in service delivery such as the emergency medical services program? How well are the results of your research put into practice? Can you give examples?

ANSWER. In our central nervous system trauma program we are currently supporting 46 research grants amounting to $2,286,000, 6 head injury clinical research centers for $2,217,246 and 5 spinal cord injury clinical research centers in the amount of $3,012,081. This work encompasses basic research, for example investigation of neurotramsmitter substances and synapse activity in the spinal cord; clinical research, such as evoked potentials for improved diagnosis in patients with spinal cord injury and applied research, for example, evaluation of therapy of the acute injury.

We are initiating a program of comprehensive central nervous system trauma centers designed to make new methods of therapy rapidly available to the public. In conjunction with establishing this program, we are interacting with Dr. David Boyd, Director of the Emergency Medical Service program, in order to maintain the coordination of our activities.

The application of research findings to practice depends to some extent on the nature of the hospital involved, with more rapid utilization in university hospitals than in community hospitals. Our program is geared to help correct this delay. One recent example of a technique proved useful in the research laboratory and now being widely accepted in clinical practice is the use of cortical evoked potentials in evaluating the status of the spinal cord in patients with spinal cord injury. Another example is assessing the appropriate use of steroids in the treatment of the acute injury to prevent edematous degeneration of the cord is now widely accepted.

NEUROSCIENCES

Mr. CONTE. To what would you attribute what appears to be a recent growth in interest in neuroscience? Has this eased the problem of finding sufficient numbers of skilled researchers in the neuroscience field?

Answer. There has undeniably been an increase in recent years in interest in the neurosciences among both scientists and the general public. There are many factors leading to this growth, but one general reason is the rapid increase in knowledge about the fundamental mechanisms operating in the central nervous system in both normal and diseased states. This has led to an increase both in number and scientific excellence of research grant applications which now far exceed our ability to fund. The increased number of exciting and challenging new problem areas for investigative research are only partially balanced by the increased numbers of young neuroscientists just completing their lengthy training, much of it at Government expense, who are now ready to devote themselves to research in the neurosciences.

BASIC RESEARCH

Mr. CONTE. What portion of your budget is devoted to basic research? Do you believe that this is an appropriate amount, or would it make more sense from a scientific standpoint to devote some of the funds presently mandated for specific purposes to more basic research?

ANSWER. Slightly over half of the Institute's budget is devoted to basic research in the sense that it is research fundamental to an understanding of the nervous system and how it malfunctions in a variety of disease processes. The results of this research will be applicable to a variety of more specifically targeted diseases and other health problems. For a large percentage of the neurological disorders confronting the Institute, this basic understanding of the normal and pathologic processes and the causes and clinical expression of diseases are not yet understood. Therefore, at least this level of effort on basic research must be maintained if we are to be able to continue to address mandated, specific areas and other disease problems from the standpoint of treatment and prevention. While increases in this basic research effort are badly needed, to do so at the expense of those mandated areas where specific research targeted toward treatment and prevention of particular diseases is possible would be unfortunate.

FUNDING PROBLEMS

Mr. CONTE. How much of your funding is actually discretionary; that is, not specifically mandated?

ANSWER. There are no specific mandated programs. However, there are certain areas of special concern that are reported to Congress each year. These represent a large percentage of the total budget.

Mr. CONTE. What percentage of your approved projects are you able to fund this year? What percentage would you expect to fund next year under your proposed budget?

ANSWER. The NINCDS expects to fund 62 percent of the total approved grants, noncompeting plus competing, in 1977 and 54 percent of the total under the 1978 budget. For competing grants only, the respective percentages are expected to be 28 percent and 30 percent.

Mr. CONTE. What is the Institute's policy on multiyear funding of research fellowships? Is it ever done?

ANSWER. We do not multiyear fund any national research service awards. As for the individual NRS awardees, if they are approved for more than 1 year of support, a 1-year award is made with the understanding that subsequent annual awards will be made if satisfactory progress is made in the first year. No awardee can receive an aggregate of more than 3 years of support under the NRSA programs.

Mr. CONTE. Don't you run into problems with a 1-year fellowship, in that 1 year really doesn't give a fellow time to get into a laboratory, master a technique, do something useful with it, and get it published? Have you done any followup work on what happens to these people at the end of their 1-year fellowships?

ANSWER. An award for only 1 year of fellowship support does not constitute a problem. Approximately 16 percent of approved applications are for 1 year only. Reviewers take into consideration whether the training program described in the application can be accomplished in the time requested. It should also be pointed out that the proposed training is frequently in the same environment and in the same general area as the applicant's doctoral training. Concerning reports emanating from the research, that is frequently accomplished after the postdoctoral training has been completed and the trainee has gone on to a teaching or research position. We have not yet done any followup work on the NRS awardees since the program has not been in operation long enough for a valid assessment.

TYPES OF RESEARCH SUPPORTED

Mr. CONTE. There have been some criticisms of the Institute, along with the others, that there is a tendency to fund predictable outcome research, that the review panels are inherently conservative. Would you care to comment on such criticisms?

ANSWER. I would like to point out that no research is fully predictable in its outcome, and this is particularly true for biomedical research. For this reason, review committees may tend to be somewhat conservative in favor of research teams and research protocols which are sound and are most likely to produce significant, useful results. This is particularly true in a tight budget year when hard priority choices must be made between many research projects of excellent quality. Still, a certain amount of risk is taken in supporting important research in areas where the outcome is very uncertain but where the problems and need for progress are of sufficient importance to take such risk.

Mr. CONTE. Can you tell me about some of the areas in which you support research into the effects of neurological disorders on human behavior? It seems that such research might tend to fall between the cracks between your Institute and the NIMH. Is that the case?

ANSWER. There are behavioral components of all neurological disorders which are of importance for both diagnosis and treatment. The comprehensive epilepsy centers program is an example of NINCDS support applied to the behavioral aspects of neurological disorders. An entire range of psychological support is offered to patients and their families through the outreach components of the centers. In addition, social services are provided at the community level. At the present time, there are five established centers with additional activities in the planning stage. At a multiple sclerosis research center in Los Angeles, there are similar, though less extensive, activities. Our clinical research centers programing has endeavored to include both psychological and sociomedical aspects of neurological disorders. We are cognizant of the problems of coordinating research in areas which cross interinstitute and interagency boundaries. We track important behavioral work by maintaining a regular liaison with the appropriate section of the NIMH. An example of this is the participation of the NIMH in the upcoming Alzheimer's disease/senile dementia and related disorders conference at NIH scheduled this coming June, for which NINCRS is the lead agency with participation also by NIA. Children from the NINCDS collaborative perinatal project are being studied for minimal brain dysfunction and its hyperactivity component, as well as behavioral and neurological factors of NINCDS collaborative perinatal project children with autism. Project data on the children of schizophrenic mothers are being analyzed by the National Institute of Mental Health.

INTRAMURAL RESEARCH

Mr. CONTE. I see that you have a fairly large increase programed for your intramural research program. Can you tell me what that increase will be primarily used for?

ANSWER. Approximately one-half the proposed budgetary increase to the intramural research program will be required to maintain the current level of effort. The remainder will be applied to the support of the following vital program extensions and new initiatives:

We would accelerate and extend the studies of Dr. Gajdusek which lead to his receiving the Nobel Prize in medicine this year. These include the possible link between slow virus infection and chronic debilitative neurologic disorders including Huntington's chorea, Parkinson's disease, amyotrophic lateral sclerosis and multiple sclerosis.

The Institute plans to extend pioneer investigations by NINCDS intramural scientists into reliable early diagnostic tests and effective enzyme replacement therapy for lipid storage disorders such as Tay-Sachs and Gaucher's diseases.

We will intensify laboratory studies of immunologic factors in multiple sclerosis and Guillian Barre syndrome, and will also establish a vigorous new program of studies of chemical factors influencing nerve growth and regeneration.

New approaches to computerized axial tomography will be explored. This is the most significant advance in neurodiagnostic technology in the past 25 years.

It is planned to extend the substantial contributions already made by intramural scientists toward the rational development of improved drug therapies for such nervous system disorders as Parkinson's disease and epilepsy.

Other planned expansion in clinical research will include revitalizing neurosurgical research with special emphasis on studies of pain, especially that occurring in the lower back, and initiating a much needed research program in clinical audiology and communicative disorders.

LEVEL OF 1978 FUNDING

Mr. CONTE. Your budget proposes an increase over last year's appropriation significantly less than the rate of inflation. In what areas will you be forced to curtail program levels? How much money would actually be required to maintain present program levels?

ANSWER. If the Institute's budget fails to keep pace with increasing costs due to inflation, we will be forced to curtail the program levels in some areas below those which are both desirable and needed. Since the vast majority of the Institute's budget is required each year to meet our commitments to ongoing activities, major curtailments will unfortunately have to be reductions in new projects, decreases in planned extensions of existing work, or the termination of competing renewal grants.

As an example, our stroke comprehensive centers program is just now in the pilot phase and implementation of fully operational centers would have to be either postponed or abolished.

Another example of this effect is that it would be impossible to significantly improve the appallingly low percentage of new and competing grant requests which can be funded, and thus truly excellent research by highly productive teams of investigators in virtually every field of concern to the Institute will go begging. To maintain current program levels, including sufficient awards of new and competing renewal grants to maintain the same level of grant portfolio, we estimate that $178 million would be required in an overall Institute budget.

NUMBER OF GRANTS FUNDED

Mr. CONTE. Why are you proposing to fund fewer regular program grants this year than last year? What accounts for the increase in the average grant amount?

ANSWER. The main reason for proposing to fund less grants in 1978 than 1977 is due to the cost per grant. The average cost for all grants in 1978 is estimated to be $98,000 per grant, an increase of $12,000 over 1977. The increase is not only due to the economy but to the cost of large center grants and program projects.

AUTISM

Mr. CONTE. Is your Institute supporting any research in the autism area? Have there been any recent developments in autism research?

ANSWER. The NINCDS has taken a number of steps to develop a program of research support on the neurobiological aspects of autism. A workshop sponsored by the NINCDS in February 1976, clearly established that research on the neurobiological aspects of autism is clearly warranted and that a program of research in this area should be pursued. The Division of Research Grants, NIH, has been requested to refer to the NINCDS, applications for grants which concern the neurobiological aspects of autism. Within the NINCDS, a section on autism and behavior disorders is planned, and active recruitment for a section head has begun. Research on autistic children in the NINCDS collaborative perinatal project has demonstrated a significant increase in uterine bleeding in their mothers during pregnancy. Studies on this group of autistic children are continuing. There is increasing evidence that autism is a neurobiological disorder, and in a recent paper in Nature, vol. 265. February 24, 1977, Michael Rutter and Susan Tolstein concluded that the "systematic study of 21 same-sexed twin pairs in which at least one twin showed the syndrome of infantile autism, indicates the importance of a genetic factor in the etiology of autism. It also indicates the importance of brain injuries, especially during the perinatal period, which may operate either by themselves or in combination with genetic predisposition involving language."

Mr. CONTE. I was interested in your comments about the differences between blood vessel involvement in American and Japanese people who suffer strokes. To what would you attribute the differences—is it largely a dietary factor?

ANSWER. No one yet knows why these differences occur. Epidemiologic studies demonstrate that there are genetic factors affecting the incidence of stroke. Yet we also know that stroke in Japanese-Americans living in the United States more closely resembles U.S. whites than Japanese living in Japan; Japanese-Americans in Hawaii are somewhat in between. Are these differences due to dietary factors? To lifestyle? To exogenous toxins? To changes in patterns of hypertension? We do not yet know but are giving priority to finding the answer.

COMMISSION REPORTS

Mr. CONTE. Could you tell me when the Commissions on Epilepsy and Huntington's Disease will be reporting?

ANSWER. The Commission on Huntington's Disease will be reporting during August 1977, to the Secretary of HEW, the President. and the Congress. The Epilepsy Commission is also expected to complete its report in August 1977.

Mr. CONTE. Can you tell me about the work done in your spinal cord injury clinical research centers?

ANSWER. The spinal cord injury clinical research centers were created to develop a better understanding of the pathophysiology of spinal cord trauma and thus develop improved methods of treatment of the spinal cord injured patient. The thrust of investigations are in the following areas: Epidemiology of spinal cord trauma, emergency and hospital care of patients with spinal cord injuries emphasizing improved methods of diagnosis and treatment to prevent or arrest cord degeneration, development of prosthetic devices to help control bladder dysfunction and to restore the use of paralyzed limbs, and laboratory studies of spinal cord and spinal column structure and function with an emphasis on cellular function and dysfunction in response to trauma. This includes studies of spinal cord regeneration and central nervous system plasticity.

CLINICAL FACILITY

Mr. CONTE. What are your plans for the creation of a clinical facility in the NIH Clinical Center? Can you tell me what will be done there?

ANSWER. Clinical facilities for communicative disorders research and patient care at the Clinical Center have been limited. Aside from many research needs, plans are being implemented to provide adequate diagnostic equipment and facilities to be able to provide competent ear, nose. and throat consultation to Clinical Center patients. For example, many patients at the Clinical Center receive experimental drugs which can affect hearing and equilibrium. In order to understand how these drugs are affecting the ear, it is important to evaluate hearing

and balance function carefully. Cancer patients, as well as other Clinical Center patients, are often very ill and have complicated problems of the sinuses, upper airways, and ear, and mastoid. This Institute is aware of a need to provide better access to sophisticated otolaryngologic care for these patients.

There are many unmet needs in research which are goals in planning for clinical facilities for communicative disorders. Research on serious otitis media and chronic ear disease; research on sudden hearing loss and fluctuating hearing loss; research on laryngeal papillomas and upper airway obstruction in children; research on early identification of laryngeal pathology and assessment of vocal disorders; research on the use of neuropharmacologic treatment for speech and language disorders, research on better communication aids for the deaf and the hard of hearing—all of these areas need tightly controlled careful clinical research that would best take place in a setting like the Clinical Center. Communicative disorders, including otolaryngology, audiology, and speech pathology is a prime example of an area where medical care can be effectively provided in an outpatient setting. We anticipate that there should be an active communicative disorders research program in the new Ambulatory Care Center under construction at the Clinical Center.

MR. ROYBAL

NOBEL LAUREATE

Mr. ROYBAL. You indicate that one of your scientists was selected as Nobel laureate in medicine for his discovery that degenerative and dementing disorders are caused by viruses. What followup studies are being done as a result of this initial discovery? Does this discovery imply that the viruses are carried within the cell and spring to life because of some occurrence of enzyme? If so, are you coordinating your research efforts with other institutes who are studying the chemical makeup of the cell?

KURU

ANSWER. The initial discovery that kuru, an heredofamilial progressive degenerative subacute fatal brain disease of the Fore people living in the Eastern Highlands of Papua, New Guinea, is caused by a serially transmissible, self-replicating, filterable virus having atypical biological and chemical properties, has led to the further discovery that some forms of presenile and senile dementias of man have a similar etiology. These dementias are of the Creutzfeldt-Jakob type, both the sporadic and familial forms, and, in at least two instances, the familial form of Alzheimer's disease. From our work we can conservatively estimate the prevalence of Creutzfeldt-Jakob disease, or CJD, to be two per million population yearly in the United States and in both central and Western Europe. Of these 10 to 12 percent are of the familial type with disease occurring in as many as 5 generations and affecting 10 to 12 people. To date only the familial form of Alzheimer's disease has been proven to be caused by a transmissible virus; in more than 30 attempts we have not been able to transmit the disease from sporadic forms of this disease. It is this later form which has the greatest impact on society since about 25 to 30 percent of the patients in mental institutions are diagnosed as having Alzheimer's disease. In addition, a third human disease, referred to in the literature as progressive supranuclear palsy or Steele-Richardson syndrome, has proven to be transmissible to nonhuman primates in which it has caused a subacute spongiform encephalopathy indistinguishable from the experimental disease induced by kuru, CJD, familial Alzheimer's and the two related diseases of animals, scrapie and transmissible mink encephalopathy. Thus, a major effort concerns the spectrum of human disease that will be found to be transmissible and the relatedness of these diseases one to another. For example, are we dealing with a syndrome in which the patients symptomatology varies clinically resulting in different descriptive diagnosis but which, in fact, are caused by the same virus? We are also concerned with the epidemiology of these diseases, their rate of occurrence and possible modes of transmission.

The striking similarity of the human disease to that of scrapie of sheep and goats both in clinical symptomatology and in neuropathological destruction at the selective level as well as the transmission of scrapie directly from natural affected sheep and goat to several species of nonhuman primate has strongly suggested that scrapie may not be innocuous for man and may, indeed, have an etiological role in the subacute central nervous system diseases we have been

studying. In the epidemiological data we have collected on the human diseases the following points are of major significance:

Kuru occurred in near-epidemic proportion in 1956 to 1957 but with the cessation of the practice of ritualistic cannibalism, this disease has virtually disappeared with disease now occurring in equal numbers of males and females all of whom are over 20 years of age indicating their involvement in the practice of cannibalism before it was outlawed in 1959.

CJD does exist in New Guinea outside of the kuru region; thus, it is possible that this disease gave rise to kuru which rapidly spread through the Fore people.

The origin of CJD is not known but could be the result of the consumption of scrapie-infected sheep and/or goat tissues that were improperly cooked, since the viruses causing both the human and animal diseases are extremely resistant to inactivation by heat, ultraviolet light, and many organic and inorganic chemicals. Further, it is well documented that scrapie in sheep is associated with asymptomatic incubation periods of 3 to 5 years; however, most sheep sent to slaughter houses are below the age of 3 years. Despite freedom from clinical disease, scrapie virus can be present. A study of natural infection in sheep raised in a scrapied environment shows that in 9 out of 16 lambs born in this environment scrapie is widely spread throughout the lymphatic system and the gastrointestinal system of such lambs as early as 10 to 14 months of age and that by 24 months of age virus is present in the central nervous system preclinically. Thus, it is entirely possible that consumption of this meat improperly cooked or butchery accidents may account for some cases of human disease.

The spread of transmissible dementias in man have now clearly been shown to be associated with, and to constitute a hazard in transplantation surgery; for example, the transmission of CJD by corneal transplantation, and in other clinical and neurosurgical procedures. For example, recently CJD has apparently been transmitted to a 17-year-old boy and a 24-year-old girl by implantation into their brains for diagnostic studies of electrodes that had been previously implanted into the brain of a patient with CJD.

The occurrence of CJD in a neurosurgeon suggests an occupational hazard.

TRANSMISSION OF VIRUSES

The strong resistance of the viruses to inactivation by heat and chemicals raises the possibility that transmission may inadvertently occur in the operating room during neurosurgical procedures that employ instruments that have not been adequately decontaminated since previous use as in the case of the electrodes referred to above. We have now shown that CJD can be transmitted to animals inoculated intracerebrally with human brain tissue that had previously been stored in formalin fixative, 4 percent formaldehyde, for 8 months.

In contrast, we have determined that the infectivity of viruses causing subacute spongiform encephalopathies can be totally inactivated by autoclaving, dry heat sterilization, and treatment with phenol and/or sodium hypochlorite. Such procedures have been recommended to the medical profession at large.

The major laboratory thrust of our program concerns the nature of the viruses causing these diseases. As previously mentioned they possess many of the properties of conventional viruses:

They are filterable. They self-replicate to high concentration frequently exceeding 1 million to 100 million infectious particles per gram of brain tissue and slightly lesser amounts in most other tissues and fluids of the infected host, such as liver, kidney, lymph node, lung, cerebrospinal fluid. They consistently reproduce the same clinical disease and histopathological lesions which are restricted to the central nervous system.

NEW GROUP OF ACTIVE AGENTS

However, they possess properties which suggest that rather than classical viruses they are a new group of biologically active agents new to microbiology and medicine. For example, they do not cause inflammatory lesions. They are not associated with a febrile response, increased cell counts in cerebrospinal fluid, or alteration of clinical chemical or blood values. They do not induce an immune response but neither do they affect the functionability of the host immune mechanism on the humoral or cellular level. They have not been visualized as recognizable virus particles by transmission, scanning, or freeze-fracture electron micros-

copy. They have not been associated with a specific nucleic acid type, RNA or DNA, and they are not inactivated by moderately high temperature, nucleases, or high energy spectrum ultraviolet light.

Thus, the laboratory work centers on the purification and unmasking of the infectious particles which are believed to comprise a small molecular weight naked nucleic acid with just enough genetic information to genetically code for itself devoid of host protein. Our data strongly suggest that the infectious material is intimately associated with the plasma membrane of the infected cell but may be more intimately associated with the ribosomes of the cells themselves. It is herein that we are concentrating our efforts on the molecular biology of the infected cells and the virus.

It should be noted that our studies, in addition to work on the "unconventional viruses," include investigations on the etiology of multiple sclerosis, amyotrophic lateral sclerosis, chronic focal epilepsy. Huntington's chorea. Parkinson's disease, and post encephalitic parkinsonism. Studies include classical virological techniques to rescue viruses in vivo and in vitro as well as molecular studies to detect specific sequences of viral genes by nucleic acid hybridization procedures employing "radioactive tagged purified virus-nucleic acid probes." Preliminary data is providing evidence that the human central nervous system does contain small amounts of poliomyelitis virus genetic sequences. Before any etiological significance can be attached to these findings appreciable additional work must be done.

Finally, it is significant to note that this work established the concept and techniques that have been successfully employed in the establishment of defective measles virus as the etiological agent of subacute sclerosing panencephalitis and CJ and SV–40 papovavirus as the etiological agents of progressive multifocal leukoencephalopathy.

VIRUSES CARRIED IN THE CELL

With regard to whether viruses are carried within the cell, there are two issues to be considered. One is the question of latency, persistence, and chronic infections or host cells and the other is the potential role of a disturbed regulatory enzyme normal to the host cell.

In the first instance ample evidence exists to establish long-term persistence and latency of viruses in human tissues which at some point in time become activated and induce a clinically recognizable and sometimes fatal disease. Examples of this are found in subacute sclerosing panencephalitis, SSPE, wherein exposure to measles virus before the age of 1 year results in an impaired immune response, associated with persistent infection and blocking of cell receptor sites, permitting a destructive invasion of the host central nervous system at some later date. A similar situation occurs in progressive multifocal leukoencephalopathy, PML, as evidenced by the widespread antibody to CJ virus in about 50 percent of children between the ages of 3 to 5 years and greater than 80 percent of young adults showing an early infection in life with this virus. In adults developing PML an antecedent illness requiring immunosuppressive therapy allows the PML-CJ virus to become reactive and invasive of the brain to result in central nervous system disease and death. Such situations form the current working hypothesis for infection as the potential etiology of MS, ALS, and a host of related diseases such as postencephalitic parkinson's disease, late onset of clinical disease following exposure to rabies and, of course, a number of nonviral human diseases such as secondary and tertiary syphilis. Such derepression of latent agents may well be involved in CJD but hard data is lacking. There are several instances wherein the onset of CJD has occurred shortly after head trauma, suggesting activation. Some of the familial cases of CJD and familial Alzheimer's, especially in twins who have not lived together for more than 50 to 60 years, suggest infection in early life.

That a regulatory enzyme could be etiologically responsible has been suggested in slow infections; however, no evidence exists to support this hypothesis. In the work of Deiner, et al., on virus-induced diseases in plants, viroids, it was early postulated that the infectious process was caused by a regulatory enzyme. This is now known to not be the case and the viroid has been clearly identified as a circular RNA of less than 100,000 daltons molecular weight.

Since the investigations thus far have not identified the true nature of the transmissible agents of the spongiform encephalopathies it is felt that the

systematic "taking apart" of infected and comparative control cells both physically and chemically is necessary to isolate and purify the infectious materials. Such studies are being conducted with scientists within the NIH community as well as a wide variety of molecular biologists, cytologists, membrane specialists, and biochemists throughout the world. Most of this work will, in the future, be conducted in the NINCDS facility nearly ready for occupancy at the Frederick Cancer Research Center, where close interactions with NCI investigators will be greatly facilitated.

FUNCTIONAL ELECTRICAL STIMULATION

Mr. ROYBAL. You indicate that if stroke patients use an electrostimulation exercise regime, normal muscles can be strengthened rather than going through atrophy from disuse. Could such a principle be used by the elderly to strengthen their resistance to disease and possibly prolong life? How long can a person safely stay on such a regimen?

ANSWER. Functional electrical stimulation has been used experimentally to prevent atrophy in the paralyzed muscles of young paraplegic patients. Instead of wasting away, their muscles increase both in mass and in strength. While such electrotherapy could certainly be used on elderly patients and might have similar beneficial effects, it has not yet been determined that this would lead to resistance to disease or prolongation of life. The limits for functional electrical stimulation have not yet been determined. Experimental animals have been stimulated for days, weeks, and even months. However, muscle hypertrophy cannot be expected to continue indefinitely.

REGENERATION

Mr. ROYBAL. We were led to believe that the Soviets have made great strides in the area of spinal cord regeneration. You indicate that you are trying to duplicate their results in the laboratory. What are your results to date?

ANSWER. Within recent months we have had the opportunity to meet with the Soviet scientists and to discuss and evaluate their work on spinal cord regeneration in the rat. We believe their results are scientifically provocative but clearly not conclusive. By research contract we are now having these experiments repeated in this country. The results of these studies are not yet available. Additional research based on the Soviet claims is being supported through grants for the evaluation and extension of the Soviet spinal cord regeneration work.

Mr. ROYBAL. What is the status of your research on otitis media, a disease of the middle ear?

OTITIS MEDIA

ANSWER. Otitis media has an incidence of about 15 to 20 percent in school age children.

Otitis media occurs in three forms; acute infection, acute otitis media, with bacteria or virus; serious otitis media with fluid filling the middle ear and causing hearing loss in school-aged children; and chronic middle ear disease with mastoiditis and cholesteatoma, a destructive process which permanently damages the middle ear and may lead to permanent deafness, loss of equilibrium and even meningitis and/or brain abscess.

NINCDS-supported research has demonstrated that all three forms are probably related, and that otitis media is associated with inadequate ventilation of the middle ear space. Research is now being supported on how the normal and the pathological Eustachian tube functions in supplying air to the middle ear. We are seeking to determine how the disease process develops in relation to, and how it is affected by, immune mechanisms. There is a possibility that the more chronic forms of middle ear disease may be related to inadequately treated acute bacterial infection of the middle ear. There is active collaboration in research supported by the Institute with vaccine therapy research supported by NIAID.

NINCDS-supported research has demonstrated that permanent sensorineural hearing loss can and does result from recurrent and chronic infection of the middle ear. It has been observed that recurrent otitis media is associated with

poor performance in school. The communicative disorders program is encouraging research in this important area. There are very few laboratories which are actively involved in research on otitis media. A much greater effort is needed. The social and economic costs of otitis media are tremendous.

AUTISM

Mr. ROYBAL. What advances have you made in the research of autism?

ANSWER. The NINCDS has taken a number of steps to develop a program of research support on the neurobiological aspects of autism. A workshop sponsored by the NINCDS in February 1976 clearly established that research on the neurobiological aspects of autism is clearly warranted.

DYSLEXIA

Mr. ROYBAL. Dyslexia is a condition where a person reads everything backward. Are you studying this problem?

ANSWER. Dyslexia is a disorder of reading which is most notable in children who have severe difficulties and delays in learning to read. We now know that children with dyslexia form at least two subgroups; one with visuospatial and sensory integration disorders and another with deficits and disorders of language performance. The first type, dyslexic children with visuospatial problems, often write letters backwards, giving the impression that they may be reading printed letters or words backwards. Recently, investigators found language deficits occur in many of these children, indicating that early detection and treatment of children with mild deficits in language could prevent at least one type of dyslexia in children. A directed research project of the communicative disorders program is studying both language-impaired children and children with dyslexia to determine what specific deficits these children have and what treatment approaches would be most appropriate for such children.

In addition, NINCDS grantees are continuing to study the neurological integrity of children with dyslexia, such as their patterns of language lateralization in the brain and their integration of sensory perceptions with language information.

SPECIAL REPORTS REQUESTED BY THE COMMITTEE

REPORT BY THE NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE TO THE CONGRESS ON MULTIPLE SCLEROSIS RESEARCH, MARCH 1, 1977

This report is in response to the requests made by the House and Senate Appropriations Subcommittees for Labor-HEW in its report accompanying the FY 1977 Appropriations Bill. At that time the National Institute of Neurological and Communicative Disorders and Stroke had submitted a detailed analysis of the implementation and funding for the recommendations made by the National Advisory Commission on Multiple Sclerosis in the Commission's final report submitted in February, 1974. However, questions arose regarding levels of research funding in terms of relevance to multiple sclerosis (MS).

The present report to the House and Senate Subcommittees consists of this summary overview plus two attachments: (A) The annual special report on MS submitted with the FY 1978 budget request for NINCDS; and (B) a special report by an ad hoc work group submitted in January, 1977 to the National Advisory Neurological and Communicative Disorders and Stroke (NANCDS) Council on the MS Commission report and recommendations.

As emphasized last year, the report of the MS Commissions are recommendations not mandates, especially with respect to specific levels of funding. The NINCDS wishes to concentrate on progress in advancing our knowledge of the causes, diagnosis, prevention and treatment of MS as a better measure of meeting the goals of the MS Commission than any specific levels of funding at a given point in time. Attachment (A) addresses the current status of progress in research on MS now being funded by NINCDS. The estimated investment for FY 1977 will total just over $11 million, actually in excess of the total originally recommended for FY 1977 by the MS Commission.

The research summarized in attachment (A) reflects vigorous activity and provocative developments in the major relevant areas of virology, immunology, genetics, biochemistry, therapeutics and diagnostic measures. What becomes more and more obvious is the fact that MS is one of the most complex problems confronting the neuroscientist and the neurologist. Over the past two years most of the reported leads have failed to withstand the test of validation by other investigators. Thus, we must face the prospect that solutions to the MS problem are not likely to be achieved as quickly as originally anticipated by the MS Commission.

The controversial question of whether or not research projects are relevant to MS has been carefully considered in Attachment (B). The report in Attachment (B) was developed by a work group with two members of

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the NANCDS Council as chairmen plus five other outside experts, all of whom are members of one of the executive or advisory boards of the National Multiple Sclerosis Society. The report addresses the questions of funding, of research relevance, of the NINCDS staff focus for MS, of collaborative coordination, and of clinical research resources.

With regard to relevance, the ad hoc group concludes (page 8): "In the final analysis, it can be said that anything that may produce answers is relevant." They distinguished two categories of relevance, proximate relevance involving research on MS patients and ultimate relevance involving research related to causes and treatment of MS. Most of the research funded by NINCDS falls into this latter category. Moreover, the ad hoc group recognized that relevance will change with time as old research leads fail and new leads appear. Thus, the NINCDS would suggest that the issue of specific relevance as raised previously is largely a non-issue, as discussed in the report by the ad hoc work group of the NANCDS Council.

Except for the question of clinical research resources, the other questions discussed in the ad hoc work group report center upon the role of the NINCDS staff serving as the focal point for MS research programs and activities supported by the Institute. As already reported to the Congress, to the NANCDS Council and to the National Multiple Sclerosis Society, the NINCDS is actively recruiting for the head of the MS program staff. Such efforts have been under way for well over a year, and it is

apparent that persons with the requisite qualifications are extremely rare. We have consulted with the National Multiple Sclerosis Society, and enlisted their help in the search. Every effort will be made to conclude the search successfully before the end of this fiscal year. With such an appointment, attention to the responsibilities and activities outlined in the report by the ad hoc group (Attachment B) can be promptly intensified.

Special consideration is needed for the problem of maintaining clinical research resources. In times of funding constraints, the provision of core support is difficult for clinics that constitute an important but potential research resource, specifically, an established group of MS patients. This problem is part of the broader problem being faced by the NINCDS for a number of chronic neurological disorders. Whether the comprehensive program approach now being evaluated for epilepsy, stroke, and nervous system trauma can or should be extended to MS and other less prevalent disorders is a question which the Institute expects to examine actively with its external advisors.

Respectfully submitted,

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REPORT OF THE NANCDS COUNCIL AD HOC WORK GROUP TO CONSIDER THE REPORT AND RECOMMENDATIONS OF THE NATIONAL ADVISORY COMMISSION ON MULTIPLE SCLEROSIS

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January 4, 1977

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INTRODUCTION:

The National Advisory Commission on Multiple Sclerosis was appointed in February 1973 by the Secretary of Health, Education and Welfare, in accordance with an Act of Congress, Public Law 92-563. The National Commission's mandate was "To determine the most effective means of finding the cause of and cures and treatments for multiple sclerosis. Such study and investigation shall give particular emphasis to the need for additional support by the Federal Government and the means by which the Federal Government can best participate in the effort to find the cause of and cures and treatments for multiple sclerosis."
In February 1974 the Commission transmitted its final report to the Secretary of Health, Education and Welfare, for transmittal to the President and the Congress. The Commission was chaired by Mr. Charles W. V. Meares of New York, and its members included Drs. Stanley M. Aronson, Lyle A. French, George B. Koelle, H. Houston Merritt, Richard P. Schmidt, Ms. Janice Dudley, Mrs. Ellen R. Grass, and Mrs. Mary El Ruffner. Dr. Harry Weaver served as Executive Director, and Dr. Leo Fox was Senior NINCDS representative to the Commission.

The Commission Report presented three types of recommendations, one which dealt with overall funding and recommended specific levels of funding, both for research in the basic biomedical sciences and for research relevant to multiple sclerosis; twenty nine recommendations dealt with specific research items which had been recommended by the Advisory Groups convened by the Commission during its deliberations, and eleven recommendations dealt essentially with administrative items.

The Report was received by Congress but the recommendations therein were not specifically implemented, in that the FY 1975 and 1976 budgets contained no additional funds above inflationary increases.

Fiscal Year	NINCDS Appropriations (in thousands)	
1974	$144,099	(includes restored funds from previous recission)
1975	142,498	
1976	144,446	

As is clear from the table, the additional funds recommended by the National Commission were not forthcoming to NINCDS and thus, implementation of the recommendations was delayed. Presumably, as the result of this delay and the disappointment of the National Multiple Sclerosis Society with what appeared to be a lack of response on the part of the most appropriate Federal Agency to participate in the effort to find "the cause of and cures and treatments for multiple sclerosis," on April 1, 1976, Hon. Paul G. Rogers, Chairman of the House Subcommittee on Health and Environment of the Committee on Interstate and Foreign Commerce, asked for an Institute assessment of its implementation of the recommendations of the National Advisory Commission on Multiple Sclerosis. Mr. Rogers asked the NMSS to assess the Institute's response and this evaluation was presented in a letter from Dr. Harry Weaver to Congressman Rogers on May 10, 1976. In the letter of transmittal dated May 10, 1976, Miss Sylvia Lawry, Executive Director of the NMSS stated, "I trust you will find the review of assistance in connection with the oversight hearing you are planning, at which time you may see fit also to examine the extent to which inadequate funding may have interfered with the full implementation of the Commission's Recommendations."

At the NANCDS Council meeting in late June 1976, Mr. Palmer Brown, President of the NMSS, addressed the Council and spoke of the continuing problem of resolving the question of the extent to which the Institute had implemented the recommendations of the Multiple Sclerosis Commission. Dr. Donald B.

Tower, Director of NINCDS, requested the Council's concurrence with the appointment of an Ad Hoc Work Group to be co-chaired by Dr. Sidney Carter and Mr. Charles W. V. Meares, members of the NANCDS Council, to provide guidance to Dr. Tower and the Institute on the problems whose background has been outlined above. The other members appointed to the Ad Hoc Work Group were Drs. Richard T. Johnson, Joseph Foley, Augustus Rose, Richard Schmidt, and Harry Zimmerman.

The Ad Hoc Work Group met in Bethesda on September 22 and November 23, 1976, in order to formulate its Report. The Group considered both the status of implementation of the National Advisory Commission on MS Report's recommendations, and the effect that these recommendations and their implementation might have on the balance of the Institute's Programs.

IMPACT OF COMMISSIONS:

The NANCDS Council Ad Hoc Work Group was convened to deal with specific problems of implementation of the recommendations of the National Advisory Commission on Multiple Sclerosis. This Commission was the first in the present series of Commissions focused on specific diseases which have an impact on the National Institutes of Health. Since that time several other Commissions have been mandated, and at present, NINCDS is host to the Commissions on Epilepsy and on Huntington's Disease. A Commission focuses on a specific disorder and, in general, the impetus for its existence comes from a group with a commitment to a particular disease. There seems little reason to believe that requests for the creation of still more Commissions related to specific diseases will be denied, unless Congress is made more aware of what the promoters of Commissions expect of them.

What might be the realistic expectations of the voluntary health agencies in asking Congress to authorize a National Advisory Commission? The National Multiple Sclerosis Society can be used as a model to answer this question. The primary purpose of the National Multiple Sclerosis Society is to discover the cause, cure, and prevention of multiple sclerosis, and incidentally, but to a less important degree, of the heterogeneous group of other demyelinative disorders. The Society acts as a coordinating center for research in Multiple Sclerosis; it stimulates research and tries to move it in appropriate directions; it raises and disburses money to qualified investigators with good and relevant ideas. The patient service function of the Society is an important one but not of concern to the present issue. In asking Congress to found a Commission on Multiple Sclerosis, the Society had several goals in mind:

(1) they wanted official recognition by the United States Government that a serious health problem exists;
(2) they wanted a mechanism that would allow them to collate what was then known about multiple sclerosis, and to identify which

investigators were working on problems that might yield suitable information directed toward the cause and cure of the disorder;

(3) they hoped to identify particular areas of special promise so that research might be targeted toward those areas in the future;

(4) they hoped to be able, on the basis of this, to present a program to Congress which would result in the disbursement of funds to move toward the objectives;

(5) they realized that the total money needed to support multiple sclerosis research was beyond the resources of the Society and hoped to increase the amount of government support targeted toward multiple sclerosis;

(6) they hoped to excite the biomedical research community on the potential of research in multiple sclerosis.

What should be the response of the National Institutes of Health to the recommendations presented by a National Advisory Commission which focuses on a specific disease? If sufficient additional resources are available to allow implementation of the recommendations, there is no difficulty. Given finite resources and infinite demands on these resources, priorities must be set. NINCDS is the component of the National Institutes of Health with specific responsibilities for research and research training in all of the neurological disorders. Approximately 45-50 million patients in the United States suffer from neurological and communicative disorders. In this population, there are some 2 million epileptics. Four to 5 million people are afflicted with the various forms of the organic dementias. There are approximately 250,000 to 500,000 multiple sclerosis patients and patients with closely related disorders in the population. It is clear that prevalence rates, cost benefit analyses, or estimates of the financial cost of any given illness must never be the sole determinant for the allocation of funding for the support of research. Multiple Sclerosis poses a major challenge to the biomedical research community and, as a disease of young adults, is clearly of vital concern to society.

In the Work Group's review of the situation posed by the recommendations of the Commission Report a number of problems became apparent.

1. The money required to operate the Commission was not separately appropriated by Congress. It was necessary for these funds to be taken out of the NINCDS appropriated budget.
2. No additional appropriations were granted to NINCDS in FY 75 or FY 76 to assist in the implementation of the National Advisory Commission's recommendations.
3. The Appropriations Bill for FY 77 indicates that both the Senate and the House Appropriations Committees expect the Institute to meet or to exceed the multiple sclerosis research support targets recommended by the Commission for both basic and applied research. The FY 77 budget, however, includes only an increase of $11.054 million over the FY 76 budget. There is evidence that at least some members of the Congress viewed this increase as sufficient to enable NINCDS to implement all the Commission's recommendations, whereas the Commission's total recommendations for increased funding over the three years following its report amounted to $19.902 million ($7.02 million for research specifically relevant to multiple sclerosis and $12.9 million for basic biomedical research in the neurological sciences). However, at the same time, the Congress directed the Institute to continue its support of research in the neurological disorders and on disorders of hearing and speech. Specific emphasis was directed to research in stroke, in spinal cord regeneration, in hearing impairment, in autism, and also to expand research and training for diabetic neuropathy.

The Work Group believes that the differences and problems between the NMSS and NINCDS have arisen in part because of failure to define in the beginning, and at the time of the submission of the recommendations, what the expectations of each party would be. In this context it is feared that similar misunderstandings will arise on the basis of divergent expectations from other Commissions which are now active. Accordingly, the Work Group discussed the basic functions of a Commission,

and in this connection, recognizes the value of Commissions in emphasizing the importance of the disease in question and in assisting those who are working with the disease to define the state of the problem at a given time. Once the problems have been defined and appropriate data have been brought together, the acquisition of funds to implement the recommendations should constitute a further separate step in the process. Any projects which emerge from the work of a Commission should be subject to the rigorous process of peer review by appropriate scientists and other concerned persons, in the manner which has made the National Institutes of Health so successful in the past. The danger in the proliferation of Commissions is that in the absence of specific additional funding, the priorities for research by any given Institute may well be taken out of the hands of the peer review group and the Advisory Council, so that the priorities of the overall health problems will not be set by those most qualified and that there will be a progressive whittling away of the funds necessary to do the basic research on which any kind of meaningful advance can be made in the general field of science or improvement of health.

As a consequence of these considerations, the Ad Hoc Work Group recommends that Congress should be advised that Commissions ought not be authorized (1) unless money is appropriated to operate the Commissions, and (2) unless it is recognized that additional funds will be needed to implement the Commission recommendations. The Work Group also emphasized that when additional funds are appropriated, they must be allocated by the NIH on the basis of the peer review and Advisory Council process, which has proven its worth in the past. Only with the input of the active biomedical research community, implicit in this dual review process, can the apportionment of funds be kept current with the 'state of the art' in research.

BASIC BIOMEDICAL AND DISEASE ORIENTED RESEARCH

The Report of the National Advisory Commission on Multiple Sclerosis recommended that support should be given for research both in basic studies in the neurological sciences and disease oriented research aimed at problems arising specifically in relation to multiple sclerosis. In evaluating implementation by NINCDS of the Commission's recommendations, a central problem is the definition of that research which is relevant to multiple sclerosis. Clearly, research carried out on patients with multiple sclerosis, attempts to recover infectious agents from patients, epidemiologic or seroepidemiological studies of multiple sclerosis patients are universally considered relevant.

Beyond these limited areas of research, the definition of relevance becomes more difficult. For a disease whose cause, pathogenesis, early diagnosis and treatment is shrouded in obscurity, relevance cannot be judged with great precision. What may be considered purely basic research may turn out to be most relevant to multiple sclerosis if it provides an answer, or even a clue, to the cause and possible treatment of this condition. It is even within the realm of possibility that research in basic neuroscience or in basic biological processes may become highly relevant to more than one disease entity, including multiple sclerosis. Further, research pursued for the purpose of helping to understand seemingly unrelated disorders or disease processes may contribute most tellingly to our understanding of multiple sclerosis.

In the final analysis, it can be said that anything that may produce answers is relevant. It is perhaps possible to consider relevance in two categories, proximate and ultimate. Proximate relevance is clear, in that it involves research on patients who have multiple sclerosis, whereas ultimate relevance involves research which may have connections to the causes or treatment of multiple sclerosis. Most of the research funded by NIH would fall into the category of ultimate relevance because, for the most part,

scientific validity is much more convincingly established for this category than for the studies which are of proximate relevance.

These varied definitions of relevance do not represent distortions of fact or subterfuge, but a difference of opinion and perspective. It is also clear that relevance varies not only with perspective but changes with time. In a disease where the cause is unknown, and where many new leads may prove to be false, continual modification of priorities is essential. In reviewing the recommendations of the Commission, which were written in 1973, it is clear that some of the recommendations might not be made today and that other studies, considered but rejected by the Commission might now be considered important and relevant. In other words, relevance is a constantly moving target and any Commission's recommendations must be judged with reference to current scientific validity.

The spirit of the Multiple Sclerosis Commission's Report, however, is still valid. New ideas must be generated in the attack on this disease. This is perhaps beyond the accomplishment of any one investigator and his colleagues. But new avenues of approach would follow from periodic informal meetings of peers, called together for the discussion of specific problems and their possible solutions. Thoughtful consideration and emphasis should be given to this approach among the recommendations provided by the Commission. A cadre of young investigators has become interested and trained in this area. Additional funding could be put to productive use. Despite the budgetary strictures of the past several years, NINCDS has expanded its multiple sclerosis-related research and basic biomedical research relevant to multiple sclerosis. However, when only 1 in 6 research grant applications approved by Study Sections for funding can be paid with presently budgeted funds, even with special emphasis given to multiple sclerosis-related grants, some relevant, worthwhile programs of investigation may not be funded.

FOCUS FOR DEMYELINATING DISORDERS

The Report of the National Advisory Commission on Multiple Sclerosis recommended that the Director of NINDS (now NINCDS) delegate to one member of his staff administrative responsibility for all research and development relevant to multiple sclerosis that is funded by NINCDS, whether conducted in-house or through extramural grants or contracts. A complete list of the Commission's recommendations for the duties of this individual will be found on pages 126 through 128 of Volume 2 of the Report and Recommendations of the National Advisory Commission on Multiple Sclerosis.

The Neurological Disorders Program of NINCDS is presently conducting a search to identify a potential staff member who will concentrate on multiple sclerosis and other demyelinating disorders to fulfill the Commission's recommendations for essentially a full-time multiple sclerosis focus. The Work Group concurred that NINCDS and NMSS share a common goal in recognizing multiple sclerosis as a significant crippling disorder of young adults and should work together in trying to determine the cause and pathogenesis of this condition, to establish criteria for early diagnosis, and to discover an effective therapy. Success of collaborative efforts between NINCDS and NMSS must rest to a large extent on the success of the recruiting effort to find the individual mentioned above. This person should have as his primary concern and responsibility problems relating to multiple sclerosis and related disorders. His responsibilities should include, but not necessarily be limited to,

(a) serving as liaison between NINCDS and NMSS
(b) being current on all research, both clinical and basic, relating to multiple sclerosis
(c) being the contact source for all would-be investigators contemplating research projects relating to multiple sclerosis to be funded by NINCDS.
(d) being responsible for establishing interinstitutional and interdisciplinary meetings through a variety of sources when empowered to do so.

The Group stressed that any position description for this person should emphasize the importance of his coordinating role. To do his work effectively, he should have as much access to the scientific meetings and deliberations of NMSS as of NINCDS. The Work Group reemphasized that in order to fulfill the role projected for this individual by all the tasks spelled out for him, he must be enthusiastically committed to the cause of multiple sclerosis, on a full time assignment, and above all, a thoughtful diplomat to reconcile to a common purpose, the (by their very nature) differing roles of the NINCDS and the leading voluntary agency, the NMSS. It is clear that the success of the collaboration depends upon the active role which this individual will play in formulating policy and the implementation and explanation of policy of one group to the other. The Work Group urged that great efforts should be devoted to the expeditious recruitment of such an individual. Time is clearly of the essence as it is of great importance that harmonious relationships be restored between NINCDS and NMSS as soon as pssible. The key role to be played by this individual becomes clear when it is realized that the current NINCDS effort in recruitment has already alleviated a great deal of the 'adversary' situation that existed between NINCDS and NMSS a few months ago.

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CONSIDERATION OF COORDINATED-COLLABORATIVE-COOPERATIVE ATTACK ON MS

The National Advisory Commission on Multiple Sclerosis recommended the launching of a coordinated--collaborative--cooperative attack on multiple sclerosis to serve as a supplement to individual investigator-designed research. This collaborative program would involve both interinstitutional and interdisciplinary cooperation. Initiation of this collaboration might be accomplished by arranging working conferences to bring together scientists active in areas which might provide leads for multiple sclerosis research to provide for a mutual exchange of ideas and perhaps even to establish an agenda for future research in a given area.

The Work Group concurred that this was a promising mechanism for the stimulation of innovative approaches to the solution of the problem of multiple sclerosis. They recommended that NINCDS consider this a suitable objective with a high priority. The Institute might also encourage interested groups to submit designs for such conferences, which would be reviewed on the basis of scientific merit, and assigned priority by an appropriate Study Section. It is thought that these kinds of small working meetings would help to reduce the dissemination time required for both results and inadequacies in the research produced in different areas and different disciplines. The Work Group recommended that the individual who is the Institute focus for MS research should be involved extensively in the coordination of these working meetings, which would be convened on an Ad Hoc basis, as appropriate. The participation in these meetings would change depending upon the topics to be considered. Some of these meetings would be funded by NINCDS, some should be funded by NMSS. It appeared to the Work Group that since this would be one of the major functions of the Institute's MS focus person, implementation should present few problems.

CONCERN FOR CLINICAL RESEARCH RESOURCES

The Report of the National Advisory Commission on Multiple Sclerosis emphasized that as multiple sclerosis is uniquely a disease of human beings and, there being no suitable animal model for study, a significant research effort should be directed toward appropriate utilization of the patient himself and of his tissues and body fluids. A reservoir of well-studied multiple sclerosis patients, carefully classified and longitudinally followed by neurologists interested in the clinical aspects of the disease, is an important and necessary resource. In acknowledging the merits and desirabilities of maintaining and establishing a limited number of clinical research centers for multiple sclerosis the Work Group recognizes that NINCDS, under present policy regulations, is restricted to the funding of research and research training, and cannot fund patient care and services. However, in the sense that clinical research centers which meet such criteria provide an essential research function which comes within the scope of the research mission of NINCDS, core support of such centers might reasonably be considered for funding. This might be done by providing salaries for one or more selected members of faculty involved in the center, or in other ways that are compatible with NIH policy. By whatever means it is done, the Work Group believes support of such centers is important to multiple sclerosis research and hopes that some way can be found for NINCDS to fund at least a part of it.

The Work Group recognizes that the number of clinical research centers, as described above for multiple sclerosis, is dependent upon the fundamental interests and clinical competencies of applicant groups. Therefore, in establishing centers, caution and careful scientific evaluation must be exerted, regardless of geographic location. It is clear that research applications should define precisely the research for which the patient resource is desired. The Work Group concurred that the clinical resources provided by clinical research centers for multiple sclerosis are essential and attempted to explore other possibilities of support for the centers.

It was concluded that hospitals in which research is carried on do not have internal funds available for such specialized clinic functions and that local community funding cannot be depended upon to provide the necessary ongoing support. The National Multiple Sclerosis Society, as the granting agency concerned with both research and patient care in multiple sclerosis, might be depended upon to carry a portion of the financial responsibility in the support of such centers, whether considered as research or as service. NINCDS, in its role of supporting research in multiple sclerosis, could perahps provide support for the coordination of clinical research being carried out in the centers. The importance of the resource was viewed as so critical by the Work Group that ways to merge private and public sector funds should be explored to greater depth. This was suggested as an important role for the individual who will serve as a focal point for NINCDS efforts in research related to multiple sclerosis.

SUMMARY

The National Advisory Neurological & Communicative Disorders & Stroke Council Ad Hoc Work Group to consider the Report of the National Advisory Commission on Multiple Sclerosis has reviewed the responses of the NMSS and the NINCDS to the Report and their interactions since the presentation of the Commission Report.

To facilitate cooperation and collaboration between NINCDS and NMSS the Ad Hoc Work Group urges that the Neurological Disorders Program of the NINCDS recruit, as soon as feasible, the individual who will serve as a focal point for the Institute for all research and development relevant to multiple sclerosis and other demyelinating disorders. This individual will function as a coordinator between NINCDS and NMSS. He will also assist NINCDS in implementing coordinated, collaborative, cooperative studies on multiple sclerosis.

The Work Group considered the problem of definition of research relevant to multiple sclerosis as distinguished from basic biomedical research in the neurological sciences. The Work Group concluded that the definition of relevance must vary not only with perspective but also must change with time. However, differences in interpretation are probably not so great as to preclude interaction. The problem of relevance will require continuing redefinition and will need to be the subject of continuing examination both by NINCDS and NMSS.

The Work Group considered the problems of support of a reservoir of well-studied multiple sclerosis patients as a clinical research resource of crucial import for the advancement of our understanding of multiple sclerosis. The Work Group urged that the NINCDS person who will be the focal point for MS research explore in depth the ways to merge private and public sector funds, so that these valuable resources can be maintained and expanded if deemed advisable.

The Work Group considered the problems implicit in the proliferation of Commissions dealing with specific diseases. In the absence of specific additional funding for the recommendations of Commissions, the priorities for research by any given Institute may well be taken out of the hands of those most qualified to judge and there may be progressive whittling away of support for fundamental research so necessary as a ground work for any meaningful advances in science or health care. The Work Group emphasized their commitment to the concept of the peer review and Advisory Council process as being most likely to produce scientifically valid, defensible ordering of priorities within any given program.

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a devastating neurological disorder of young adults. Its unpredictable episodes attack the brain and spinal cord and destroy the protective nerve covering called myelin. When myelin destruction, or "demyelination" occurs, messages from nerves to muscles and sensory organs are impeded or lost, causing varying degrees of impairment. The extent and location of demyelination determines symptoms and severity. These can include impairment of muscle strength, control, or movement or they can result in sensory disturbances such as blurred vision or speech problems. When myelin destruction is either widespread or critically located, its effects are crippling.

Because myelin destruction is sporadic and myelin repair is only partial, MS symptoms follow a totally unpredictable course. MS patients may have symptoms which occur once with no additional episodes; or they may have a progressive series of episodes with varying periods of exacerbation (worsening of symptoms) followed by remission (cessation of symptoms); or they may have chronic progressive symptoms. This course differs for each person with MS.

Thus, each young man or woman afflicted with MS must endure the burden not only of coping with the symptoms, but the uncertainty of how to carry out life's activities without knowing how often the symptoms will strike, how long they will last, or how severe or incapacitating they may become.

It is estimated that 250,000 American men and women between the ages of 20 and 40 are victims of MS; another 250,000 suffer from closely related demyelinating disorders.

The cause and cure of MS are as yet unknown. The prognosis is uncertain. But remarkable advances in understanding "slow" viruses, coupled with important discoveries concerning the immune (defense) system, as well as an increased understanding of myelin have brought new levels of sophistication to MS research. It may well be that the key to demyelination and to MS lies in an integration of these three components.

Obligations for Programs in Multiple Sclerosis and Related Disorders

	1974	1975	1976	1977 estimate	1978 estimate
National Institutes of Health:					
National Institute of Neurological and Communicative Disorders and Stroke	$5,390,000	$6,980,000	$9,590,000	$11,060,000	$11,436,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

The National Advisory Commission on Multiple Sclerosis wrote in its 1974 report, "...the time is now for a concerted, well-managed effort to unravel the mysteries of MS." The Institute has incorporated many recommendations made by the nine-member Multiple Sclerosis Commission, appointed by the Secretary of Health, Education, and Welfare in accordance with Public Law 92-563.

As suggested by the Commission and occasioned by important research leads, the NINCDS has greatly intensified its MS research here at the NINCDS and at other institutions, including support of five major MS Clinical Research Centers. In addition, MS research continues to be a major concern of the Institute's intramural program. The two major NINCDS laboratories currently engaged in viral research have been augmented by a recently established Neuroimmunology Branch, headed by a leading neuroimmunologist, who is conducting both basic and clinical MS research. Basic research directly related to the neurochemistry of myelin is being conducted in two other NINCDS laboratories.

Also, as suggested by the Commission, a contract has been awarded to ascertain the overall impact of MS by determining incidence, prevalence and costs. The country's 6,448 neurologists and neurosurgeons and 2,002 primary care physicians (selected at random) have been asked to identify all possible and probable MS patients seen during the six-year period 1970 through 1975. The same information is being collected from the nations' 267 teaching hospitals and a sample of 458 non-teaching hospitals to provide a comprehensive assessment of incidence and prevalence. After duplication is eliminated, patients will be asked to provide information on the direct and indirect costs of the disease by keeping a 90-day diary of all health related expenditures.

Viral Involvement in MS?

Work on the possible viral origins of MS received a tremendous boost after the brilliant demonstration of the existence of "slow viruses" by this year's Nobel Laureate in Medicine and Physiology, Dr. D. Carleton Gajdusek, working with Dr. Clarence Gibbs and colleagues. The scientists showed that at least two disorders affecting the central nervous system (CNS) are caused by atypical viruses which lie dormant in the body for years before some mechanism triggers them into action.

While MS bears no resemblance to these other two slow virus disorders, slow viruses may cause several different types of diseases. Arguing against the theory of slow viral involvement in MS is the inability, as yet, to transmit it to laboratory animals in the classical proof of a

virus. However, several important factors implicate viral involvement: first, there is an inflammation around blood vessels, consistent with viral infection. Second, epidemiological studies of the pattern and distribution of MS suggests a latent viral infection. Such studies have shown that persons who migrate from areas of high risk for MS to a low risk area before age 15 (and possibly as early as before age 5) adopt the low risk of their new country; while those who migrate after age 15 maintain the high risk of their homeland. This suggests that some factor or combination of events operating early in life leads to the subsequent development of MS. Third, many MS patients have elevated cerebrospinal levels of immunoglobulin G which is consistent with a viral infection. Immunoglobulin G is an antibody against measles. Significantly, high levels of this antibody have been found among all patients with another neurological disorder, subacute sclerosing panencephalitis (SSPE), caused by a slow, defective measles virus which strikes in the teenage years.

Because both SSPE and MS patients have increased immunoglobulin G levels, and since SSPE is known to be caused by defective measles virus, there is speculation that MS also may be caused by a defective virus which might be measles. Dr. John Sever and colleagues at the Institute's Bethesda laboratories found that the SSPE measles virus has a defective maturation process which may account for the virus' slow infection rate. Additional knowledge on how viral infection may be slowed is emerging from intensive studies by NINCDS scientist Dr. Robert Lazzerini and colleagues, and others, of viral fragments which are accidently formed by certain viruses during replication. They are called defective interfering (DI) particles and are not infectious. But importantly when they enter a cell with the infectious virus, they slow down viral infection by successfully competing with the infectious virus for materials needed for replication. In addition preliminary studies suggest that DI particles may also stimulate at least one part of the body's immune (defense) system. Work is under way to determine whether DI particles may be involved in the slowdown of the SSPE measles virus.

Further implication of measles occurred just a few months ago with a report by Drs. Louis Pertschuk, Albert Cook, and Jagdish Gupta of Long Island College Hospital and Kings County Hospital. Measles antigen was reportedly found in the small bowel of 30 MS patients but in none of the 24 non-MS controls. The scientists have postulated that a chronic measles infection of the small bowel could have a cross reactivity to the CNS, essentially making the body "allergic" to its own cells. If further investigations substantiate the findings, it may be one of the strongest leads to date linking measles virus to MS. Institute scientists currently are evaluating the findings to determine whether additional studies are needed.

Studies of other possible MS causing viruses, besides measles, also are being actively pursued. Dr. Richard Carp and colleagues at the New York State Institute for Basic Research in Mental Retardation initially reported isolating an agent from MS patients' brain tissue and sera. These findings, based on extremely difficult and complex tests, were not confirmed until last year when Dr. Werner Henle and colleagues from Philadelphia Childrens Hospital reported substantiation and extension of the studies. Work is continuing to further investigate these findings.

Immune System Alterations in MS?

If a common virus is involved in MS, why are only a few people affected by it? Bearing on this question are important studies reported this year concerning the immune (defense) system of MS patients. Preliminary evidence now suggests that there may be some association between susceptibility to MS and inherited "histocompatability antigens". During the past few years, increasingly convincing evidence of a genetic predisposition to MS has been amassed. Initial interest derived from studies of tissue rejection in transplant patients, where histocompatability (HLA) antigens were found to evoke tissue rejection. These antigens serve as markers of an individuals' underlying histocompatability genes; significantly, in mice these genes have been shown by a number of studies to be closely linked to genes which control specific immune responses.

HLA antigens are strategically located on the cell surface, and are thought to serve as receptors for viruses. Initially, 40 percent of MS patients were found to have two specific histocompatability antigens, labeled HLA-A3 and HLA-B7. Subsequent studies showed an even higher incidence (70 percent) of another antigen, HLA-DW2. Now, in an exciting new development this year, two laboratories have found that B-cell (a type of white cell) antigens, occur in 90 to 100 percent of MS patients tested. Intensive studies are in progress at NINCDS by Drs. Dale McFarlin and Henry McFarland to substantiate these findings by Drs. H. J. Winchester and associates at Rockefeller University, New York, and Dr. P. I. Terasaki and colleagues, at UCLA, under contract to NINCDS.

In order to analyze this association between HLA types and MS in greater detail, four important studies have been initiated. First, the Neuroimmunology and Infectious Disease Branches in the Institute's Intramural Research Program are conducting studies of families in which more than one member has MS.

Secondly, a massive study is being conducted in the Scottish Orkney and Shetland Islands where an astounding 250 persons per every 100,000 have MS (the highest known prevalence of MS in the world). Dr. David Poskanzer and colleagues at Massachusetts General Hospital, Boston, conducting the study under contract to the NINCDS, is exploring the

relationship between MS and histocompatability antigens and other possibly related biological factors. Additionally, NINCDS contractor Dr. Derek Roberts, University of Newcastle, is investigating the genetic lineage--going back 200 years--of MS patients, their families and non-MS controls. This is possible because the Islands have extraordinarily well kept records from parish marriage and death certificates. Information gained from interviews will be verified and will show whether MS incidence can be traced back to a particular family, as was the case in this country with another neurological disorder, Huntington's disease.

Third, 100 patients with MS are being studied by Dr. Donald Silberberg and colleagues at the Institute-supported MS Clinical Research Center at the University of Pennsylvania.

Fourth, NINCDS grantee Dr. Roger Dotels and colleagues at UCLA are following 150 families with at least two members with MS, including 75 families with MS among primary relatives. Of particular additional interest is a cluster of MS patients in King County, Washington, where 8 students of the same high school graduating class of 1953 now have MS. The investigators also are obtaining data on the costs of MS in their study population.

What Role Does Myelin Play?

If a virus or immune system defects--or both--are operating in MS, what is their role in demyelination? NINCDS chemists Drs. Richard Quarles and Joseph Poduslo have shown that mammals have a high molecular weight glycoprotein which accounts for a major proportion of the myelin surface. These glycoproteins are the first to be destroyed by toxic agents. Furthermore, in other cells, they are known to be receptors for certain viruses. Scientists believe changes in glycoproteins may be involved in the regulation of viral replication.

In addition, one of the most exciting advances in MS research this year concerns a protein component of myelin, called myelin basic protein. In two separate studies supported by the National Multiple Sclerosis Society, one by Drs. Guy McKhann, Robert Herndon and Steven Cohen at The Johns Hopkins University, Baltimore, the other by Dr. John Whittier at the University of Tennessee, Memphis, myelin basic protein was found in the cerebrospinal fluid of patients with MS but seldom in fluid from patients with other neurological disorders. These observations were made possible through a new technique (radioimmunoassay), which employs radioactivity to reveal the presence of a specific protein. Moreover, increased amounts of myelin basic protein correlated with increased MS activity. Patients with inactive MS had no cerebrospinal fluid myelin basic protein; those with slowly progressive MS had low protein levels; while patients with an acute MS attack had very high protein levels. Thus, this technique has great potential for evaluating potential MS drugs; those which effectively reduce myelin basic protein levels could reasonably be expected to produce an improved clinical picture. Furthermore,

drug evaluation would be objective. This would be a tremendous advantage over the current subjective assessment by patients which is wrought with difficulties since MS symptoms can disappear for no apparent reason and may be totally unrelated to drug efficacy.

Treatment

Myelin basic protein potentially also may be a treatment for MS. When injected into animals, this protein causes a disease in animals, called Experimental Allergic Encephalomyelitis (EAE) which is similar to MS. But interestingly, subsequent injections of the protein arrest EAE's further progress. Therefore, can myelin basic protein also arrest the progress of MS? To answer this, a limited clinical study under Dr. Richard Eylar, University of Toronto, using myelin basic protein has just been planned, supported by the MS Society of Canada. Dr. Murray Bornstein, head of the Institute-supported MS Clinical Research Center at Yeshiva University will use sera from participating patients to determine whether the demyelinating activity of their blood corresponds with clinical changes in the disease. They will then compare results with those from non-treated MS patients.

During the past several years, two other experimental approaches to treatment--both involving the immune system--have been under investigation. Conflicting results have been reported concerning immunosuppressive therapy (lowering the immune response) using transfer factor. This consists essentially of transferring white cells from healthy donors to MS patients. Dr. John Zabriskie, Rockefeller University, N. Y., has found negative results, while Dr. Torben Fog of Denmark has reported more favorable data. Scientists are awaiting further substantiation from other scientists. The other approach, which consists of increasing the immune response of MS patients, still is under investigation in several studies. At the NINCDS-supported MS Clinical research Center at Emory University under Dr. Richard Kibbler, the immunoreactive drug levamisole is being clinically tested in 25 MS patients.

In addition to seeking curative treatment of MS, several studies are pursuing methods of ameliorating MS symptoms. These include the experimental combined use of chloropromazine and dilantin to suppress spasticity in MS patients being conducted by Dr. Stanley Cohan and colleagues at Georgetown University, Washington, D.C. Scientists at the UCLA Clinical Research Center under Dr. Frederick Wolfgram are using two drugs, methyl-dopa and dibenzyline for relief of bladder spasticity which causes incontinence. This is not only a difficult and embarrassing physical complication of MS, but can lead to infections which can be fatal. The drugs' action on bladder sphincters produce relief of urinary urgency. In one of the most important clinical advances to date, Dr. Keith Schneider, Albert Einstein College of Medicine, reported adapting a surgical technique for bladder incontinence to patients with MS.

The technique involves making an incision in the bladder which is kept closed except when the patient inserts a catheter to void, four times daily. In addition, work is continuing on possible development of electrical stimulation to provide bladder control. To date, experimental animal tests by Dr. Emil Tanagho and colleagues at the University of California, San Francisco, under contract to the NINCDS neural prosthesis program, indicate it may be possible to simultaneously stimulate contraction of muscles in the bladder wall while relaxing exit sphincters, similar to the natural urinary process. This procedure, which is still in the animal testing stage, may have potential for helping not only MS patients but those with spinal injury as well.

Diagnosis

Another finding this year (which needs further substantiation) may have dramatic implications for diagnosing MS. Dr. Nelson Levy and colleagues at Duke University have reported that white blood cells from MS patients, when mixed with cells that have been infected with measles virus, stuck together in a large rosette pattern. This pattern occurred much more frequently with MS blood samples than with samples provided by non-MS controls. If the test is found to be effective, it would mark a major advance since diagnosis currently is based on clinical findings. However, Dr. Ryoichi Mori, Kyushu University, Japan, found diametrically opposite results using this same test. Therefore work is under way to determine why the results varied so dramatically and whether results from either test can be substantiated.

Studies during the past years continue to offer hope that the disorder can be brought under control and that effective methods for diagnosis, treatment, and ultimately prevention can be found. Advances this year have made that goal a closer reality.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Amounts Available for Obligation 1/

	1977	1978
Appropriation	$155,500,000	$161,461,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $30,000; 1978 - $30,000.

National Institute of Neurological and Communicative Disorders and Stroke

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	Number	FTE 1/	Amount	Number	FTE 1/	Amount
Grants:						
Regular Program:						
Non-competing	798	--	$64,754,000	597	--	$58,200,000
Competing	142	--	13,825,000	187	--	18,320,000
New	113	--	10,923,000	148	--	14,376,000
Supplemental	(55)	--	1,000,000	(55)	--	1,000,000
Subtotal	1,053	--	90,502,000	932	--	91,896,000
Special Programs:						
Specialized Research Centers	--	--	8,714,000	--	--	9,700,000
Research Career Program	106	106	2,445,000	112	112	2,612,000
Subtotal	106	106	11,159,000	112	112	12,312,000
Total Grants	1,159	106	101,661,000	1,044	112	104,208,000
Training Programs:						
Individual Awards						
Non-competing	114	114	1,618,000	201	201	2,840,000
Competing	14	14	186,000	20	20	266,000
New	228	228	3,188,000	73	73	1,007,000
Supplemental	--	--	--	--	--	--
Subtotal	356	356	4,992,000	294	294	4,113,000
Institutional Awards						
Non-competing	17	93	1,461,000	32	149	2,459,000
Competing	--	--	--	--	--	--
New	10	38	647,000	--	--	--
Supplemental	--	--	--	--	--	--
Subtotal	27	131	2,108,000	32	149	2,459,000
Total Training Programs	383	487	7,100,000	326	443	6,572,000
Intramural Research	--	--	23,924,000	--	--	26,344,000
Direct Operations	--	--	9,815,000	--	--	10,312,000
Research and Development Contracts	65	--	11,604,000	78	--	12,593,000
Program Management	--	--	1,396,000	--	--	1,432,000
Total	--	--	155,500,000	--	--	161,461,000

1/ Full-time equivalents

DHEW - National Institutes of Health

CROSSWALK - 1977 COLUMN 1978 JUSTIFICATION

INSTITUTE: National Institute of Neurological and Communicative Disorders and Stroke
(Dollars in thousands)

Program	Research Grants				Training Programs		Intramural Research	Direct Operations	Research and Development Contracts	Program Management	Total
	Regular Program		Special Programs								
	Non-Competing	Competing	Multi-disciplinary Centers	Other	Individual Awards	Institutional Awards					
1. Communicative Disorders.....	12,167	6,701	711	356	657	686			429		21,707
2. Neurological Disorders.....	27,579	9,125	2,898	1,598	3,895	1,104			5,483		51,682
3. Stroke and Nervous System Trauma.....	9,865	6,792	5,105	78					456		22,296
4. Fundamental Neurosciences....	15,143	3,130		413	440	318			1,746		21,190
5. Intramural Research.....							23,924		3,490		27,414
6. Direct Operations.								9,815			9,815
7. Program Management.....										1,396	1,396
Total Obligations....	64,754	25,748	8,714	2,445	4,992	2,108	23,924	9,815	11,604	1,396	155,500

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DHEW - National Institutes of Health

CROSSWALK - 1978 COLUMN 1978 JUSTIFICATION

INSTITUTE: National Institute of Neurological and Communicative Disorders and Stroke
(Dollars in thousands)

Program	Research Grants: Regular Program Non-Competing	Research Grants: Regular Program Competing	Research Grants: Special Programs Multi-disciplinary Centers	Research Grants: Special Programs Other	Training Programs: Individual Awards	Training Programs: Institutional Awards	Intramural Research	Direct Operations	Research and Development Contracts	Program Management	Total
1. Communicative Disorders.....	13,613	5,088	718	399	646	851			571		21,886
2. Neurological Disorders.....	23,830	13,421	3,176	1,674	3,130	1,290			6,098		52,619
3. Stroke and Nervous System Trauma.....	10,035	6,771	5,806	100					499		23,211
4. Fundamental Neurosciences....	10,722	8,416		439	337	318			1,750		21,982
5. Intramural Research.....							26,344		3,675		30,019
6. Direct Operations.								10,312			10,312
7. Program Management.....										1,432	1,432
Total Obligations....	58,200	33,696	9,700	2,612	4,113	2,459	26,344	10,312	12,593	1,432	161,461

Summary of Changes

1977 Estimated obligations	$155,550,000
1978 Estimated obligations	161,461,000
Net change	+5,961,000

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Within grade salary increases	--	$ 44,000	--	+240,000
2. Wage board salary increases	--	192,000	--	+7,000
3. Federal Employees Compensation Fund increase	--	25,000	--	+24,000
4. Service and supply fund increase	--	1,893,000	--	+283,000
5. Federal Telecommunications rate increase	--	111,000	--	+9,000
6. Payment for centrally furnished services	--	10,094,000	--	+994,000
(Standard Level User Charge)	--	(338,000)	--	(+50,000)
Subtotal				+1,557,000
B. Program:				
1. Research Grants:				
a. Non-competing from 254 competing awards in prior years	--	74,375,000	--	+25,011,000
b. Research grants, new and competing	--	27,286,000	--	+8,349,000
2. Research and development contracts	--	11,604,000	--	+989,000
3. Intramural research	--	23,924,000	--	+1,316,000
4. Direct Operations	--	9,815,000	--	+154,000
5. Program Management	--	1,396,000	--	+10,000
Subtotal			--	+35,829,000
Total Increases				+37,386,000
Decreases:				
A. Built-in:				
1. One less day of pay in 1978	--	14,383,000	--	-45,000
Subtotal			--	-45,000
B. Program				
1. Decrease of 2 positions from 1977	543	39,000	-2	-39,000
2. Research Grants:				
a. Non-competing terminated in 1977	--	74,375,000	--	-30,813,000
3. Fellowships				
a. Phase out of post doctoral research fellowship awards	--	14,000	--	-14,000
b. National Research Service Awards	--	7,086,000	--	-514,000
Subtotal			-2	-31,380,000
Total, decreases			-2	-31,425,000
Total, net change			-2	+5,961,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
195	Communicative Disorders	---	$ 21,707,000	---	$ 21,886,000	--	$ +179,000
197	Neurological Disorders	---	51,682,000	---	52,619,000	--	+937,000
201	Stroke and Nervous System Trauma	---	22,296,000	---	23,211,000	--	+915,000
203	Fundamental Neurosciences	---	21,190,000	---	21,982,000	--	+792,000
205	Intramural Research	324	27,414,000	324	30,019,000	--	+2,605,000
	(Standard Level User Charge)		(158,000)		(196,000)		(+38,000)
298	Direct Operations	169	9,815,000	167	10,312,000	-2	+497,000
	(Standard Level User Charge)		(180,000)		(192,000)		(+12,000)
210	Program Management	50	1,396,000	50	1,432,000	--	+36,000
	Total obligations	543	155,500,000	541	161,461,000	-2	+5,961,000
	(Standard Level User Charge)		(338,000)		(388,000)		(+50,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	543	541	-2
Full-time equivalent of all other positions	55	55	--
Average number of all employees	591	589	-2
Personnel compensation:			
Permanent positions	$10,982,000	$11,092,000	+$110,000
Positions other than permanent	1,503,000	1,532,000	+29,000
Other personnel compensation	293,000	320,000	+27,000
Subtotal, personnel compensation	12,778,000	12,944,000	+166,000
Personnel benefits	1,605,000	1,626,000	+21,000
Travel and transportation of persons	525,000	467,000	-58,000
Transportation of things	83,000	86,000	+3,000
Rent, communications and utilities	801,000	880,000	+79,000
Printing and reproduction	279,000	295,000	+16,000
Other services	4,702,000	5,470,000	+768,000
Project contracts	11,604,000	12,593,000	+989,000
Payment for centrally furnished services	10,094,000	11,088,000	+994,000
Supplies and materials	1,968,000	2,332,000	+364,000
Equipment	2,300,000	2,900,000	+600,000
Grants, subsidies and contributions	108,761,000	110,780,000	+2,019,000
Total obligations by object	155,500,000	161,461,000	+5,961,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1977 House Report	
1. The Committee expects that with the additional funds provided in the bill, the total funding level for research specifically relevant to multiple sclerosis will be $10,000,000 in fiscal year 1977. The Committee has long held the tenet that the support of research mandates cooperaperation and collaboration of the public and private sector and thus, supports the recommendations of the Advisory Commission on Multiple Sclerosis that this should apply to multiple sclerosis research. The Institute is requested to provide this Committee with a report, prior to hearings on the 1978 budget, on the implementation of the Commission's recommendations.	1. The NINCDS Advisory Council has submitted a report to the Congress detailing the funding levels for MS research projects and showing the MS-related purpose of the projects. NINCDS will spend at least $10,000,000 in fiscal year 1977 specifically for MS research, and will continue to carry out the recommendations of the Advisory Commission on Multiple Sclerosis.
1977 Senate Report	
1. The Committee expects the Institute to continue to meet or exceed the multiple sclerosis research support targets recommended by the MS Commission for both basic and applied research. The Committee considers this to be a very high priority area and directs the Institute to submit a report detailing, specifically, levels of funding on MS research projects funded and a brief justification as to their relevance to MS research. This report should be received no later than 6 months following the enactment of this bill.	1. The NINCDS Advisory Council has submitted a report to the Congress detailing the funding levels for MS research projects and showing the MS-related purpose of the projects. NINCDS will spend at least $10,000,000 in fiscal year 1977 specifically for MS research, and will continue to carry out the recommendations of the Advisory Commission on Multiple Sclerosis.

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act Section 301--Research and Investigations in general.....	Indefinite	
Title IV, Part D--National Institute of Neurological Diseases and Blindness.....	Indefinite	$154,889,000 2/
Public Law 90-639, Sec. 7--National Institute of Neurological Diseases and Stroke.....	Indefinite	
Title IV, Part I--National Research Service Awards.....	1/	$ 6,572,000 2/

1/ Authorization expires September 30, 1977; extension legislation is pending.

2/ Funding estimate only.

National Institute of Neurological and Communicative Disorders and Stroke

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	120,285,000	120,285,000	125,310,000	120,269,000
1969	123,765,000	119,244,000	125,244,000	121,504,500
1970	97,667,000 1/	95,438,000	106,187,000	91,497,000
1971	89,475,000	95,073,000	110,073,000	100,073,000
1972	91,015,000	103,454,000	133,454,000	111,445,000
1973	111,394,000	122,405,000	129,735,000	124,005,000 2/
1974	100,769,000	119,644,000	124,571,000	119,529,000 3/
1975	119,494,000	131,496,000 4/	143,536,000	142,034,000
1976	115,216,000	136,807,000 5/	136,807,000 5/	144,707,000 6/
1977	146,532,000	153,132,000	163,132,000	155,500,000
1978	161,461,000			

1/ $21,519,000 transferred to National Eye Institute
2/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.
3/ Appropriation after reduction as authorized by PL 93-192.
4/ Excludes contracts not considered by House due to lacking authorization.
5/ Excludes fellowships and training grants not considered due to pending legislation ($7,900,000).
6/ Includes $7,900,000 training programs authorized by the continuing resolution.

Note: The figures presented in this table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsiblity for funding of general research support grants is no longer the function of this institute in 1978. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

National Institute of Neurological and Communicative Disorders and Stroke

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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 1/	103,485,000	101,256,000	112,700,000	97,315,000
1971	96,972,000	100,807,000	115,807,000	103,502,000
1972	96,521,000	108,590,000	139,187,000	116,731,000
1973	117,877,000	130,672,000	145,000,000	130,672,000 2/
1974	101,198,000	120,073,000	125,000,000	121,358,000 3/
1975	119,958,000	131,960,000 4/	144,000,000	142,498,000
1976	114,955,000	136,546,000 5/	136,546,000 5/	144,446,000 6/
1977	146,532,000	153,132,000	163,132,000	155,500,000
1978	161,461,000			

1/ Excludes funds for blindness, established as a separate appropriation "National Eye Institute" in 1970.
2/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.
3/ Appropriation after reduction as authorized by PL 93-192.
4/ Excludes contracts not considered by House due to lacking authorization.
5/ Excludes fellowships and training grants not considered due to pending legislation ($7,900,000).
6/ Includes $7,900,000 training programs authorized by the continuing resolution.

Justification

Program	1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
1. Communicative Disorders.....	---	$ 21,707,000	---	$ 21,886,000	---	$ +179,000
2. Neurological Disorders.....	---	51,682,000	---	52,619,000	---	+937,000
3. Stroke and Nervous System Trauma.....	---	22,296,000	---	23,211,000	---	+915,000
4. Fundamental Neurosciences.....	---	21,190,000	---	21,982,000	---	+792,000
5. Intramural Research.....	324	27,414,000	324	30,019,000	---	+2,605,000
6. Direct Operations.....	169	9,815,000	167	10,312,000	-2	+497,000
7. Program Management.....	50	1,396,000	50	1,432,000	---	+36,000
Total obligations..	543	155,500,000	541	161,461,000	-2	+5,961,000

General Statement

Research conducted and supported by the National Institute of Neurological and Communicative Disorders and Stroke is intended to increase understanding of the structure and function of the brain, the spinal cord, and the related nervous and sensory systems; and to combat the many disorders which afflict these organs. Many of these disorders such as cerebral palsy, multiple sclerosis, muscular dystrophy and Parkinson's disease, interfere with physical mobility and cause long-term disability. Others interfere with education and employment; such as epilepsy, deafness, and speech disorders. Stroke is the third leading cause of death in this country; and head and spinal cord injury are major causes of serious and permanent disability.

The successful prevention and treatment of most of this broad spectrum of diseases is still a goal to attain. The eventual prevention and treatment of most of these conditions is still dependent on basic understanding of how the brain and nervous system develops and functions. Because basic research is vital to our efforts to cope with neurological and sensory disorders, NINCDS' efforts remain focused toward knowledge development. As new knowledge leads to new opportunities to prevent or treat disease, NINCDS is prepared to move decisively in their application. Efforts to improve drug treatment for epilepsy and Parkinson's disease; screening techniques for hereditary lipid storage disorders; and attention to conditions which seem to foretell cerebrovascular accidents are examples of NINCDS efforts to hasten the application of basic knowledge to the treatment of human disease.

The overall NINCDS research program represents a balanced, and coordinated, attack on health and scientific problems. This program more specifically addresses itself to the following problems:

The neurological disorders of early life, including cerebral palsy and metabolic diseases such as Tay-Sachs;

The neurological disorders of adult life including Parkinson's disease and Huntington's disease;

The cerebrovascular disorders, particularly stroke;

Epilepsy and related paroxysmal disorders including migraine headaches;

Multiple sclerosis and related disorders;

Neuromuscular disorders, particularly muscular dystrophy and myasthenia gravis;

Infectious diseases of the nervous system, including those chronic degenerative diseases caused by slow and latent viruses;

Spinal cord and head injury, and central nervous system regeneration;

Tumors of the nervous system;

Neuroendocrine studies, including studies on the autonomic nervous system, and on the control of body temperature, the bladder, and respiration;

Neural aspects of learning and behavior, such as sensory and motor behavior, perception, memory, learning, and locomotion;

Normal nervous system functions, including the subcategories of anatomy, biochemistry, pharmacology and physiology; and

Communicative disorders including disorders of hearing and equilibrium, speech and language, and other higher brain fuctions, and disorders of other senses.

In addition to the conduct and support of research, the NINCDS will continue its training programs which emphasize professional development of outstanding scientists who are interested in the neurological and communicative disorders. Both individual and institutional National Research Service Awards are used to support training programs in developmental neurology, neurobiology, neuroimmunology, neuropathology, neurovirology, and in sensory physiology and biophysics.

The budget requested in 1978 for support of these research efforts is $161,461,000, an increase of $5,961,000 over the 1977 appropriation. The requested amount will permit the four extramural research programs and the intramural research programs to proceed as noted below.

Communicative Disorders Program

	1977 Appropriation	1978 Estimate	Increase or Decrease
Communicative Disorders.....	$21,707,000	$21,886,000	+$179,000
Subactivities:			
Hearing and equilibrium...	16,767,000	16,752,000	-15,000
Speech and language.....	3,241,000	3,238,000	-3,000
Research career programs.....	356,000	399,999	+43,000
Training programs.....	1,343,000	1,497,000	+154,000
Total.....	21,707,000	21,886,000	+179,000
Budget Mechanism:			
Research Grants			
Regular.....	18,868,000	18,701,000	-167,000
Special.....	1,067,000	1,117,000	+50,000
Subtotal.....	19,935,000	19,818,000	-117,000
Training programs.....	1,343,000	1,497,000	+154,000
Research and development contracts.....	429,000	571,000	+142,000
Total.....	21,707,000	21,886,000	+179,000

The Communicative Disorders Program is concerned with research efforts to improve the diagnosis, treatment, and prevention of diseases and disorders of the ear, nose and throat and problems relating to hearing, language, and speech. The disorders of human communication are among the most frequent disabilities in our society. Approximately 10 percent of the population, or over 20 million individuals, are so affected. Of these disorders, hearing loss is the most prevalent. The most recent census of the deaf indicates that between 13 and 14 million persons have sufficient hearing loss to significantly affect their ability to function effectively in everyday activities. In addition, an estimated 11 million persons have speech and/or language disorders, some of whom are also hearing impaired. Children delayed in language development cannot enter the normal educational process and are prevented from learning the skills they need to function as self-sufficient members of society. Since the communicative disorders usually do not cause death, the problem is often downgraded. However, one cannot overlook the economic factors of: Cost for special education and rehabilitation; and loss of potential earning power for self-support. Even more important for the individual and the family involved is the change in the quality of life caused by such disabilities.

The communication process may be impaired by a multitude of problems including: Inaccurate speech production; inadequte amplification of incoming speech; distortion of speech producing diminished intelligibility; and interference with either the memory of language information or the generation of meaningful language. Speech disorders may result from structural defects or impaired neuromuscular control of the lips, tongue, oral cavity, larynx or pharynx. Both speech and language disorders may result from limited exposure to language and speech in deafness, or from brain injury. In each of these areas where the potential for a break in the communicative process is present, significant gaps in our knowledge still exist.

Individual research grants, program projects, and clinical research centers are all being utilized by the NINCDS to study in depth the basis of human communication and its disorders. The primary emphasis is on prevention, but where disorders of function already exist, the emphasis is on improvements in diagnosis and treatment. The Laboratory of Neuro-Otolaryngology on the Bethesda campus is providing leadership in revealing some of the inner ear functions which were previously not understood. Chief among these is the process of transduction, whereby sound waves (mechanical energy) entering the ear are converted into nerve impulses (electrical signals) for transmission to the brain for processing, utilization, and storage. Understanding of this mechanism is the key to the development of rational methods of dealing with the most prevalent type of hearing loss and the type which up to now has not been amenable to treatment, i.e., sensori-neural hearing loss.

Clinical studies are in progress to determine the effects of neuro-pharmacological treatments on the speech and language functioning of children and adults with various neurological disorders. The results should indicate new approaches to treatment of many of these disorders.

The NINCDS has indicated a special interest in certain areas of research at this time. One of these is the possibility of stimulating the nerve endings of the inner ear through the so-called cochlear implant. Workshops which were sponsored by the Institute recommended a number of projects which should be carried out in this area. One of these, evaluation of the limited number of humans who have received a cochlear implant, has been completed. From the information gained, new directions for research involving further development of the cochlear implant are projected and as a result a contract will be awarded in 1977 for further development of multi-channeled electrodes to be used in the cochlear implant.

A second area of special emphasis is concerned with the problem of serous (secretory) otitis media, a common middle ear affliction in young children; which is a major cause of hearing loss. The NINCDS helped make available to the professional community the results of a recent International Workshop in this subject. A study of the epidemiological aspects of serous otitis media is currently being developed in response to the Workshop's recommendations.

A third area of special emphasis is the study of agents which cause damage to the functioning of the ear. Knowledge in this area should provide better protection of the ear from such agents. Common examples of such agents include noise and various ototoxic drugs which are sometimes required for therapeutic use.

In addition, directed research supported by research contracts includes several projects such as: Development of a measure of everyday communication skills in aphasic (language impaired) adults; evaluation of newly developed speech tests to determine the potential of hearing aid use; evaluation of a wearable master hearing aid for possible utilization to improve hearing aid fitting; assessment of the process of language acquisition in language disordered children; differential diagnosis of the sensory and perceptual abilities of language impaired, reading impaired and speech impaired children; development of methods for screening for language and speech problems in preschool children; and determining the feasibility of screening high risk populations for early signs of laryngeal pathology.

Neurological Disorders Program

	1977 Appropriation	1978 Estimate	Increase or Decrease
Neurological Disorders.....	$51,682,000	$52,619,000	+$937,000
Subactivities:			
Neurological disorders of early life.....	8,628,000	8,881,000	+253,000
Neurological disorders of adult life.....	3,171,000	3,264,000	+93,000
Epilepsy.....	7,080,000	7,290,000	+210,000
Sclerosing disorders.....	7,500,000	7,720,000	+220,000
Neuromuscular disorders...	5,605,000	5,769,000	+164,000
Infectious disease of the central nervous system.....	1,069,000	1,100,000	+31,000
Tumors of the nervous system.....	664,000	683,000	+19,000
Neuroendocrine studies....	3,171,000	3,264,000	+93,000
Learning and behavior.....	2,249,000	2,315,000	+66,000
Other sensory disorders...	5,236,000	5,389,000	+153,000
Research career programs.....	1,598,000	1,674,000	+76,000
Scientific evaluation.....	712,000	850,000	+138,000
Training programs.....	4,999,000	4,420,000	-579,000
Total.....	51,682,000	52,619,000	+937,000
Budget Mechanism:			
Research Grants			
Regular.....	36,704,000	37,251,000	+547,000
Special.....	4,496,000	4,850,000	+354,000
Subtotal.....	41,200,000	42,101,000	+901,000
Training programs.....	4,985,000	4,420,000	-565,000
Old Fellowship programs.....	14,000	--	-14,000
Research and development contracts.....	5,483,000	6,098,000	+615,000
Total.....	51,682,000	52,619,000	+937,000

Neurological Disorders of Early Life

NINCDS will support research on the developmental disorders of early life, including cerebral palsy and other motor disorders, autism and behavioral disorders, mental retardation and learning disorders, and central nervous system birth defects and heritable muscle and neurological disorders. This research will be focused on understanding the etiology, and improving diagnosis and treatment of these disorders. NINCDS continues to support research involving cerebral spinal fluid formation and absorption in relation to pathophysiology of hydrocephalus, regulation of protein synthesis in brain development, myelin membrane structure, synaptogenesis in tissue culture, neurogenesis, environmental factors affecting brain development and other related subjects. In the area of catabolic deficiency disorders, emphasis is on the causes, control and therapy of hereditary lipid storage diseases,

such as Menkes' disease, Wilson's disease, Zellweger's cerebro-hepato-renal syndrome, phytanic acid storage disease, Neimann-Pick disease, Tay Sachs disease, Krabbe's disease, Metachromatic Leukodystrophy and other storage diseases of unknown etiology.

In addition, reports from the major analyses of Collaborative Perinatal Project data will be published in the following areas: cerebral palsy and motor disorders; mental retardation, vision abnormalities; convulsive disorders; learning disorders, minimal brain dysfunction; communicative disorders (problems of speech, language and hearing); congenital malformations; multiple problems associated with low birth-weight and gestational age (prematurity); and the children who died during the interval of the Study, with particular emphasis on the abnormalities found in the central nervous system. The analysis of these data has identified groups of children with special interest and these subgroups of children will receive extended follow-up and study. The subgroups are children with febrile seizures and convulsive disorders, cerebral palsy, learning and behavior disorders and communicative disorders. A controlled study of children with febrile seizures will evaluate whether preventive therapy will reduce the number of children who subsequently develop epilepsy or other disabilities.

Epilepsy

An estimated 70% of grant funds to epilepsy and epilepsy-related research are channeled to scientists for the accumulation of new information about this disease. Areas under study include pharmacokinetics of anticonvulsant drugs, mechanisms of epileptogenesis, electrical activity of the brain, seizure control using non-pharmacological means, progressive pathology resulting from seizure activity, development of animal models, role of the cerebellum in epilepsy, computerized data reduction and analysis of EEG, and synaptic factors in epilepsy. In addition five clinical research centers have been developed countrywide. These centers combine the best efforts of basic and clinical investigators working in concert to acquire an understanding of all aspects of the epilepsies. These clinical research centers function as a bridge between basic research efforts and the development of new therapies.

The commission for the Control of Epilepsy and Its Consequences, mandated by the Congress in 1975, began deliberations in 1976. It will report its findings and recommendations to the Secretary of Health, Education, and Welfare and to the Congress in 1977. The Comprehensive National Plan for the Control of Epilepsy and Its Consequences will contain specific recommendations for expanded research, treatment, socioeconomic and rehabilitation efforts. The Institute will continue its support and collaboration in clinical research of investigational new antiepileptic drugs in the search for agents providing greater seizure control and fewer side effects. The Institute has established five comprehensive research and treatment programs for epilepsy and related convulsive disorders. Primary emphasis of these programs is on the application of new research findings to patients. The programs will demonstrate the relationship of vigorous basic and clinical research efforts to optimal care of patients in varied settings. At NIH, intramural research is directed towards improved seizure control through intensive monitoring of patients with complex partial seizures; also the metabolism of investigational and marketed antiepileptic drugs is being studied in animals and man.

Multiple Sclerosis and other Demyelinating Diseases

A comprehensive hypothesis for the demyelinating disorders might state that there may be an early childhood insult, perhaps a virus attack, which interacts with the human organizm of a particular genetic background to result in the preservation of the putative etiologic agent, either in its intact form or in a severely modified form, which will in later life produce the clinical picture. In both the Extramural and Intramural Research Programs,

the major research efforts in multiple sclerosis are targeted to virological, immunological, and epidemiological tests of this hypothesis. Approximately 60 research projects are currently supported by NINCDS, with three-fourths of these concerned with etiology and the remainder dealing with diagnosis and treatment. The seven Clinical Research Centers supported by NINCDS provide a cadre of patients who have been relatively well defined clinically who can be followed and tested for some of the new approaches to therapy which involve manipulation of the patient's immune response. Because myelin appears to be the target for damage in these diseases much research is concerned with the biochemistry and chemistry of myelin. The brain enzymes involved in the synthesis, modification and breakdown of myelin have been studied and their specificity is being determined. If the demyelinating disorders of man are caused by an early infection by a virus or a combination of viruses, then pathology could result by at least two major mechanisms which need not occur independently. First, immune responses directly against virus or viral coded unmasked tissue antigens could result in tissue injury. Secondly, the virus itself could slowly alter the biochemical function of specialized cells in the nervous system without destroying the cells. Research indicates that the immune responses may be paradoxical in that one may have either aberrant hyperimmune responses or immunosuppression. The assocation between multiple sclerosis and the genetically determined histocompatability antigens is provocative and is being intensively investigated. The study of the high multiple sclerosis incidence cluster in the Shetland and Orkney Islands which includes epidemiological, virological, and immunogenetic analysis has been completed. Analysis of these data should provide further understanding of the possible interaction of these factors. A national survey of incidence, prevalence and cost of multiple sclerosis in the United States is in progress.

Muscular Dystrophy, Myasthenia Gravis, and other Neuromuscular Diseases

The Institute's activities in supporting research in the neuromuscular disorders include approximately 127 research projects, three clinical research centers and one program project. Extramural research support is currently focused on work on the neurotransmitters, the neuromuscular junction and nerve-to-nerve junction (synapses and the properties of membranes). It is widely accepted in the scientific medical community that rational therapies for neuromuscular diseases require an understanding of sensitive membranes, neurotransmitters and synapses. Other support efforts relate directly to dystrophies, myasthenia gravis, peripheral neuropathies and general enruomuscular facilities. The three clinical research centers are concerned primarily with the dystrophies, myasthenia gravis, and the other neuromuscular disorders and the program project included within this program effort is primarily concerned with the development of drugs to ameliorate the symptoms of these diseases. Activities include tissue culture studies of differentiating muscle cells aimed at elucidating the nature of intrinsic muscle disorders like muscular dystrophy; immunochemical studies utilizing antibodies against pure nerve-to-muscle receptor proteins--studies which provide animal models closely resembling human myasthenia gravis; the use of freeze-fracture electron microscopy to obtain a panoramic view of cell membrane surfaces--a technique which has provided for the first time visualization of distinctive structural differences between nerve-to-junctions which are excitatory and those that are inhibitory.

Infectious Diseases of the Central Nervous System.

In addition to the Institute's program in slow and atypical viruses described in the section on the Intramural Research Program, the Institute has a highly significant program carried on by its grantees and contractors. Recent advances have been made in studies of the effects of herpes virus infections, toxoplasmosis, cytomegalovirus infections, and rubella vaccine

during pregnancy. The role of measles virus in the causation of subacute sclerosing panencephalitis, a fatal disease in children, has been clarified.

Degenerative Disorders.

Research under this category includes work related to Parkinsonism, Huntington's Disease and other involuntary movements and hyperkineses, and general extrapyramidal studies. Although levodopa produces remarkable improvement in most Parkinsonism patients at times it has unpleasant side effects and some patients do not respond to it at all. Approximately 27 research grants are concerned with improving the efficacy of levodopa, exploring other treatments, and examining hypotheses that deal with the etiology of Parkinson's Disease.

Four research grants are concerned with early diagnosis and treatment of Huntington's Disease. Although physostigmine has been demonstrated to be effective in treating the involuntary movements associated with this disease, other agents are being examined. Public Law 94-63 established the Commission for Control of Huntington's Disease and Its Consequences. The Commission operates out of the Office of the Director, NINCDS, which provides the administrative and logistical support for the conduct of its mission.

Certain studies focus on Alzheimer's Dementia utilizing clinical, biochemical, light microscopic ultrastructural, and other experimental approaches. Related work is concerned with the determination of a defect in axonal or dendritic flow of particulate matter in cortical neurons of patients suffering from dementia. Other studies emphasize the development of experimental models for the analysis of the immunobiology of age-dependent CNS disease. About 25 research grants support activities in this area.

Five research centers have been established to focus efforts on studies of degenerative disorders.

Neoplasms (Tumors) of the Brain and Nervous System.

Tumors of the brain and nervous system constitute an important health problem for children and the aged. Nearly one-half of all those who die each year of neurological disorders other than stroke succomb to brain tumors. Because of the special characteristics of nervous system tissue, these neoplasms do not respond to therapies found useful on tumors in other organs. Also, there is preliminary but substantial evidence that the nervous system is an important reservoir of viruses suspected of being tumor causing (oncogenic). In collaboration with the National Cancer Institute, the Institute is continuing to explore these leads on the unique problem of tumors of brain and other nervous tissue.

Stroke and Nervous System Trauma Program

	1977 Appropriation	1978 Estimate	Increase or Decrease
Stroke and Nervous System Trauma.....	$22,296,000	$23,211,000	+$915,000
Subactivities:			
Stroke.....	10,554,000	10,978,000	+424,000
Trauma and injury.....	11,664,000	12,133,000	+469,000
Research career programs.....	78,000	100,000	+22,000
Total.....	22,296,000	23,211,000	+915,000
Budget Mechanism:			
Research Grants			
Regular.....	16,657,000	16,806,000	+149,000
Special.....	5,183,000	5,906,000	+723,000
Subtotal.....	21,840,000	22,712,000	+872,000
Research and development contracts.....	456,000	499,999	+43,000
Total.....	22,296,000	23,211,000	+915,000

Within this program, there are six major scientific program efforts: Stroke, Head Injury, Spinal Cord Injury, Nervous System Regeneration, Tumors of the Nervous System, and Chiropractic and Manipulative Therapy.

Stroke, the third leading cause of death in the United States, has an annual mortality rate of over 200,000. Moreover, each year an additional 300,000 persons who survive strokes suffer permanent physical and mental disabilities. The Institute is continuing to give the highest priority to a coordinated research program in this area by means of investigator-initiated research, research and development contracts, and stroke clinical research centers (fourteen of which are now active). In addition, a pilot program of comprehensive stroke centers was initiated last year. This pilot program will focus on the evaluation and dissemination in the community of laboratory and university clinical findings, with special attention to the correlation of early diagnosis and treatment with subsequent outcome. The stroke comprehensive center program offers promise for seeing that applied research is fostered and that these clinical findings are brought to use for patient care. Recent developments in improved methods of diagnosis also offer promise of early intervention and prevention; these leads are being vigorously pursued. In addition, techniques for monitoring acutely ill stroke patients are being developed to bring to the brain techniques using the equipment and knowledge which have been so successful in caring for patients with acute heart disease.

Head Injury. Head Injury is one of the major causes of death resulting from trauma (e.g., traffic accidents, industrial accidents, sports). The physiological and metabolic consequences of head injury, the physical forces involved in brain damage, the structure and function of the blood-brain barrier, and the evaluation of new diagnostic and therapeutic procedures in the management of head injury are the several approaches being fostered

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in the Institute's head injury research program. A major clinical problem continuing to confront the physician is the evaluation of coma following injury to the brain. In order to resolve this dilemma, a national cooperative study, which is in its final stages, will provide the means of differentiating between head injured patients who have incurred irreversible damage at the time of the injury and those who are comatose as a result of reversible complications of the injury. To parallel this, improved therapeutic methods of dealing with brain swelling, the most common cause of coma following head injury, are being developed. Through its clinical research center activity, five regional head injury clinical research centers are serving as focal points for the coordination, evaluation and dissemination of laboratory and clinical data in this research area. A program of comprehensive trauma centers is being launched to coordinate and increase community based activities as a basis for evaluating the efficacy of clinical procedures.

Spinal Cord Injury. Spinal cord injury as a result of traffic and recreational accidents continues to be a serious problem to the victim, his family, and the community. In light of this, the Institute has focused special attention on the problem of preventing permanent damage to the injured spinal cord and at the least, preventing the cord's self-destruction. Preliminary data indicate that if the acutely injured cord is treated immediately and adequately, permanent damage may be minimized or prevented; however, more information is needed in regard to improved methods for identifying the specific site and extent of injury and to improved approaches to both specific and general therapy of the injured person. The applicability of computerized tomography scanning to these problems is being evaluated. In addition, there is need to exploit further existing opportunities at the regional spinal cord injury clinical research centers to demonstrate how best to translate the newest scientific information into better methods of clinical therapy. The Institute currently supports five spinal cord injury clinical research centers and through a new program of comprehensive trauma centers, will coordinate and develop community based clinical evaluation activities.

Central Nervous System Regeneration. Paralleling research efforts on Stroke, Head Injury and Spinal Cord Injury is the Institute's targeted program on central nervous system regeneration. If the function of destroyed segments of the brain and spinal cord could be restored, then many of the millions of now permanently disabled citizens could enjoy a partial return of function. The solution of this problem is one of the most complex in the entire field of the biomedical sciences and will demand focused attention for several years before its solution is achieved. To help identify and focus needed research efforts in this area, the Institute's National Advisory Council comprehensive report on "Growth and Regeneration in the Central Nervous System" is serving as a basis for stimulating increased research efforts in this important area.

Research on Manipulative Therapy. At the direction of the Congress, the pilot phase of a coordinated national effort on research on chiropractic and manipulative therapy has been completed. Research workshops identifying the state of the art in these research areas have been completed and the proceedings of these symposia are being made available to the scientific community. A modest number of pilot research programs have already been initiated, focused particularly on the biomechanics and neurophysiology of subluxation and altered vertebral mechanics. Also, a pilot program to evaluate the efficacy of manipulative therapy has been initiated. In addition, a modest program of research training has been identified which will provide manipulative clinicians (chiropractors, osteopaths and medical physicians) with the opportunity for increasing their research skills for application to these problems.

Fundamental Neurosciences Program

	1977 Appropriation	1978 Estimate	Increase or Decrease
Fundamental Neurosciences....	$21,190,000	$21,982,000	+$792,000
Subactivities:			
Nervous System Studies related to normal function.....	15,475,000	16,146,000	+671,000
Multicategorical.....	4,544,000	4,742,000	+198,000
Research career programs...	413,000	439,000	+26,000
Training programs.....	758,000	655,000	-103,000
Total.....	21,190,000	21,982,000	+792,000
Budget Mechanism:			
Research Grants			
Regular.....	18,273,000	19,138,000	+865,000
Special.....	413,000	439,000	+26,000
Subtotal.....	18,686,000	19,577,000	+891,000
Training programs.....	758,000	655,000	-103,000
Research and development contracts.....	1,746,000	1,750,000	+4,000
Total.....	21,190,000	21,982,000	+792,000

All biomedical research may ultimately lead to solutions of health problems. However, it is the firm belief of the vast majority of biomedical scientists that the more fundamental questions toward which research is directed, the greater will be the return in ultimately applicable results. Because basic understanding of how the brain and nervous system develop, work, and are constructed is essential to a successful attack upon the varied neurological and sensory disorders; and because so little is known about the mysteries of the nervous system; NINCDS continues to support and conduct basic research in the fundamental neurosciences.

In the wide range of research grant and contract proposals from which the NINCDS selects its programs, some are more directly applicable to specific diseases and disorders. These are assigned to the disease categorical programs, Neurological Disorders, Communicative Disorders, and Stroke and Trauma. Other research proposals are directed at more fundamental questions about the basic structure and function of the nervous system, its chemistry, the action of drugs on it, and on the individual nerve cells with their tiny terminal processes by which they communicate with one another. The answers to such fundamental questions about the normal nervous system are required in order to understand the even more complex processes of disease. It is the basic research efforts such as these which constitute the Fundamental Neurosciences Program.

Even within this program there is a wide variability in the lead time required before research findings can be applied to treatment of disease. For example, there is increased effort in application of computers to neurobiological problems of pattern recognition in studying how groups of nerve cells work together to control muscle movement, and problems of computer assisted analysis

of brain waves (EEG). Sleep is classified into different types and the normal and abnormal balance between these different types can be studied with the help of computers. Basic mechanisms in sensory neurophysiology must be understood in order to learn how to preprocess sound so that electrical stimulation of the nervous system of deaf individuals can be utilized for intelligible speech communication.

Some of the most fundamental studies in this program relate to the manner in which interconnections between nerve cells affect the function of the nervous system. The nervous system is not "hard-wired" like a telephone switchboard, rather, it is thought, the synapses or connections at nerve endings continue to change with time, new ones forming and old ones dissolving. Such changes in "connectivity" are stimulated by changes in usage or activity of nerve pathways. Increased efforts are planned for these studies of the functional modification of the nervous system with usage.

Targeted studies continue to explore the mechanisms by which electrical stimulation of the nervous system can be used to induce useful patterns of nerve cell activity. Other studies emphasize the damage which such electrical nerve stimulation may produce and search for techniques to maximize the safety factor between effective stimulation and irreversible damage. Implanted electronic devices can be used to stimulate the spinal cord and its nerve roots in such a way that urinary bladder evacuation occurs. Failure of the bladder to drain properly is one of the major causes of urinary infection and death in paraplegic patients. Thus, in this area fundamental studies of the normal bladder reflex mechanisms and the development of successful techniques for nervous system stimulation by remote control may lead very directly to relief of human disease.

The research efforts capable of solving such basic questions about the nervous system required the long term nurture of highly skilled scientists. These teams cannot be "turned on and off" from year to year. An opportunity to try out new research ideas is as important as the continued support over the years required to realize long range research goals. In FY 1977 NINCDS will concentrate its resources on the maintenance of the best basic research efforts across the broad spectrum of the basic biomedical sciences related to the neurological and sensory disorders. A directed research program will continue to explore the feasibility of new types of neural prostheses (nerve substitutes) and fundamental techniques of bioengineering.

A program of workshops are planned to facilitate the exchange of new information between the Fundamental Neurosciences Program staff, acting as an information hub, and grantee principal investigators and contractors. These workshops provide the means at a modest cost to accelerate the exchange of highly specialized scientific information, focus and direct the efforts of investigators toward issues of concern to NINCDS, and obtain the best scientific advice for program planning and development.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Research	324	$ 27,414,000	324	$ 30,019,000	---	$ 2,605,000

The Intramural Research Program of NINCDS conducts research related to the nervous system and its disorders in laboratories and clinics in Bethesda, Maryland. There are currently 227 active research projects: approximately 57% of intramural resources are devoted to fundamental research and 43% to clinically applied studies. In the basic research areas, major budgetary support currently is devoted to neurophysiologic (16%) and biochemical (10%) approaches to the understanding of brain function as well as to the basic mechanisms by which viruses and other infectious agents modify the structure and activity of nervous system tissues (12%). In the clinical research areas, demyelinating conditions (8.5%), infectious diseases (5.1%), and congenital disorders (4.4%) of the nervous system presently command the largest resource allocations. Some of the most promising research areas to be pursued during the next fiscal year are summarized below. Also included in the activity is the Institute's Office of Biometry and Epidemiology.

Clinical Research Programs. The Institute conducts clinical research on a variety of neurological and communicative disorders arising as a result of maldevelopment or malfunction of the nervous system. Emphasis continues to be placed on the rapid application of new knowledge developed from basic research with the goal of improved preventive, diagnostic, and therapeutic measures for nervous system disease.

In the medical neurology area, studies will continue on the causes and treatments of motor neuron disease such as amyotrophic lateral sclerosis, the myopathies, including muscular dystrophy, and diseases of the neuromuscular junction such as myasthenia gravis. Increased emphasis is being placed on immunological and viral aspects of a number of central nervous system disorders, including multiple sclerosis, motor neuron disease, Alzheimer's disease and Parkinson's disease. New strategies are being undertaken in experimental therapy of Parkinson's disease, Huntington's disease, epilepsy and certain drug-induced disorders of movement.

In the developmental and metabolic neurology areas, research continues to be directed towards the development of improved diagnostic and therapeutic techniques for such inherited disorders of lipid metabolism as Fabry's, Tay Sachs, Gaucher's, and Niemann-Pick disease. Each of these disorders arises as a result of a genetically determined defect in a single enzyme. Efforts to perfect biochemical tests for the antenatal diagnosis of these conditions--as well as to expand clinical trials of enzyme replacement therapy--are a major priority.

In the surgical neurology area, research is focused on vascular disease of the nervous system, head injury, and cerebral tumors. Special attention is being directed towards the development of experimental stroke models; clinical trials of improved chemotherapeutic and immunosuppressive therapies for central nervous system tumors; and treatment of preclinical and clinical testing of microsurgical therapeutic approaches to cerebrovascular insufficiency. An effort is also underway in the treatment of chronic pain--an adjunctive condition associated with many tumors and cerebrovascular disorders.

An expansion of clinical research has also taken place into the communicative disorders. Recently initiated studies of speech production disorders in patients with Parkinson's disease using speech science instrumentation should provide objective measures of speech dysfunction applicable to patients with a variety of neurologic disorders.

Laboratory Research Programs. The Institute's research laboratories conduct a broad array of projects devoted to creating the knowledge base for developmental and applied work. The projects are investigator-initiated and are carried on within the laboratories by individual scientists or groups, depending on the type of activity necessary. The recognition that progress depends on the creativity and ingenuity of an individual who makes important discoveries of broad applicability to medicine justifies support for investigator-initiated research. The most efficient way to generate discoveries important to the prevention or treatment of disease is to encourage creative individuals or small groups to pursue ideas arising from their own knowledge and expertise. Although not often highly visible in the final application of the discovery, the investigator-initiated research effort is the predominant mechanism to create the new knowledge with which to achieve progress.

With the discovery that transmissible viruses or virus-like agents cause certain degenerative disease of the human brain, it becomes imperative that these agents be isolated, identified and chemically characterized. Four degenerative diseases of the brain can now be attributed to transmissible agents. Whether other important diseases of the nervous system such as multiple sclerosis, amyotrophic lateral sclerosis or Huntington's disease are also caused by similar agents remains unknown. It is therefore expected that the efforts to identify transmissible causes of degenerative neurological disorders will expand. Elucidation of the mechanisms of interference between complete viruses and defective virus particles continues. The studies examine the possibility that harmless defective virus particles may be useful in preventing or treating viral infections of the nervous system. Understanding virus diseases of the brain and how to treat them requires the gaining of new knowledge about the immunological responses of nerve cells and, consequently, efforts in immunological research related to virus diseases of the nervous system will expand.

Vigorous efforts to gain new knowledge about the function of nerve cells and the networks they form will continue. The basic mechanisms through which nerve cells transfer information between themselves remain poorly understood. Also inadequate is our knowledge of the metabolic and chemical environment that allows nerve cells to exist for scores of years--alive and functioning. Much more information is needed about the electrical activity of individual nerve cells and the chemicals released when the cells become active. It is especially necessary to define which chemicals are released and to determine the location of their activating or inhibiting effects on other cells. Also needed are extensive studies of the storage and release of brain cell chemicals and of possible methods to activate or block that storage or release through the use of drugs or other means. Biochemical, microspectrophotometric, neurophysiological and cytological studies of invertebrates and vertebrates, electrical recording from single cells, electron microscopy (especially with scanning and freeze fracturing techniques) are some of the important approaches used for data collection. One focus of effort will be the study of molecular excitation phenomenon. Particular study will be given to the ions involved and the nature of the channels through which they flow. Also examined will be the enzyme composition of the membranes and how the enzymes function in relation to excitation and ionic or molecular transport.

There is an increasing need for the knowledge and techniques of molecular biology and biochemistry applying to the problems of the normal functioning or damaged nervous system. Since the ultimate understanding of nerve function will

require a detailed knowledge of the molecular interaction that occurs within and between nerve cells, there are many and varied research approaches being pursued within these two research areas. The studies encompass enzymological aspects of neural function, metabolism of neurohumoral transmitter substances, composition of cellular membranes, regulation of metabolism and synthesis of complex lipids, myelination of the nervous system, genetic regulation in human cells, regulation of viral nucleic acids and many other areas.

The evaluation of the basic reactions of the nervous system to injury and disease remains a primary focus of the Institute's work. The elucidation of the pathological mechanism of cerebral stroke and the demyelinative mechanisms involved in multiple sclerosis are two important research areas. The permeability of the blood brain barrier, the study of cerebral ischemia and edema as they relate to stroke, and the structure of synaptic junctions are also areas of considerable importance for the understanding of nervous system function. Yet another important question is how to initiate or control effective regeneration of axons after their destruction in the spinal cord or brain. Recent research findings indicate the desirability of further expanding efforts to obtain new knowledge about nerve growth and regeneration. The neural mechanisms of learning and behavior are investigated in lower animal forms where simpler nervous systems increase the probability of progress.

Also emphasized are studies on motor control systems in the spinal cord or cerebral cortex, and techniques for obtaining information transfer within the nervous system. An effort to study the biologic mechanisms of hearing continues. An increased understanding of the afferent and efferent neural components of the auditory system is sought.

Office of Biometry and Epidemiology. The Office of Biometry and Epidemiology is concerned with research into the epidemiology of neurological disorders and with biometric and data systems support of ongoing Institute research. This includes the conduct of investigations, surveys, either with in-house staff or under contract or with collaborative institutions, to determine unusual patterns of disease occurrence, trends, social impact on the U.S. population, and provide a basic planning and improved program geared to assist individuals affected with neurologic disorders. Statistics surveys reflect incident, prevalence and economic costs of neurological disorders, the distribution and effectiveness of treatment centers and associated measures of disability.

In addition to providing its biometric support to the Institute research effort, the Office of Biometry and Epidemiology will have underway during the fiscal year 1978 significant investigations using the contract mechanism. A pilot study for a national survey of epilepsies will be conducted to provide more precise information as to the incident and prevalence and identification of treatment centers for purpose of improving total program planning and correlating research budgets with mortality and morbidity data. The study will test a new design for the identification of epileptics by those who are using anti-convulsant drugs. A study of the prevalence of cerebrovascular diseases, convulsive disorders, cerebral palsy, mental retardation, Parkinson, dementia, and deafness in Coprah County, Mississippi, will be made in a well-defined population of southern whites and blacks. A number of studies suggest that Parkinson's disease is less common among blacks and stroke being more common within this group. The study will reflect the magnitude of these neurological disorders and provide an identification as to whether there is a racial and sex differential in the frequency of this sample. The disorder of Dementia, thought to be largely a problem among the elderly, will be studied to provide accurate statistics on morbidity and measure this disease in the population. This effort will be carried out with the cooperation of the National Institute on Aging. Next fiscal year, a pilot study will be underway to test the collection of incident and prevalence of Neurological Disorders and Stroke from the Hospital Discharge Survey by the National Center for

Health Statistics. The key objective of this study is to develop a program for the annual collection of data so that trends can be established for disorder incident and prevalence.

Multiple sclerosis is a demyelinating disease of the central nervous system usually characterized by exacerbations and remissions. By a study with multiple sclerosis patients prospectively and in detail, an effort will be made to analyze the periodicity of the disease, related factors and its overall course. Other studies to be conducted under contract include the study of long-term effects of levodopa drug for treatment of Parkinson's disease; a case-control study of Motor Neuron Disease (ALS), including a well-coordinated multi-center investigation to explore all currently suggested risk factors.

Among other subjects to be investigated will be a planning study to measure the incident and prevalence of debilitating headaches in the population by type (migraine, tension, etc.) and a scale to measure their intensity.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations	169	$9,815,000	167	$10,312,000	-2	+$497,000

The recent reorganization of the Institute established four major research programs; communicative disorders, neurological disorders, stroke and nervous system trauma, and fundamental neurosciences. This activity includes the program directors and their staffs who are responsible for the scientific direction, administration, and review and approval functions of the Institute's grant and contract research programs. Two administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Services.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management	50	$1,396,000	50	$1,432,000	--	+$36,000

This activity supports the immediate Office of the Director, and those staff units which assist the Director in management and direction of the total program. These units include: program planning and evaluation, scientific and health reporting, and administrative management, including the financial management section.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Communicative Disorders (Speech and Hearing) [Public Health Service Act, Public Law 410, Title IV, Parts D and I]

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$21,707,000	Indefinite	--	$21,886,000

Purpose: The Communicative Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke is concerned with research on improving the diagnosis, treatment, and prevention of diseases and disorders which affect the ear, hearing, language and speech.

Explanation: The Institute's programs combine extramural research and training grants, intramural laboratory research, and contract-supported collaborative, clinical, and applied research and are directed at improving understanding of the underlying functions involved in hearing, expressing ideas through speech, and in the central neural processing of language.

Accomplishments in 1977: In 1977, under this program 229 research grants, 57 individual training awards, and 7 research contracts were awarded. The Institute's programs in 1977 were directed towards improving understanding of the underlying functions involved in hearing, expressing ideas through speech, and in the central neural (brain) processing of language. Also programs were directed at learning how specific diseases interfere with these functions and at applying this understanding to the diagnosis, treatment, and prevention of these disorders.

Objectives for 1978: The estimate for 1978 provides for 202 research grants, 59 individual training awards, and 8 research contracts. The Institute will continue to support clinical research in oto-rhinolaryngology, audiology, speech pathology and basic research in the communicative sciences and related fields through investigator-initiated research grant awards of the Extramural Programs. Ongoing basic research in neurosciences relating to communicative disorders will continue in the Intramural Research Program.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Neurological Disorders (Public Health Service Act, Public Law 410, Title IV, Parts D and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$ 51,682,000	Indefinite	--	$ 52,619,000

Purpose: Of the four major research program segments, the Neurological Disorders Program contains the largest grouping of subprograms. These neurological diseases fall into ten separate areas, each subject of a specifically focused research effort and directed at significantly advancing knowledge of the human nervous system and of how it functions in health and disease.

Explanation: Research support is directed towards the neurological diseases of adulthood, epilepsy, tumors of the nervous system, neuromuscular disorders, sclerosing disorders, neurological diseases of childhood, neurological aspects of learning and behavior, infectious diseases of the nervous system, and other sensory disorders.

Accomplishments in 1977: In 1977, 470 research grants, 290 individual training awards, and 14 research contracts were awarded. Research was directed towards all the neurological disorders with emphasis in the fields of epilepsy, sclerosing disorders, parkinsonism and infectious diseases of the central nervous system.

Objectives for 1978; The estimate for 1978 provides for 417 research grants, 239 individual training awards, and 20 research contracts. Research emphasis in 1978 will be focused on: epilepsy including the establishment of one or more comprehensive programs centered on research and treatment of epilepsy; on multiple sclerosis; genetic and developmental disorders; on the further analysis of data collected from the collaborative perinatal project; and on virological and immunological aspects of infectious disorders.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Stroke, Nervous System Trauma (Public Health Service Act, Public Law 410, Title IV, Parts D and I)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$ 22,296,000	Indefinite	--	$ 23,211,000

Purpose: Research under this Program is directed towards cerebrovascular disease and stroke, head injury, spinal cord injury, and nerve growth and regeneration.

Explanation: This program includes the support of stroke or head injury clinical research centers, acute spinal cord injury centers, stroke acute care research units and national trials of improved methods of prevention, diagnosis and therapy.

Accomplishments in 1977: In 1977, support was provided for 165 research grants and 7 research contracts. Research was directed towards stroke, head injury, spinal cord injury, and nerve growth and regeneration.

Objectives for 1978: The estimate for 1978 provides for 151 research grants and 7 research contracts. Research programs on stroke will be directed towards the problems of prevention, diagnosis, and acute care and long-term care. In the fields of head injury, spinal cord injury and regeneration, plans include the exploitation of recent leads in central nervous system regeneration as well as the protection of the brain and spinal cord during the acute phase of the trauma.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Fundamental Neurosciences (Public Health Service Act, Public Law 410, Title IV, Parts D and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$21,190,000	Indefinite	--	$21,982,000

Purpose: Support of research in those areas of the fundamental neurosciences not identifiable with the other three NINCDS program areas is basic to the Institute's mission to elucidate the mechanisms responsible for normal functioning of the human nervous system and to understand the nature of its diseases and disorders.

Explanation: This program supports research grants in ongoing projects and new highly meritorious scientific projects, such as studies related to normal nervous system function including anatomy, biochemistry, physiology, and pharmacology.

Accomplishments in 1977: In 1977, 295 research grants, 36 individual training awards and 12 research contracts were awarded. Research was directed towards the mechanisms responsible for normal functioning of the human nervous system and to the understanding of the nature of its diseases and disorders.

Objectives in 1978: The estimate for 1978 provides for 274 research grants, 28 individual training awards, and 12 research contracts. The amount requested is for continued support of research in the fundamental neurosciences. These funds will be used to support research grants in ongoing projects, and to start new highly meritorous scientific projects, such as studies related to normal nervous system function including anatomy, biochemistry, physiology, and pharmacology.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act, Public Law 410, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
325	$27,414,000	Indefinite	324	$30,019,000

Purpose: The intramural research activities of the Institute comprise a broad program of investigation of the basic characteristics of the nervous system and its diseases.

Explanation: Supporting the intramural program effort are five branches and ten laboratories. The following are in the Clinical Research area: Medical Neurology, Surgical Neurology, Developmental and Metabolic Neurology, Electroencephalography, and Neuroimmunology. Under the Laboratory Research area are: Biophysics, Neurochemistry, Neurophysiology, Molecular Biology, Experimental Neurology, Neural Control, Neuropathology and Neuroanatomical Sciences, Perinatal Physiology, Central Nervous System Studies, Neuro-otology, and Neuropharmacology. This program also includes support for the Office of Biometry and Epidemiology which conducts investigations and surveys to determine unusual patterns of occurrence, trends, and social impact of neurological disorders.

Accomplishments in 1977: Several promising new therapies were developed for treatment of epilepsy, and understanding the burst of abnormal electrical activity of brain cells during the epileptic seizure. In the Laboratory Research area, advancement in knowledge has been obtained of the structure of the nervous system and interpreting basic abnormal changes, the blood-brain barrier and its functions, and the chemical organization of the brain and nerves.

Objectives for 1978: In 1978 the Institute will continue basic and clinical research in neurological and communicative disorders including genetic disorders of the nervous system, parkinsonism, epilepsy, spinal cord injury and communicative disorders.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Public Law 410, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
169	$9,815,000	Indefinite	167	$10,312,000

Purpose: This activity provides the administration and program direction of the Institute's four extramural research programs.

Explanation: Included in this program are the four Directors of each of the Institute's extramural programs and staff for the administration of grants and contracts as they relate to these program areas. They are: Communicative Disorders; Neurological Disorders; Stroke and Nervous System Trauma; and Fundamental Neurosciences.

Accomplishments in 1977: In 1977, 1,159 research grants, 383 individual training awards, and 40 research contracts were awarded.

Objectives for 1978: The estimate for 1978 provides for 1,044 research grants, 326 individual training awards, and 47 research contract awards.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological and Communicative Disorders and Stroke

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Public Law 410, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
50	$ 1,396,000	Indefinite	--	$ 1,432,000

Purpose: This activity provides the overall administration and program direction for the Institute.

Explanation: Included is the immediate Office of the Director, the Office of Administrative Management including personnel and finance, the Office of Program Planning and Evaluation, and the Office of Scientific and Health Reports.

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WEDNESDAY, MARCH 9, 1977.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

WITNESSES

DR. RUTH L. KIRSCHSTEIN, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. LEO HANS VON EULER, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
DR. ARTHUR E. HEMING, ASSOCIATE DIRECTOR FOR PROGRAM ACTIVITIES, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
GORDON J. KLOVDAHL, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
MRS. EMMA LOUISE AKERS, FINANCIAL MANAGEMENT OFFICER, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
MS. ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. We continue this morning with the National Institutes of Health. This is the National Institute of General Medical Sciences.

The presentation will be made by Dr. Ruth L. Kisrchstein, the Director.

Doctor, we have your biographical sketch which we will place in the record at this point.

[The biographical sketch follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

BIOGRAPHICAL SKETCH

Name: Ruth L. Kirschstein.
Position: Director, National Institute of General Medical Sciences.
Birthplace and date: Brooklyn, N.Y., October 12, 1926.
Education: A.B., maga cum laude, Long Island University, 1947; M.D., Tulane University School of Medicine, 1951.
Experience: Director, National Institute of General Medical Sciences, September 1974 to present; Deputy Associate Commissioner for Science, FDA, 1973–74; Acting Deputy Director, Bureau of Biologics, FDA, 1972–73; Assistant Director, Division of Biologics Standards, NIH, 1971–72; Chief, Laboratory of Pathology, DBS, NIH, 1965–72; Acting Chief, Laboratory of Pathology, DBS, NIH, 1964–65; Assistant Chief, Laboratory of Viral Immunology, and Chief, Section of Pathology, DBS, NIH, 1962–64; Chief, Section of Pathology, Laboratory of Viral Immunology, DBS, NIH, 1960–62; Medical Officer, Pathologist, Laboratory of Viral Products, DBS, NIH, 1957–60; Medical Officer, Resident in Pathology, Clinical Pathology, Clinical Center, NIH, 1956–57; Trainee of National Heart Institute and Instructor in Pathology, Tulane University School of Medicine, 1954–55; Resident, Pathology, Providence Hospital, Detroit, Mich., 1952–54; Assistant Resident, Pathology, Veterans Administration Hospital, Chamblee, Ga., 1952; Internship, Medicine and Surgery, Kings County Hospital, Brooklyn, N.Y., 1951–52.
Association memberships: American Association of Immunologists; American Association of Pathologists; American Society of Microbiology.

Special awards or citations: Invited member of World Health Organization Expert Group on International Requirements for Biological Substances, Geneva, Switzerland, March 1965 and 1971; Invited consultants to World Health Organization concerning problems related to the use of Poliovirus Vaccine, Live, Oral, Geneva, Switzerland, March 1967; DHEW Superior Service Award, 1971; Member, Board of Consultants, Journal of Medical Primatology; Member, National Commission on Diabetes; Member, National Commission on Arthritis and Related Musculoskeletal Diseases; Member, Ad Hoc Committee on Reserpine and Breast Cancer; Chairperson, NIH Grants Peer Review Study Team; Member, Editorial Board, Journal of Toxicology and Environmental Health.

Selected publications: Kirschstein, R. L., Baron, S., Borman, G., Murray, R., Perkins, F. T., and Hottle, G.; Neurovirulence of attenuated Type I poliovirus vaccine strains after intramuscular inoculation of rhesus monkeys. Virology 11:300–302, May 1960; Kirschstein, R. L. and Gerber, P.: Ependymomas produced after intracerebral inoculation of SV40 into new-born hamsters. Nature 195:299–300, July 1962; Kirschstein, R. L., Rabson, A. S., and Peters, E. A.: Oncogenic activity of adenovirus 12 in thymectomized BALB/c and C3H/HeN mice. Proc. Soc. Exp. Biol. Med. 117:198–200, 1964; Kirschstein, R. L. Rabson, A. S., and O'Conor, G. T.; Ependymomas produced in Syrian hamsters by adenovirus 7, strain E46 ("hybrid" of adenovirus 7 and SV40). Proc. Soc. Exp. Biol. Med. 120:484–487, 1965; Kirschstein, R. L. Rabson, A. S., Paul, F. J., and Peters, E. A.: Double infection of newborn Syrian hamsters with simian virus 40 and human adenovirus 12. Cancer Res. 26:1361–1364, July 1966; Kirschstein, R. L.: Value of neurovirulence tests for attenuated vaccine assessment. International Symposium on Neurovirulence, Munich 1965. Symp. Series Immunobiol. Standard 2:267–268 (Karger, Basel/New York 1966); Kirschstein, R. L., Smith, K. O., and Peters, E. A.: Inhibition of adenovirus 12 oncogenicity by adeno-associated virus. Proc. Soc. Exp. Biol. Med. 128:670–673, 1968; Kirschstein, R. L. and Palmer, A. E.: A primate program developed for the testing of biological products. Proceedings of the Second Conference on Experimental Medicine and Surgery in Primates, Medical Primatology 886–894, Ed.—E. I. Goldsmith and J. Moor-Jankowski, Basel S. Karger, 1970; Kirschstein, R. L.: Cyclamates. Human Pathology, 5:498, July 1974; Kirschstein, R. L.: Toxicology and carcinogenicity of preservatives used in the preparation of biological products. International Symposium on Preservatives in Biological Products, San Francisco, 1973, Develop. Biol. Standard, 24:203–212, 1974; Hoel, D. G., Gaylor, D. W., Kirschstein, R. L., Saffiotti, U., and Schneiderman, M. A.: Estimation of risks of irreversible delayed toxicity. J. of Tox. and Environ. Health, 1:133–151, 1975.

Mr. FLOOD. Do you have some people with us you would like us to meet?

Dr. KIRSCHSTEIN. Yes.

To my right is Dr. Leo von Euler, the Deputy Director. To my left, Mr. Gordon Klovdahl, Executive Officer; Mrs. Emma Louise Akers, Financial Management Officer; and Dr. Arthur Heming, Associate Director for Program Activities.

Mr. FLOOD. I see we have your statement, Doctor, which we will place in the record at this point.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health

STATEMENT BY DIRECTOR, NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES ON "NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES"

Mr. Chairman, members of the committee, I appear before you for the third consecutive time and am privileged to do so.

The National Institute of General Medical Sciences is often called the basic science institute of the NIH because of its longstanding mission to support

research in sciences basic to medicine. Approximately four-fifths of the Institute's resources each year serve to support such research in order to elaborate and increase the understanding of human biology in health and disease and with the expectation of generating new concepts and tools which are broadly applicable to clinical research. Most disease, unfortunately, is not susceptible to a magic bullet or wonder drug approach; but, rather, effective treatment must depend on a fundamental understanding of molecular, cellular, genetic, or environmental factors.

GENETICS PROGRAM

Mr. Chairman, as part of its responsibilities in regard to genetics research, the NIGMS has established an Office of Recombinant DNA Activities. This office is responsible for surveying the research in recombinant DNA by all NIH-supported scientists to assure that it is done under the guidelines issued in June 1976 and that the proper containment is used. The NIH assigned this responsibility to the NIGMS because of its major role in support of such research.

The Institute's program in genetics supports both basic and clinical studies and these are tightly interwoven in many of the projects supported.

For example, Dr. Frank Ruddle of Yale University has been using individual human chromosomes or even fragments of chromosomes in an attempt to map human genes, in other words, to determine on which chromosome and at which location there are genes which are specific for certain characteristics. Dr. Ruddle has shown that, when cells which are genetically deficient in a certain enzyme are grown in cell culture in the laboratory and are mixed with isolated human chromosomes, a specific piece of one of the chromosomes is taken up by some of the deficient cells. If this piece contains the gene required to make the enzyme lacking in the deficient cells, it can be shown that these cells now will produce the missing enzyme. This work is of great importance for two reasons. First, by using this technique of mixing cells with isolated individual chromosomes or pieces of them, human genes can be functionally mapped; secondly, the correction of an enzyme deficiency by use of specific genetic fragments may lead to a new approach for treatment of genetic disease.

BIOMEDICAL ENGINEERING PROGRAM

A problem encountered when considering enzyme replacement therapy to correct genetic defects is that enzymes, other than those of human origin, may provoke the body's immunologic defenses and give rise to antibodies that rapidly remove them from circulation. This not only leads to serious immunologic reactions but provides for very limited therapeutic activity. To overcome this problem a grantee of the biomedical engineering program has been developing a biomaterial; namely, polyethylene glycol, which forms flexible strands that can be attached to these "foreign" or nonhuman enzymes prepared for infusion. Polyethylene glycol is related to an antifreeze commonly used in automobile cooling systems. Studies are underway to determine whether this material, in the form of strands, is nontoxic, will elicit less of an immunologic reaction, and will provide for attachment of enzymes which are then no longer identified as "foreign" and thus can be safely infused and allowed to circulate freely in the blood. An NIGMS grantee is working with an enzyme obtained from a fungus which he has bound to these strands of polyethylene glycol and injected into mice deficient in the same enzyme to determine whether the blood enzyme levels of the mice would be raised for extended periods of time and if the process is safe even when injections are repeated many times. It is known that enzyme not bound to and chemically modified by polyethylene glycol cannot be injected more than two to three times because of severe immunologic reactions.

Thus, correction of genetically induced deficiencies may be approached in many ways.

PHARMACOLOGY-TOXICOLOGY PROGRAM

The Pharmacology-Toxicology program of the Institute has been concerned with the specific effects of drugs in certain populations and also in relation to other drugs. As this committee suggested last year, efforts to increase research in pediatric pharmacology are underway. To this end, NIGMS in collaboration with the Child Health Institute held a meeting in November of last year at which current studies in pediatric pharmacology were summarized and areas

requiring further study were delineated. This Institute is now evaluating proposed research in which the effectiveness in children of a variety of important drugs will be studied.

As you know, along with its beneficial effects, penicillin often causes allergic reactions which are responsible for 70–80 percent of all such reactions to drugs. Fatal allergic reactions to penicillin have been thought to be due solely to respiratory distress. However, an NIGMS grantee, Dr. Roberto Levi, has shown that allergic reactions to penicillin may fatally affect the cardiovascular system by release of histamine by the heart tissue. Patients who are being treated with digitalis, a drug used in about 4 million people in the United States to control heart failure, may develop severe cardiac dysfunction as a result of allergic reactions to penicillin. Using the guinea pig as a model, this investigator has shown that, in an allergic response to penicillin, the heart beats very rapidly and arrhythmically and the blood pumping action becomes less efficient. This adverse effect is markedly enhanced by very small doses of digitalis. Studies are now underway to develop a method to pharmacologically inhibit this allergic impairment of cardiac function, in order that patients on digitalis whose hearts have already been in failure and who have little cardiac reserve may be protected from infections by the use of penicillin.

CLINICAL AND PHYSIOLOGICAL SCIENCES PROGRAM

The NIGMS, as we have reported to you on previous occasions, actively supports research in trauma and burns. In January 1977, the Institute held a workshop in this area in order to evaluate the status of the research activities to find the most effective means of furthering them and to determine what areas of endeavor are being neglected and what studies should be encouraged. The report of this meeting will be made available to you as soon as it is published. At this meeting, several speakers reiterated that, although a great deal of progress had been made in the treatment of severe burns, the problem of infection in burn patients remains a very serious one and, indeed, because the causative bacteria of the infections are so often found not to be susceptible to antibiotics, this is still a major reason for the high mortality rate in burned patients. Furthermore, although, as I reported to you last year, the prevention of weight loss in severely burned patients is possible by the use of both intravenous feeding and delivery of nutrients into the stomach by nasogastric tube, there is still a need for research in regard to the amounts of protein, carbohydrate, or fat needed by such patients to provide appropriate energy metabolism.

Studies in both these areas are currently being supported by the NIGMS Trauma and Burn Program and we are actively seeking to support further research in this vital area. It should be noted that in 1976 the American College of Surgeons produced a manual which was distributed to practicing physicians and was on the early care of the injured patient, including a chapter on the initial management of burns. This manual was based extensively on the studies of Dr. Charles Baxter, an NIGMS grantee.

CELLULAR AND MOLECULAR BASIS OF DISEASE PROGRAM

The research of many surgeons and other clinicians has been made possible because of basic studies of cellular and molecular biology and chemistry supported by, among others, the Cellular and Molecular Basis of Disease program. The research sponsored by this program is very broad as is illustrated in the following examples:

Although sugars have been studied for many years, biochemists have only recently turned their attention to the way in which biological processes, such as sugar production, are regulated. One very important question has been how lactose, the major nutrient sugar of both human and animal milk, is synthesized. Lactose is only formed in the mammary glands of females following childbirth. It turns out that two proteins are required for the synthesis of lactose and the formation of these is controlled by hormone levels. During pregnancy, only one of these two proteins is synthesized. After the birth occurs, the changes in hormone levels allow the synthesis of the second protein as well. Dr. Keith Brew, an NIGMS grantee who has been studying this process, has recently shown that certain specific minerals, magnesium and calcium, are required for these two

proteins to operate efficiently in the synthesis of lactose. If the levels of both of these minerals are not high enough in the mammary gland, lactose will not be efficiently produced. These studies, showing the interaction of hormonal and nutritional factors in forming this important ingredient of milk, could be very significant in correcting abnormalities in milk production in both humans and milk-producing animals.

The NIGMS Cellular and Molecular Basis of Disease Program supports many of the Nation's outstanding scientists. An example is the work of Dr. William N. Lipscomb of Harvard University, this year's winner of the Nobel Prize in chemistry, supported under the aegis of this program of the NIGMS. The Nobel Award was made to Dr. Lipscomb for studies of molecules containing the chemical element, boron. This research has led to a deeper understanding of the nature of the chemical bond. Although this work had no obvious relationship to biomedical science, it has led other scientists and clinicians to use compounds containing boron for radiation treatment of brain tumors.

Dr. Lipscomb has recently become engaged in chemical and structural studies of an enzyme which regulates the bacterium, Escherichia coli. Enzymes of the type under investigation by Dr. Lipscomb are known to control the metabolism of living organisms from bacteria to man. However, how this very complex enzyme functions is almost completely unknown. In attacking this problem, Dr. Lipscomb is attempting to determine the detailed structure of this enzyme, using the same techniques which he applied so successfully to analyzing the structure of the boron compounds. The major approach to be used is the technique of X-ray crystallography, a method which allows the scientists to construct a three-dimensional model of the molecule. The most famous applications of this technique to date has been the determination of the structure of the genetic material, DNA, which revolutionized the field of genetics and led directly to so many of the studies currently being performed with the support of NIGMS. At the moment, any such direct applicability of enzyme crystallography being performed by Dr. Lipscomb has not yet developed; but the basic information obtained is essential even when not clearly and directly applicable, since, as in the above cited situations, application frequently arises several years after the initial studies. Knowledge development in basic science is indispensable to future progress.

It is important to stress that Dr. Lipscomb, like most other fine basic scientists, is also a teacher, and his laboratory has been a training ground for some of the Nation's most promising young chemists and biochemists. As the committee knows, the NIGMS has supported a program of research training of young, highly qualified scientists for many years and continues such support in the belief that quality training will produce fine scientists for tomorrow who will carry on the outstanding work of persons such as Dr. Lipscomb.

MINORITY ACCESS TO RESEARCH CAREERS PROGRAM

In an effort to provide biomedical research training opportunities for all, the NIGMS has established a sixth program, the Minority Access to Research Careers Program (MARC). This program supports research training for faculty members coming from institutions with a large number of minority students and also supports visiting scientists from majority schools who help minority schools to establish or improve their ersearch and research training programs. For a number of years, NIGMS has been attempting to establish a pregraduate training program for the most promising students at minority institutions in order to give them the background in biomedical science and research that would enable them to compete successfully for positions as graduate students at the outstanding academic institutions of this Nation. The NIGMS is currently attempting to begin such an Undergraduate Honors Program in the MARC Program as encouraged by the Congress.

Mr. Chairman, in order to support all the programs described above, the budget request for the National Institute of General Medical Sciences for 1978 is $219,896,000. I shall be pleased to try to answer any questions and supply additional information desired for the record.

Mr. FLOOD. We have some questions for you, Doctor.

We notice in your budget proposal for this year that you propose an increase of $14,896,000 over the 1977 budget. How do you plan to use this increase?

Dr. KIRSCHSTEIN. The largest proportion of this increase, Mr. Chairman, will be for research activities, both the investigator initiated research grants and some increase in activities in our special programs, particularly in burn research activities.

SPECIAL RESEARCH CENTERS

Mr. FLOOD. Now even though you have this overall increase in the budget there are some program areas that are reduced.

For example, under your special grants program you have reduced the former pharmacology-toxicology grants for research centers.

Mr. FLOOD. Why have you cut these centers?

We thought you had a great deal of work to do in this area.

Dr. KIRSCHSTEIN. Yes, Mr. Chairman.

These are among our oldest centers. They have been in existence for a considerable period of time. Many of them, upon review, have been found to perhaps not have activities that are quite as meritorious as they were to begin with. Some of these centers will no longer be in existence and we will substitute for them newer centers and these will start at funding levels that are somewhat lower and will perhaps gradually increase.

Mr. FLOOD. But you are not affecting the area of pharmacology-toxicology research?

Dr. KIRSCHSTEIN. No, sir.

Mr. FLOOD. Another area you cut is the genetic research centers. Now I am sure you realize that there is a great deal of pressure on everybody and from our constituents to support genetic research. That being so, why this reduction?

Dr. KIRSCHSTEIN. We, too, feel that our Genetics Research Program is essential, Mr. Chairman. Indeed it is one of our emphasis areas. However, again the same situation holds. We have had 10 Genetic Research Centers in existence for about five years now. Several of these have come in with renewal applications which were found to be somewhat less meritorious and will be no longer funded.

But we will be planning new centers that will start again at somewhat lower levels.

Mr. FLOOD. But would that affect genetic research?

Dr. KIRSCHSTEIN. No, sir. The genetics area is one that we emphasize considerably and we will be putting a great deal of effort into it.

TRAINING PROGRAMS

Mr. FLOOD. The largest reduction is in the training programs. How do you see that reduction and what is the impact there?

Dr. KIRSCHSTEIN. It is a very significant impact. As you know, the National Institute of General Medical Sciences is the Institute that has had the largest share of the research training programs of the entire NIH. In the past and up to this year we have supported one-third of all the research training at NIH. Of the research training for predoctoral trainees, we support two-thirds. Most of this has been through support of institutional fellowship awards.

Dr. KIRSCHSTEIN. Yes, sir. Since it has been stated that there will no longer be institutional awards, this has caused the NIGMS program to be substantially reduced.

Mr. FLOOD. Under the training budget you have, where will the emphasis be, on predoctoral training or postdoctoral training?

Dr. KIRSCHSTEIN. In the 1978 budget, Mr. Chairman, based on an administration decision, it will be on postdoctoral training.

RECOMBINANT DNA RESEARCH

Mr. FLOOD. We talked about this last week some. How much do you spend to support DNA recombinant research?

Dr. KIRSCHSTEIN. The National Institute of General Medical Sciences spending $2,600,000 on DNA recombinant research.

Mr. FLOOD. Have your grantees been able to comply with the containment guidelines?

Dr. KIRSCHSTEIN. In general, yes. There may be some requirement that there be construction and renovation of facilities. There were some funds specifically allocated for that purpose. As you know, sir, the National Institutes of Health has set up an Office of Recombinant DNA activities which has been assigned to our Institute to administer.

Mr. FLOOD. This has almost overnight become highly controversial nationwide so there should be no doubt insofar as the regulations and guidelines, out of an abundance of caution.

Dr. KIRSCHSTEIN. Most of our grantees have filed the memoranda of understanding and agreement that are required and are following our guidelines.

Mr. FLOOD. Why not all of them?

Dr. KIRSCHSTEIN. Most of them are in. There have been 84 memoranda of understanding and agreement and Institutional Biohazards Committees have been set up. This is just about all of them.

Mr. FLOOD. You are aware of how delicate this situation is?

Dr. KIRSCHSTEIN. Yes, indeed, sir.

Mr. FLOOD. Is it correct that you are currently considering setting up a central repository to hold the host cells in this DNA research?

Dr. KIRSCHSTEIN. The Institute, at the suggestion of the Recombinant DNA Advisory Committee, requested of the scientific community by publication of a letter in the journal, Science, back in early December, advice as to whether it would be scientifically reasonable and feasible to develop a bank of fragments of DNA recombinant materials that could be used to provide grantees with these materials.

Mr. FLOOD. Are you setting up a center repository?

Dr. KIRSCHSTEIN. We are thinking of doing so, yes, sir.

Mr. FLOOD. Is there any target date or time or place?

Dr. KIRSCHSTEIN. If it is decided to establish such a bank, it will probably be in the next fiscal year, in 1978.

Mr. FLOOD. Where?

Dr. KIRSCHSTEIN. We have not completely decided on this. If the NIH sets up a national facility, a P–4 facility, at the Frederick Cancer Center for work with the most hazardous materials, this might be a logical place for the central repository to be.

Mr. FLOOD. Can you tell us what is involved in setting up all of this reporting and what this is going to cost? Who is going to maintain this operation and basically why is it necessary?

Dr. KIRSCHSTEIN. In order to assure that the guidelines are being met and that the reporting is done properly, the NIH established an Office of Recombinant DNA activities in the National Institute of General Medical Sciences. The Director of that Office reports directly to me. He is in the Office of the Director of the Institute.

The activities have cost us something in the order of $100,000 thus far in this year. This includes publishing the guidelines, mailing them out, answering the inquiries. The Director of the Office has to travel to the various institutions to see them and answer questions concerning the guidelines and keep in contact with the international community.

Mr. FLOOD. Who is going to maintain it?

Dr. KIRSCHSTEIN. The National Institute of General Medical Sciences is maintaining these activities.

Mr. FLOOD. I repeat for the purpose of emphasis now, why is it necessary?

Dr. KIRSCHSTEIN. It is necessary to do this so that there is appropriate monitoring and assurance that the guidelines are being complied with and that there is evidence that the scientific community will comply appropriately. We have every expectation that there will be compliance and thus far the scientific community has complied with the guidelines.

Dr. FREDRICKSON. Mr. Chairman, it is the view of the interagency committee, about which I spoke earlier in my testimony, that the important elements in the regulation of this activity include registration so that we know where the use and production of recombinant DNA molecules is taking place in the United States.

At the present time, NIH, in coordination with the rest of the Federal agencies that are funding this activity, have already come to a preliminary agreement as to a common pool of information relative to all Federal support.

Now eventually—and before very long, I think—if legislation is passed relative to regulation, there will be a full registry of all activities including the private as well as the Federal sector.

For the present NIH, is developing that capability. If and when we have a regulatory agency that works as a companion to NIH in standard setting, then we may move the registry to that organization. But we are taking the initiative now to see that it is created.

Mr. FLOOD. You obviously are on top of the thing.

Dr. KIRSCHSTEIN. I think so, sir.

GENETIC DISEASES

Mr. FLOOD. What advances have been made in the prevention and control of genetic disease?

Dr. KIRSCHSTEIN. Mr. Chairman, we now have the ability to diagnose a large number of genetic diseases prenatally by many techniques, the major one of which is the performance of a procedure known as amniocentesis in which fluid and cells representing the fetus are removed during pregnancy and can be studied.

Based on that, there would be ability to diagnose whether or not the child that is to be born is indeed suffering from a genetic disease. A great deal of this activity has been possible based on the basic re-

search in genetics which has been performed by the NIGMS grantees both in individual grants and also through the genetics research centers which combine basic and clinical research activities.

Mr. FLOOD. Remember last year you mentioned the studies for genetice research laboratory, very important in the undertaking of and the ability to detect cancers and cancer-causing chemicals. Are you finding any new links between the genetic factors and possible predisposition to certain types and kinds of cancer?

Dr. KIRSCHSTEIN. Yes, sir. These are activities that we would like to undertake in genetics now. Whereas up to now we have been concentrating primarily on genetic diseases that are caused by single gene defects, it seems that this is an appropriate time to begin studies on polygenic diseases, diseases that may indeed be caused by more than one genetic defect.

Many of the so-called chronic diseases and some cancers seem to have some relationship to a multifactorial genetic disposition. Such diseases as diabetes, atherosclerosis and some other forms of heart disease fall into this category. We will be making new initiatives in this regard.

PEDIATRIC PHARMACOLOGY

Mr. FLOOD. In the 1977 appropriation bill funds were made available to develop a program of pediatric pharmacology. What does that involve?

Dr. KIRSCHSTEIN. We have just gotten underway with this program. In order to be assured that we knew what areas to undertake, we sponsored a workshop in pediatric pharmacology last year along with the Institute of Child Health and Human Development in which pharmacologists came to discuss with us areas that needed investigation in the realm of pediatric pharmacology.

We are currently considering several awards in areas that we will work in, in pediatric pharmacology.

Mr. FLOOD. How much have you budgeted in 1978 for pediatric pharmacology?

Dr. KIRSCHSTEIN. About $1 million.

Mr. FLOOD. Is your Institute involved in the research on the amniocentesis technique?

Dr. KIRSCHSTEIN. We were involved originally in some of the basic research that led to this. This technique has now been fairly well established, sir. As such then, the activities that go on in regard to amniocentesis are undertaken by other institutes and other agencies to perform the services that are needed.

Mr. FLOOD. How widely used is the technique? Is it a highly accurate and safe procedure?

Dr. KIRSCHSTEIN. There was a report that came out, I believe, last fall that Dr. Cooper presented as the Assistant Secretary of Health which indicated that the procedure was very safe and quite effective. There was a recommendation that there be activities undertaken in this regard throughout the country.

Mr. FLOOD. We have heard that it is now possible to determine the presence of Cooley's anemia prenatally through a process known as placentocentesis. Is this process similiar?

Dr. KIRSCHSTEIN. I believe it may be a variant of it.

Mr. FLOOD. It is a similar technique?

Dr. KIRSCHSTEIN. I believe it may be a similar technique. The National Institute of General Medical Sciences supports basic studies in genetics. Once these studies relate more directly to diseases of blood or childhood diseases, these activities are supported by other institutes. Cooley's anemia is supported by the National Heart, Lung and Blood Institute.

Mr. FLOOD. Placentocentesis is something in itself?

Dr. FREDRICKSON. For that test a sample of fetal blood is required. That is a special problem in amniocentesis, rather than just getting the fluid.

Mr. FLOOD. But as far as Cooley's anemia, it fits in?

Dr. FREDRICKSON. It fits in. It is an important question and still a matter of research.

BURN RESEARCH

Mr. FLOOD. You reported last year that one of your grantees was developing an artificial skin to be used in treating the burn patients. What is the status of that research?

Dr. KIRSCHSTEIN. That research has gone on quite well, Mr. Chairman. The work is being done in Boston by Dr. John Burke at the Massachusetts General Hospital in conjunction with biomedical engineers at the Massachusetts Institute of Technology. They have recently shown that, as opposed to using materials from pigskin, it is better to use fibers from bovine skin. This has been tried in a number of burned animals and has been shown to be very successful.

As I understand it, they have now been able to show that, whereas this material could cover the surface and remain in place previously for 6 to 8 weks, this can be extended for about 3 months after which it is possible for the animal's own skin to fill in the burned area.

There are plans to start testing this in man very soon.

Mr. FLOOD. We understand that infection is a very serious problem in a burn patient.

Dr. KIRSCHSTEIN. That is correct.

Mr. FLOOD. Are you making any progress in controlling that particular problem?

Dr. KIRSCHSTEIN. Yes, sir.

One of the ways in which one can prevent infection is to place seriously burned patients in a sterile environment, in a "sterile island". This has indeed been successful in preventing infection.

The other problem that arises in regard to infection in patients with burns is antibiotic resistance. Many of the organisms that cause infection are resistant to the antibiotics which is why it is so important to prevent infection.

Mr. FLOOD. Are there any other promising developments in burn research?

Dr. KIRSCHSTEIN. The entire field of burn research has been moving slowly in attempting to save the lives of severely burned patients. The situation is such that a whole series of activities have to occur at once in order to do so.

The patient's nutrition must be maintained, infection must be prevented or treated. The rehabilitation and grafting of skin, first with perhaps an artificial skin or, as today, mostly with skin from a close relative or the patient's own skin from the area that has not been burned, must occur. Then rehabilitation must occur.

The problem is a very difficult one. It takes many, many months for severely burned patients to recover.

TRAUMA RESEARCH

Mr. FLOOD. What other kinds of trauma research are you supporting?

Dr. KIRSCHSTEIN. We support research in general trauma, trauma due to automobile accidents or severe injuries. The problems of such patients are similar to those of burned patients to some extent. There is very often multiple organ failure in these patients such that a severe injury will lead to kidney failure, liver failure and severe circulatory disturbances.

All of these have to be treated at one time in order for the patients to survive.

Mr. FLOOD. Mr. Natcher?

Mr. NATCHER. Doctor, as you point out in your statement, the National Institute of General Medical Sciences is often called the basic science institute of NIH because of its longstanding mission to support research in sciences basic to medicine.

You are requesting $219,896,000 for fiscal 1978.

Dr. KIRSCHSTEIN. That is correct.

CELLULAR AND MOLECULAR BASIS OF DISEASE

Mr. NATCHER. Doctor, if I asked you to come down to Kentucky and make a speech and discuss three of your major achievements since you were here last year other than the matters in your statement, what would you talk about?

Dr. KIRSCHSTEIN. Mr. Natcher, I would talk about the activities of our Institute in our basic programs such as our Cellular Molecular Basis of Disease Program where studies of the structure compared to the function of large molecules such as proteins and proteins combined with fats and carbohydrates such as glycoproteins and lipoproteins are under study in an attempt to understand the basic mechanisms of the action of these materials in the cell. This has very widespread effects on the study of specific diseases.

Once one understands the molecules that normally constitute a cell and their structure and how that relates to the functions of the cell, one can move from this to understand abnormal cells such as cancer cells or cells that have genetic defects, cells that have changed surface membranes and so forth.

That is one of the major achievements of our Institute, to begin to understand the structure and functional relationship of these very large molecules in the cells.

In the area of genetics, we have continued to support basic genetics in attempts to determine what are the specific defects. As we said last

year, for example, the defect in patients who have a familial disease known as hypercholesterolemia is being elucidated. This is a marked increase in the level of cholesterol in the blood that leads to a predisposition for atherosclerosis which then could lead to early coronary artery disease.

Thirdly, in our pharmacology program, there have been studies going on concerning the relationship of substances which will induce a material known as interferon which is an antiviral substance and their effect on the metabolism of drugs.

An individual or an animal that is infected by a virus and begins to produce this antiviral substance, if given a drug, may show increased toxicity to that drug. This needs to be studied further.

CENTRAL REPOSITORY

Mr. NATCHER. Doctor, the chairman asked you about the establishment of a central repository to hold host cells used in recombinant DNA research. Why is it necessary to set up such a repository?

Dr. KIRSCHSTEIN. Mr. Natcher, in order to be able to have investigators do the research they feel is necessary in the recombinant DNA area and yet keep the hazards to a minimum, it may be deemed reasonable to set up such a central repository such that only in one location where all the precautions can be taken and where there is a facility known as a P–4 facility, for example, where there is total containment; in only that one location would this material be handled in the process of the recombination, the splicing. Then these pieces could be stored and sent relatively safely to investigators who could work on them using less containment facilities.

It is a method of increasing the safety of the activity.

Mr. NATCHER. Doctor, what would it cost to maintain this repository?

Dr. KIRSCHSTEIN. We have not totally determined this as yet, but we believe that probably something in the order of half a million dollars a year.

Mr. NATCHER. Would this involve the transporting of different types of DNA material from one part of the country to another?

Dr. KIRSCHSTEIN. There would eventually be transportation of the material from the repository to investigators who need the material. But it would be transport of material which is inactive unless it is placed within an organism. It would be material that would be safe to transport because if there is any hazard, the hazardous activities would have been performed at the original site of the repository.

Dr. FREDRICKSON. I think it might be safe to say, Mr. Natcher, that the danger of transporting such materials is expected to be far less than materials that are now transported across State lines under very strict codes required by the Hazardous Materials Transportation Act and other similar regulatory statutes. We are already transmitting, across the country and around the world, viruses, bacteria, and other materials which are certainly far more hazardous than these DNA materials.

There already exist excellent regulatory agencies and statutes for maintaining great care in this form of transportation and they will all be abided by.

Mr. NATCHER. Thank you, Mr. Chairman.

Mr. FLOOD. Doctor, in your justification you state that one of the goals of the anesthesiology centers is to understand the basic mechanism of pain. What kind of research are you supporting in that area?

Dr. KIRSCHSTEIN. Yes, sir, this is an area that has really begun to come to fruition very recently, Mr. Chairman. There is a grantee of ours who has been a grantee for a number of years, Dr. C. H. Li at the University of California in San Francisco, who has been working on materials, proteins, he has isolated from the brain. For many, many years some of these materials did not seem to have any specific function. Recently it has been shown that one of these materials is related to, and may, indeed, be a precursor, although this is not quite known as yet, to some indigenous materials in the brain which are similar to the opiates. These are called endorphins.

These materials seem to act, as do the opiates, in reducing pain. So there now seems to be a mechanism which under certain circumstances, allows release within the brain, of materials which actually are antagonists of pain and will prevent or decrease pain.

Dr. Li started all this work by isolating what seems probably to be a precursor of these materials.

ACUPUNCTURE RESEARCH

Mr. FLOOD. Do your anesthesiology centers support acupuncture research?

Dr. KIRSCHSTEIN. Yes, sir, this whole story is coming together now. We have been supporting some acupuncture research for many years. There are currently five such projects. For some time, there was some discouragement about this area because it did not seem to be leading to any goal. Very recently it seems likely that these materials I was just talking about, the endorphins, do seem to play a part in the relief of pain or in anesthesia caused by acupuncture.

There seems to be evidence that if, the points that one talks about as being acupuncture points, are stimulated, there is release in the brain of these endorphins which, indeed, then decrease pain.

Mr. FLOOD. Do you view acupuncture as an alternative to anesthetic drugs, some of which have adverse side effects?

Dr. KIRSCHSTEIN. I don't think we can go that far yet, but I think we can perhaps understand the physiologic basis of what acupuncture might have been doing all along. But there is a long way to go before one can say that this would be a method that one could substitute for anything else.

BIOMEDICAL ENGINEERING

Mr. FLOOD. I believe your biomedical engineering program has been developing a material called bioglass to be used in replacement of joints such as hip joints. What is the status of that project?

Dr. KIRSCHSTEIN. The project has been progressing well. There has been considerable further study of this material in the use of hip joints in animals, primarily in sheep and dogs. One of the problems is that evaluation of artificial hip joints in four-legged animals is rather different than evaluating them in man whose weight bearing is on two legs.

So there are attempts to make biomechanical models which will give an indication of whether or not it is possible for an artificial hip joint such as this to continue to be effective.

Now as you know, artificial hip joints are used quite extensively in man now. The problem is that there is considerable wear and tear of the artificial material and very often these hip joints need to be replaced by new artificial joints.

Mr. FLOOD. If this material is found to be suitable for the replacement of joints, is it going to be very, very expensive or are you making efforts to keep down the cost of this material?

Dr. KIRSCHSTEIN. I think there will be efforts made to keep down the cost. It will clearly be more expensive in the beginning for the prototype joints, but presumably, if this proves satisfactory, one could develop methods for reducing the cost. That is something that would be looked into.

Mr. FLOOD. Your budget for the Biomedical Engineering Program is close to $17 million. What are some of the other projects you are supporting which appear to have some kind of promise for the future?

Dr. KIRSCHSTEIN. There are considerable efforts in ultrasound and as a noninvasive technique as a method for diagnosis of various conditions. Previously the use of ultrasound has been such that one could look at the body as a whole. There are efforts, now particularly by Dr. Meindl at Stanford University in an attempt to be able to make specific determinations as to what tissues are involved in whatever abnormalities are noted by using ultrasonic techniques.

So there is an effort in tissue ultrasound work.

Mr. FLOOD. How many individuals have received support under the so-called MARC program since fiscal 1975? I mean Minority Access to Research Careers.

Dr. KIRSCHSTEIN. There have been 122 individuals supported since 1975 by the MARC Program.

Mr. FLOOD. Is there a great deal of interest?

Dr. KIRSCHSTEIN. Yes, a great deal.

Mr. FLOOD. How many applications did you receive in 1977 and how many were approved?

Dr. KIRSCHSTEIN. The approval rate is quite high. To date we have received 29 MARC Faculty Fellowships Applications, of which 24 were approved and 18 funded. For the May Council we have 15 applications and its is expected approximately 12 to 14 of these will be approved and funded.

In addition, the Institute is planning to implement a MARC Honors Undergraduate Research Training Program which is designed to support highly selected undergraduate honor students who subsequently plan to seek enrollment in the Nation's biomedical graduate schools as candidates for the Ph. D. degree. Initially this program will provide a small number, five to seven, of institutional fellowship awards to a limited number of fellows.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. CONTE

BASIC SCIENCE

Mr. CONTE. Dr. Kirschstein, in your opening remarks, you hinted at something that has been of major concern to a number of people involved in our national policy on biomedical research, and that is the fact that most disease is not susceptable to a magic bullet or wonder drug approach. In your professional judgment, is adequate support being given by the Federal Government to basic science, as opposed to applied or targeted research?

ANSWER. An ideal proportion of basic to applied research is difficult to derive from anything other than impressions. In my professional judgment, it is a good long-range investment to fund about 60 percent of approved research grant applications in basic research. Last year's budget for National Institute of General Medical Sciences allowed only 25 percent to be funded, while the requested budget would fund 50 percent, somewhat short of the desirable level of support.

RECOMBINANT DNA

Mr. CONTE. How much research on recombinant DNA is currently going on? How many of those projects involving recombinant DNA are supported by the National Institute of General Medical Sciences? Would you tell me about some of those projects?

ANSWER. The National Institutes of Health is supporting research projects worth $18,319,000 using recombinant DNA techniques. The NIGMS supports about 75 research projects totaling $2,677,000.

Recombinant DNA techniques enable scientists to isolate a specific piece of DNA, representing the information in a gene, and splice in onto a simple DNA structure, a plasmid. The latter can be propagated in bacteria, reisolated, and the original piece of DNA excised, now in greatly increased amounts. In other words, a gene, representing perhaps one-millionth of the total DNA of an organism, can be amplified about 1 million times and thus studied in pure form. This makes it easier to study both the biology, its function, and the chemistry structure and composition of a gene. This technique has made available pure materials, most of which could not be obtained at all in the past. One or two genes had been laboriously synthesized before in the laboratory after many man-years of skilled effort.

In essence, the technique bridges the work of the chemist, the molecular biologist, and the morphologist, all of whom have been using different techniques to study how genes work. For the first time, the chemistry, the mode of action, and the location of the same bit of DNA in an organism can be studied at different levels, and with different approaches.

Mr. CONTE. Is recombinant DNA research being supported by any of the other National Institutes? Can you tell me generally what sorts of containment procedures and safeguards are used in this type of research?

ANSWER. Yes, recombinant DNA research is being supported by other Institutes, particularly NCI and NIAID. The containment procedures and safeguards are matched to the degree of perceived hazard according to the NIH guidelines. Thus, recombination of DNA from the same bacterial species in the test tube, an event known to occur in nature, would require less stringent safeguards than recombination of DNA from different species. Experiments utilizing human DNA require the most stringent safeguards. Certain experiments, for example, those using known microbiologic pathogens, are prohibited.

PEDIATRIC PHARMACOLOGY

Mr. CONTE. How much are you allocating for pediatric pharmacology this year? What are some of the areas which were identified as requiring further study at your November meeting?

ANSWER. We have not allocated a specific amount this year to pediatric pharmacology because so few good research projects are proposed in the field. We are making determined efforts to encourage increased numbers of good investigators to enter this field, and fully intend to support all projects of high scientific merit. We anticipate that during fiscal year 1978 the funds required to support these programs will be about $1 million.

The participants in the November 1977 meeting identified the following areas in pediatric pharmacology for emphasis; the effect of one drug on the efficacy or toxicity of another; means for calculating optimum drug dosage; effect of chronic drug administration on physical and mental development; analytic methodology; and good animal models for pediatric conditions.

CELLULAR AND MOLECULAR BASIS OF DISEASE

Mr. CONTE. In your Cellular and Molecular Basis of Disease Program, do you engage in any joint funding of projects with other Institutes which may also support basic research? How much cooperation do you receive from the other Institutes, particularly some of the large ones, in this area?

ANSWER. The NIGMS does not support research projects through joint funding because we have found it to be administratively cumbersome. However, 15–20 percent of research grant applications may be assigned simultaneously to two Institutes for possible funding with that Institute designated as primary whose mission most closely corresponds to the thrust of the research proposal. If that Institute is unable to fund a meritorious application, the other tries to. There is close communication and cooperation among NIGMS and such other Institutes as the NCI, NHLBI, NIAMDD, and NINCDS, in this regard.

CLINICAL RESEARCH

Mr. CONTE. Your justification mentioned that the Institute encourages clinical research on major medical problems that are not in the purview of the categorical institutes—problems such as anesthesiology. Can you give me examples of other areas in which NIGMS has picked up medical research problems which would otherwise have fallen through the cracks?

ANSWER. Clinical research areas of a similar kind are research on trauma and burns and clinical pharmacology.

TRAINING PROGRAMS

Mr. CONTE. Your Institute has traditionally had the leading role in support of predoctoral research training. What has been the level of support for predoctoral research training over the past few years by the Federal Government as a whole, and specifically by the Institute of General Medical Sciences? What are the requested levels for predoctoral research training support for 1978 by the entire Federal Government and by your Institute?

ANSWER. As you know, a congressionally mandated manpower review has been undertaken by the National Academy of Sciences, its latest annual report having been issued in May 1976. The long-range task of the review is to obtain more accurate figures on research manpower expenditures and future needs in the various biomedical science fields. To date, the available overall information has been approximate and incomplete, but probably good enough to show trends and magnitude.

About 90 percent of Federal predoctoral training support in the health-relevant biological sciences is funded by three agencies: NIH, ADAMHA, and NSF. This support has decreased from about $61 million for 7,600 individuals in fiscal year 1974 to $55 million for 5,400 individuals projected for fiscal year 1978. The corresponding figures for NIGMS are $31 million for 3,800 individuals in fiscal year 1974, to $30 million for 3,200 individuals in fiscal year 1978. The 1978 figures show an increased cost per trainee, which is due to both increased stipends and tuition costs.

Mr. CONTE. Could you give me a brief explanation of the importance of support for these predoctoral training programs?

ANSWER. The main purpose of the predoctoral training programs is to strengthen and improve the quality of the training that institutions can offer. The awards remove the temptation for the trainees to take undesirable training shortcuts, by providing them with stipend and tuition support, 75 percent of the overall award. In addition, these awards include support for necessary equipment, supplies, seminar speakers, and personnel. In our opinion, these predoctoral grants insure that the performers of research 10 years from now will have been given the best possible training for that task.

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Mr. CONTE. I notice that you are requesting a significant decrease in your institutional training assistance programs. Would you explain the reason for that decrease? How much money did you request of OMB for institutional training assistance?

ANSWER. It was decided by the administration not to request funds for new institutional National Research Service Awards. We had originally requested $4.461 million for the funding of institutional training grants.

FUNDING REDUCTIONS

Mr. CONTE. Would you explain why you are proposing reductions in funding for your Pharmacology-Toxicology and your Clinical and Physiological Sciences Programs?

ANSWER. The Pharmacology-Toxicology Program has supported 10 Pharmacology-Toxicology Research Centers for a number of years. These are among the oldest research centers supported by NIGMS. Many of them, upon peer review for scientific and technical merit have been found to be performing some research endeavors that are not quite as meritorious as they were during the earlier award periods. Some of these centers will be phased out and discontinued. We will be reviewing new research center grant applications and will make awards for new centers which will start at lower funding levels but will perhaps gradually increase. Therefore, the funding in the Pharmacology-Toxicology Program in fiscal year 1978 will be at a reduced level.

In regard to the proposed reduction in funding for the clinical and physiological sciences program there has been some difficulty in finding highly meritorious grant applications in the areas of anesthesiology and trauma and burn research. In order to overcome this difficulty, the NIGMS has announced a special grants program in anesthesiology in order to encourage young investigators to enter this field. In addition, as projects which were supported by NIGMS in the area of anesthesiology research become more focused on categorical areas such as pulmonary disease or in the area of trauma research such as head trauma, support, appropriately is provided by the categorical institutes such as NHLBI and NINCDS.

PEDIATRIC PHARMACOLOGY

Mr. CONTE. How do you intend to place new emphasis on pediatric pharmacology while reducing your overall pharmacology program by $180,000? Tell me what areas of research you will be unable to continue because of this budget request.

ANSWER. The new emphasis on pediatric pharmacology is important programmatically, but is not expected to require much money initially. The net decrease in the overall Pharmacology-Toxicology Program is due primarily to the conjunction of a large number of ongoing research centers undergoing competitive review and the fact that not all were successful. In their place we expect to fund a few new research centers, but at a lower level initially. No general research area will be discontinued, and we hope to fund about 50 percent of approval applications.

FUNDING—APPROVED RESEARCH GRANT APPLICATIONS

Mr. CONTE. What portion of your approved grant applications did you fund last year? What portion will you be able to fund with the proposed budget? How much money would be required to maintain the percentage of approved applications which are funded at last year's level?

ANSWER. In fiscal year 1976 we funded 61 percent of our approved competing research grants applications.

The proposed budget will allow us to fund about 50 percent of our competing research grant applications.

To fund the same percentage of competing research grant applications as in fiscal year 1976 an additional $9.5 million would be required.

PAIN

Mr. CONTE. I understand you are supporting research on the basic mechanisms of pain, particularly chronic pain. Have there been any recent developments in this area? Is research being conducted on acupuncture?

ANSWER. The NIGMS is supporting research on the basic mechanisms of pain. There is a very important recent development in this area. One of the NIGMS grantees, Dr. C. H. Li at the University of California has been studying a protein isolated from the brain, which, for many years did not seem to have any specific function. Recently it has been shown that this protein may be related to, or may be a precursor of materials released in the brain upon stimulation. The proteins are known as endorphins which are similar to and act like opiates to reduce or prevent pain.

The NIGMS has been supporting acupuncture research for a number of years and currently supports five such projects. However, for some time, this research did not seem to be very fruitful. There now is some evidence that the endorphins, can be released in the brain when the known acupuncture points are stimulated and this might explain the action of acupuncture in decreasing pain or causing anesthetic effects.

The NIGMS currently funds five Anesthesiology Research Center grants. Several of these centers have studies which concentrate heavily on learning about the basic mechanism and control of pain.

DIRECT OPERATIONS

Mr. CONTE. Does your request for direct operations provide adequate support for the effective review and administration of your grants and contracts? How can you provide adequate supervision and administration of almost 200 more grants without any additional personnel—in fact with the loss of one position?

ANSWER. In my professional judgment, an increase of 17 positions would be required. Six additional positions would be used for the Pharmacology-Toxicology Research Associates Program: three for the Recombinant DNA Program, three positions in the Office of the Director and five positions for Direct Operations.

MR. MICHEL

PROGRAM INCREASES

Mr. MICHEL. Your Institute is budgeted for the largest increase of any of the institutes. What do you attribute that to, and perhaps Dr. Fredrickson may also wish to respond?

ANSWER. The solutions to the basic, underlying defects in many important diseases will come from basic research studies in the fields of cellular and molecular biology, genetics, immunology, and virology. Thus, it is essential to give special support to these areas and, since the National Institute of General Medical Sciences, as the basic science Institute supports activities in all four areas but particularly in cellular and molecular biology and genetics, much of the funds allocated for research in these areas was allocated to NIGMS. This is with the anticipation that support of basic biomedical research today, will, tomorrow, lead to prevention or treatment of diseases of man.

BASIC RESEARCH

Mr. MICHEL. Do you have a formal working arrangement with the other institutes in order that the basic research finding coming from your Institute can be made available to the other more specialty areas?

ANSWER. While we do not have a formal working arrangement with other institutes, in point of fact, the Division of Research Grants which is responsible for the assignment of research grant applications to a particular institute, assigns those grant applications in which the thrust of the research is basic and noncategorical to the National Institute of General Medical Sciences. When, under such grants, the research becomes more focused on a particular disease, support of the work is transferred to one of the categorical institutes. For example, as we reported previously, an NIGMS grantee, Dr. Charles Shaw of the University of Texas, Houston, has been studying the induction of an enzyme, aryl hydrocarbon hydroxylase, by a wide variety of chemicals and drugs. He has found a suggestive association between the fact that such an enzyme can be induced at a high level in certain persons and that these people are susceptible to lung cancer. This was interpreted as being due to increased conversion of potentially carcinogenic substances in cigarette smoke to frank carcinogens. This work of Dr. Shaw and other further studies of this finding are now being supported by the National Cancer Institute. Also reported previously, work by

Dr. Joseph Goldstein in Dallas supported by NIGMS has shown how certain forms of hypercholesterolemia, an increased blood level of cholesterol, are associated with a cell membrane defect that is inherited. These original studies are now focusing, through work in a number of other laboratories, on the relationship of this phenomenon to coronary artery disease and heart attacks supported by the National Heart, Lung, and Blood Institute.

Mr. MICHEL. In the fields covered by your institute, what percentage of the grant applications received this year are being funded, and second, what percentage of the applications approved by the study sections are being funded.

ANSWER. We expect to fund 21 percent of the grant applications received this year; about 25 percent of the applications approved by study sections will be funded.

TRAINING PROGRAMS

Mr. MICHEL. I note that about 90 percent of your training funds go to institutions, rather than individuals. Why is that?

ANSWER. Just as the research supported by the Institute lays the foundation for the research of the other Institutes, predoctoral research training support insures that the scientists who will conduct such research in the future will have received the best possible training. To this end, the National Institute of General Medical Sciences funds two-thirds of the predoctoral training at NIH. In accord with NIH policy and NAS recommendations, this support is limited to institutional awards for several reasons. First, the selection of the best qualified candidates having the strongest motivation to become creative scientists can be accomplished more knowledgeably and reliably by the proposed sponsors and faculty who have first-hand knowledge of the candidates. Second, the cost of review per trainee is lower for an institutional award than for individual awards. Third, the main purpose of NIGMS support of predoctoral training is to strengthen and improve the quality of the training that institutions can offer. The institutional awards are planned with this specific intent. The awards remove the temptation to take undesirable training shortcuts by providing the trainees with stipend and tuition support, 75 percent of the overall award. In addition these awards include support for necessary equipment, supplies, seminar speakers, and personnel, of up to a total of 25 percent of the overall award.

At the post doctoral level of training, the Institute offers both individual and institutional awards. This is a period of specialization and, depending on the size of the training program, individual or institutional awards may be most appropriate. This is also a period when candidates holding the M.D. degree are recruited into special areas with serious shortages of research manpower, such as anesthesiology and trauma and burns.

Mr. MICHEL. What types of training programs are undertaken by the institutions with these funds, and what specifically are the funds used for?

ANSWER. The Institute supports predoctoral, institutional research training programs in the areas of molecular, genetic, or cellular biology and in the pharmacological sciences. Postdoctoral research training of both the institutional and individual type is offered in such areas as clinical pharmacology, anesthesiology, trauma and burns, and medical genetics. Allowable budget items on the institutional awards include stipends, tuition, trainee travel, for example, to scientific meetings, necessary equipment and supplies, consultant fees, seminar speakers, and salaries for faculty and support personnel commensurate with time dedicated to the training program.

Mr. MICHEL. Where do we stand currently as far as total numbers of research scientitsts are concerned versus the need? Has the supply virtually caught up to the need.

ANSWER. As requested by Congress, the NAS is making a continuing study of Personnel Needs and Training for Biomedical and Behavioral Research. Its latest report was issued in May 1976. The supply and demand picture for biomedical scientists varies for the different major categories.

With regard to predoctoral training of Ph. D. candidates, the need that they are intended to meet is 7 to 10 years in the future. Since it is most difficult to anticipate specific needs that far ahead, the National Institute of General Medical Sciences is placing its entire emphasis on broad, interdisciplinary research training that will equip the graduates to enter any of a number of fields, and to later switch fields, if necessary. The NAS recommended that NIH as a whole

reduce the total number of predoctoral trainees in the basic biomedical sciences to 90 percent of the fiscal year 1975 level. This we have done. The emphasis remains on the quality of the research training rather than on the numbers being trained.

With regard to postdoctoral training, the Institute consultants and the NAS have identified certain areas of clinical research training which still suffer marked shortages of research manpower. Unfortunately, these shortages exist because of general recruitment difficulties, and the postdoctoral research training programs are overcoming them only slowly.

CLINICAL TRIALS

Mr. MICHEL. Are you funding any clinical trials, and if so, to what extent and in what areas?

ANSWER. The National Institute of General Medical Sciences does not fund any clinical trials because most of its research is in fundamental sciences with some efforts in clinical investigations related to trauma, burns, and anesthesiology.

RECOMBINANT DNA GUIDELINES

Mr. MICHEL. Are you satisfied that your guidelines pertaining to genetic research are strong enough to prevent any major disasters from occurring if some of this research should get out of hand?

ANSWER. The guidelines pertaining to research utilizing recombinant DNA techniques in studies of genetic characteristics were developed after many months of discussion by scientists, Government officials, and members of the lay public including ethicists, regulators, and legal staff. It is the conclusion of the NIH that adherence to these guidelines will provide the needed assurance to permit this research to be carried out without hazard.

Mr. MICHEL. Do you think these guidelines ought to be applied to private industry?

ANSWER. It is the position of the NIH that the guidelines pertaining to research involving DNA recombinant techniques should be followed by all scientists undertaking such activities, including those in industry. To this end, the NIH has been in close communication with the Pharmaceutical Manufacturers Association and an Interagency Committee has been established to develop collaborative efforts to assure compliance with the guidelines.

Mr. MICHEL. What's your opinion regarding the efforts of some local communities to restrict genetic research that may be conducted within their boundaries?

ANSWER. In my opinion, the NIH guidelines provide adequate protection. However, local community governments have a responsibility to their citizens to assure, to the best of their ability, that they will be protected and it seems reasonable that each such community engage in full discussion of the issues and reach decisions which are appropriate for the particular community and are representative of the needs and wishes of that community. However, in order to assure uniformity throughout the country, Federal regulations based on the NIH guidelines may be needed to supersede local rules.

Mr. MICHEL. Do you think Congress ought to establish any restrictions on such research?

ANSWER. In order to assure that research involving recombinant DNA techniques, conducted by all sectors of the scientific community, is carried out in accordance with the guidelines, new legislation is probably needed. The NIH favors the establishment of legislation for regulation by an appropriate regulatory agency of all such endeavors to comply with guidelines.

RESEARCH PROJECT

Mr. MICHEL. What is the average length of funding for a research project under your Institute?

ANSWER. The average length of funding for a research project in this Institute is 3 years.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Amounts Available for Obligation

	1977	1978
Appropriation	$205,000,000	$219,896,000

National Institute of General Medical Sciences

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	Number	FTE 1/	Amount	Number	FTE 1/	Amount
Research Grants:						
Regular Program:						
Noncompeting	1,548	---	$99,699,000	1,406	---	$94,968,000
Competing	127	---	11,024,000	270	---	24,049,000
New	176	---	9,273,000	379	---	20,872,000
Supplemental	(131)	---	2,300,000	(83)	---	1,500,000
Subtotal, Regular	1,851	---	122,296,000	2,055	---	141,389,000
Special Programs:						
Pharmacology-Toxicology Res. Ctrs.	9	---	5,643,000	9	---	4,700,000
Biomedical Engineering Res. Ctrs.	5	---	2,200,000	5	---	2,200,000
Diagnostic Radiology Res. Ctrs.	2	---	1,200,000	2	---	1,200,000
Anesthesiology Res. Ctrs.	5	---	3,190,000	4	---	3,000,000
Trauma & Burn Res. Ctrs.	12	---	4,650,000	12	---	4,850,000
Genetic Res. Ctrs.	10	---	6,500,000	10	---	6,000,000
Molecular Pathology Res. Ctrs.	1	---	425,000	2	---	1,029,000
Research Career Program	216	---	5,376,000	201	---	5,000,000
Subtotal, Special	260	---	29,184,000	245	---	27,979,000
Total Research Grants	2,111	---	151,480,000	2,300	---	169,368,000
Training Programs:						
Individual:						
Noncompeting	135	135	1,804,000	129	129	1,844,000
Competing	---	---	---	---	---	---
New	79	79	1,150,000	156	156	2,206,000
Supplemental	---	---	---	---	---	---
Subtotal, Indiv.	214	214	2,954,000	285	285	4,050,000
Institutional:						
Noncompeting	311	4,406	39,047,000	250	3,617	35,340,000
Competing	---	---	---	---	---	---
New	20	128	1,850,000	1	8	240,000
Supplemental	---	---	---	---	---	---
Subtotal, Instit.	331	4,534	40,897,000	251	3,625	35,580,000
Total Training Programs	545	4,748	43,851,000	536	3,910	39,630,000
R & D Contracts	13	---	1,500,000	13	---	1,500,000
Intramural Research	---	---	467,000	---	---	487,000
Direct Operations	---	---	6,409,000	---	---	7,562,000
(Standard Level User Charge)	(---)	(---)	(100,000)	(---)	(---)	(123,000)
Program Management	---	---	1,293,000	---	---	1,349,000
TOTAL	2,669	4,748	205,000,000	2,849	3,910	219,896,000

1/ Full time equivalent.

DHEW - National Institutes of Health

Crosswalk - 1977 Column of 1978 Justification

INSTITUTE: National Institute of General Medical Sciences

(Dollars in Thousands)

Program \ Mechanism	Research Grants: Regular Program: Non-Comp.	Research Grants: Regular Program: Comp.	Research Grants: Special Programs: Multi-discip. Centers	Research Grants: Special Programs: Other	Training Programs: Indiv.	Training Programs: Instit.	Res. & Develop. Contracts	Intramural Research	Direct Opers.	Program Mgmt.	Total
1. Cellular & Molecular Basis of Disease...	$36,910	$8,371	$425	$1,773	$670	$20,899	---	---	---	---	$69,048
2. Genetics.....	38,188	7,067	6,500	2,305	1,005	5,722	$409	---	---	---	61,196
3. Pharmacology-Toxicology.....	11,415	2,950	5,643	630	99	5,289	333	---	---	---	26,359
4. Clinical & Physiological Sciences.....	5,706	2,029	7,840	325	231	5,619	---	---	---	---	21,750
5. Biomedical Engineering.....	7,480	2,180	3,400	343	128	2,483	758	---	---	---	16,772
6. Minority Access to Research Careers...	---	---	---	---	821	885	---	---	---	---	1,706
7. Intramural Research..	---	---	---	---	---	---	---	$467	---	---	467
8. Direct Operations....	---	---	---	---	---	---	---	---	$6,409	---	6,409
9. Program Management...	---	---	---	---	---	---	---	---	---	$1,293	1,293
Total Obligations....	99,699	22,597	23,808	5,176	2,954	40,897	1,500	467	6,409	1,293	205,000

DHEW - National Institutes of Health

Crosswalk - 1978 Column of 1978 Justification

INSTITUTE: National Institute of General Medical Sciences

(Dollars in Thousands)

Program (Mechanism)	Research Grants: Regular Program: Non-Comp.	Research Grants: Regular Program: Comp.	Research Grants: Special Programs: Multi-discip. Centers	Research Grants: Special Programs: Other	Training Programs: Indiv.	Training Programs: Instit.	Res. & Develop. Contracts	Intramural Research	Direct Opers.	Program Mgmt.	Total
1. Cellular and Molecular Basis of Disease	$35,347	$19,141	$1,029	$1,596	$921	$17,625	---	---	---	---	$75,659
2. Genetics	35,036	18,729	6,000	2,155	1,198	5,270	$409	---	---	---	68,797
3. Pharmacology-Toxicology	10,702	4,433	4,700	505	280	5,226	333	---	---	---	26,179
4. Clinical and Physiological Sciences	6,279	1,764	7,850	426	370	4,241	---	---	---	---	20,930
5. Biomedical Engineering	7,604	2,354	3,400	318	284	2,093	758	---	---	---	16,811
6. Minority Access to Research Careers	---	---	---	---	997	1,125	---	---	---	---	2,122
7. Intramural Research	---	---	---	---	---	---	---	$487	---	---	487
8. Direct Operations	---	---	---	---	---	---	---	---	$7,562	---	7,562
9. Program Management	---	---	---	---	---	---	---	---	---	$1,349	1,349
Total Obligations	94,968	46,421	22,979	5,000	4,050	35,580	1,500	487	7,562	1,349	219,896

Summary and Explanation of Changes

1977 Estimated obligations	$205,000,000
1978 Estimated obligations	219,896,000
Net change	+14,896,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increase cost	---	$30,000	---	+$30,000
2. FTS rate increase	---	41,000	---	+3,000
3. Federal Employees' Compensation Fund rate increase	---	7,000	---	+7,000
4. Payment for centrally furnished services	---	2,076,000	---	+511,000
(Standard Level User Charge)	(---)	(100,000)	(---)	(+23,000)
Subtotal	---	---	---	+551,000
B. Program:				
1. Research grants:				
a. +475 noncompeting continuation research grants	---	99,699,000	---	+35,058,000
b. +649 competing (new, continuation and supplemental)	---	22,597,000	---	+46,421,000
2. Individual training awards: +156 new fellowships	---	1,150,000	---	+2,206,000
3. Institutional training awards: +1 new institutional (MARC) award	---	1,850,000	---	+240,000
4. Increased costs for program evaluation	---	1,275,000	---	+485,000
5. Intramural Research	---	467,000	---	+18,000
6. Direct Operations	---	6,409,000	---	+167,000
7. Program Management	---	1,293,000	---	+40,000
Subtotal	---	---	---	84,635,000
Total, increases	---	---	---	85,186,000
Decreases				
A. Built-in:				
1. One less day of pay	---	3,621,000	---	-13,000
B. Program:				
1. Research grants:				
a. -617 noncompeting completed or converted to competing status	---	99,699,000	---	-39,789,000
b. -303 competing completed or converted to noncompeting continuations	---	22,597,000	---	-22,597,000
2. -15 Special programs	---	29,184,000	---	-1,205,000
3. Individual training awards:				
a. -85 Noncompeting awards completed or converted to competing status	---	1,713,000	---	-1,110,000

Summary and Explanation of Changes - Continued

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
4. Institutional training awards: -81 Noncompeting Fellowships completed or converted to competing status	---	$17,620,000	---	-$5,557,000
5. Positions	164	3,621,000	-1	-19,000
Subtotal	---	---	-1	-70,277,000
Total, decrease	---	---	-1	-70,290,000
Total, net change	---	---	-1	+14,896,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
15	Cellular and Molecular Basis of Disease.....	---	$69,048,000	---	$75,659,000	---	+$6,611,000
17	Genetics.....	---	61,196,000	---	68,797,000	---	+7,601,000
18	Pharmacology-Toxicology.....	---	26,359,000	---	26,179,000	---	-180,000
20	Clinical and Physiological Sciences.....	---	21,750,000	---	20,930,000	---	-820,000
21	Biomedical Engineering.	---	16,772,000	---	16,811,000	---	+39,000
22	Minority Access to Research Careers.....	---	1,706,000	---	2,122,000	---	+416,000
24	Intramural Research....	18	467,000	18	487,000	---	+20,000
25	Direct Operations.....	108	6,409,000	107	7,562,000	-1	+1,153,000
	(Standard Level User Charge).....	(---)	(100,000)	(---)	(123,000)	(---)	(+23,000)
26	Program Management.....	38	1,293,000	38	1,349,000	---	+56,000
	Total.....	164	205,000,000	163	219,896,000	-1	+14,896,000

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions.....	164	163	-1
Full-time equivalent of all other positions.....	6	6	---
Average number of all employees.....	167	166	-1
Personnel Compensation:			
Permanent positions.....	$3,046,000	$3,180,000	+$134,000
Positions other than permanent.....	93,000	96,000	+3,000
Other personnel compensation.....	81,000	84,000	+3,000
Subtotal, personnel compensation.....	3,220,000	3,360,000	+140,000
Personnel benefits.....	401,000	426,000	+25,000
Travel and transportation of persons.....	100,000	100,000	---
Transportation of things.....	20,000	20,000	---
Rent, communications, and utilities.....	250,000	253,000	+3,000
Printing and reproduction.....	220,000	220,000	---
Other services:			
Project contracts.....	1,500,000	1,500,000	-
Payment for centrally furnished services...	2,076,000	2,587,000	+511,000
Other.....	1,732,000	2,282,000	+550,000
Supplies and materials.....	75,000	75,000	---
Equipment.....	75,000	75,000	---
Grants, subsidies, and contributions.....	195,331,000	208,998,000	+13,667,000
Total obligations by object.....	205,000,000	219,896,000	+14,896,000

Significant Items in House and Senate
Appropriations Committee Reports

Item	Action taken or to be taken
1977 Senate Report	
Minority Access to Research Careers (MARC)	
1. The Committee has allowed an increase of up to $3.7 million for the MARC Program. The Committee is very clear in earmarking a substantial portion of this amount for undergraduate training programs. Any other use of these funds would not follow the intent for which they were provided. The Committee directs the Institute to report to the Committee as to their spending plan for these funds (page 57).	1. A special report reflecting the spending plan of the Minority Access to Research Careers Program is being prepared.
Burn Research	
1. In light of the importance which the committee has placed on fully implementing a comprehensive burn treatment and research program, the Committee will expect a very thorough and comprehensive report - including organizational, position, and funding recommendations. In addition, the mission and goals of this burn program should also be clearly defined for both the Health Services Administration and the National Institute of General Medical Sciences (page 28).	1. The National Institute of General Medical Sciences forwarded their portion of the burn research report to the Health Services Administration, who in turn submitted the entire comprehensive report on the burn research program to the Committee.

Authorizing Legislation

Legislation	1978 Authorized	1978 Appropriation requested
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	$192,532,000 2/
Title IV, Part I - National Research Service Awards Act	1/	27,364,000 3/

1/ Authorization expires September 30, 1977; extension legislation is pending.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $12,266,000 for old training programs.

National Institute of General Medical Sciences

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1967	$130,734,000	$136,172,000	$138,672,000	$138,672,000
1968	152,295,000	152,295,000	156,295,000	152,295,000
1969	157,650,000	153,123,000	158,123,000	155,386,500
1970	146,685,000	146,685,000	167,397,000	140,691,300
1971	141,398,000	159,094,000	164,094,000	159,094,000
1972	143,274,000	161,364,000	172,192,000	166,348,000
1973	173,377,000	180,588,000	203,417,000	180,588,000
1974	138,573,000	175,778,000	183,500,000	168,329,000 1/
1975	168,399,000	178,178,000 2/	198,070,000	187,470,000
1976	161,706,000	146,537,000 3/	146,537,000 3/	187,388,000 4/
1977	193,435,000	198,435,000	218,435,000	205,000,000
1978	219,896,000			

1/ Appropriation after reduction as authorized by Public Law 93-192.

2/ Excludes contracts not considered by House due to lack of authorization ($3,993,000).

3/ Excludes fellowships and training grants not considered due to pending legislation ($40,851,000).

4/ Includes $40,851,000 for training programs authorized by the continuing resolution.

Note: The figures presented in this Table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

National Institute of General Medical Sciences

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	154,288,000	175,000,000	148,294,300
1971	148,376,000	166,072,000	171,072,000	166,072,000
1972	150,400,000	168,490,000	179,318,000	173,474,000
1973	175,960,000	183,171,000	206,000,000	183,171,000
1974	138,573,000	175,778,000	183,500,000	168,329,000 1/
1975	168,329,000	178,108,000 2/	198,000,000	187,400,000
1976	161,630,000	146,461,000 3/	146,461,000 3/	187,312,000 4/
1977	193,435,000	198,435,000	218,435,000	205,000,000
1978	219,896,000			

1/ Appropriation after reduction as authorized by Public Law 93-192.

2/ Excludes contracts not considered by House due to lack of authorization ($3,993,000).

3/ Excludes fellowships and training grants not considered due to pending legislation ($40,851,000).

4/ Includes $40,851,000 for training programs authorized by the continuing resolution.

Justification

National Institute of General Medical Sciences

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Cellular and Molecular Basis of Disease.....	---	$69,048,000	---	$75,659,000	---	+$6,611,000
Genetics.....	---	61,196,000	---	68,797,000	---	+7,601,000
Pharmacology-Toxicology.....	---	26,359,000	---	26,179,000	---	-180,000
Clinical and Physiological Sciences.....	---	21,750,000	---	20,930,000	---	-820,000
Biomedical Engineering.	---	16,772,000	---	16,811,000	---	+39,000
Minority Access to Research Careers.....	---	1,706,000	---	2,122,000	---	+416,000
Intramural Research....	18	467,000	18	487,000	---	+20,000
Direct Operations.....	108	6,409,000	107	7,562,000	-1	+1,153,000
(Standard Level User Charge).....	(---)	(100,000)	(---)	(123,000)	(---)	(+23,000)
Program Management.....	38	1,293,000	38	1,349,000	---	+56,000
Total.....	164	205,000,000	163	219,896,000	-1	+14,896,000

General Statement

The National Institute of General Medical Sciences supports a broad base of research on life processes the understanding of which is essential to progress in prevention, diagnosis and treatment of all disease. In addition, the Institute encourages clinical research on major medical problems that are not in the purview of the categorical Institutes, e.g. anesthesiology. In order to facilitate and assist these activities the NIGMS supports the development of necessary resources, such as research tools and instruments, technologies for improved diagnosis, and research manpower.

The Institute supports research and training in such scientific areas as Cellular and Molecular Basis of Disease, Genetics, Pharmacology-Toxicology, Clinical and Physiological Sciences, and Biomedical Engineering.

In accord with its basic mission, the Institute is preeminent at NIH in the support of predoctoral research training. This training is designed to be broad and multidisciplinary so that the graduates will be versatile and creative enough to work successfully on future biomedical research problems, some of which cannot even be foreseen. Postdoctoral research training for individuals with either the M.D. or Ph.D. degree is also encouraged in areas of specialized need. Special research training is offered through the Minority Access to Research Careers (MARC) Program which is dedicated to the goal of increasing the proportion of biomedical scientists of minority origin.

Cellular and Molecular Basis of Disease

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Cellular and Molecular Basis of Disease.....	996	$69,048,000	1,101	$75,659,000	+105	+$6,611,000
Budget Mechanism:						
Research Grants:						
Regular Program:						
Noncompeting.....	620	36,910,000	585	35,347,000	-35	-1,563,000
Competing.....	121	8,371,000	283	19,141,000	+162	+10,770,000
Subtotal, Regular..	741	45,281,000	868	54,488,000	+127	+9,207,000
Special Programs:						
Molecular Pathology Research Centers...	1	425,000	2	1,029,000	+1	+604,000
Research Career.....	71	1,773,000	64	1,596,000	-7	-177,000
Subtotal, Special..	72	2,198,000	66	2,625,000	-6	+427,000
Training Programs:						
Individual.....	51	670,000	68	921,000	+17	+251,000
Institutional.....	132	20,899,000	99	17,625,000	-33	-3,274,000
Total.....	996	69,048,000	1,101	75,659,000	+105	+6,611,000

The objectives of this program are to gain a greater knowledge of the complex structure and function of human cells and their subcellular components and biochemical systems, and of the interactions between cells and their surroundings. Most diseases of the body are associated with abnormal cellular function. The body's response to infection, injury, drugs, environmental agents and chemicals are all dependent on events occurring at the cellular level. Structural changes of cell membranes or subcellular organelles and malfunction of their molecular components may seriously affect the whole organism and lead to disease. Continued success and achievements in basic research in cellular and molecular biology will further contribute significantly to the ultimate prevention of many diseases, more effective treatment, and the reduction and containment of the cost of medical care.

Of particular importance among the studies at the cellular level are those on cell division, cell mobility, cell/cell recognition and communication, and cellular differentiation. Biophysicists, organic and biological chemists, and cell biologists are major contributors to these fundamental studies. In recent years, pathologists and other clinical scientists have increasingly collaborated with them to study the cellular and molecular basis of disease, trauma, and aging. Emphasis is given to the rapid dissemination of new research findings through publications, workshops, conferences, and international meetings for cellular and molecular biologists and related clinical investigators. Concomitant with its long-range objectives, the Cellular and Molecular Basis of Disease Program fosters and supports the research training of young investigators in cellular and molecular sciences. This includes training in the newly developing area of molecular pathology so as to provide patholgists with the tools and knowledge

needed for fundamental cellular and molecular research on the causes and mechanisms of disease. Exciting new progress is being made on the detailed structure of the cell membrane, which is now seen as a highly organized mosaic made up of a large number of different kinds of molecules serving a variety of functions. Prominent among these molecules are the proteins, which serve as a path of communication and transport of sugars, amino acids, hormones, and drugs between cells' internal parts and the external environment. Other proteins in the cell membranes serve a vital role as the site of contact for hormones and drugs that circulate in the body. Another exciting area concerns the so-called microtubules, tiny organelles in the cells which are capable of contracting and consequently have a role in the movement of phagocytic cells, the transport of materials and vesicles within the cell, and some of the changes that occur during cell division.

Genetics

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Genetics	869	$61,196,000	961	$68,797,000	+92	+$7,601,000
Budget Mechanism:						
Research Grants:						
Regular Program:						
Noncompeting	548	38,188,000	483	35,036,000	-65	-3,152,000
Competing	91	7,067,000	255	18,729,000	+164	+11,662,000
Subtotal, Regular	639	45,255,000	738	53,765,000	+99	+8,510,000
Special Programs:						
Genetic Research Centers	10	6,500,000	10	6,000,000	---	-500,000
Research Career	94	2,305,000	87	2,155,000	-7	-150,000
Subtotal, Special	104	8,805,000	97	8,155,000	-7	-650,000
Training Programs:						
Individual	70	1,005,000	83	1,198,000	+13	+193,000
Institutional	54	5,722,000	41	5,270,000	-13	-452,000
Research and Development Contracts	2	409,000	2	409,000	---	---
Total	869	61,196,000	961	68,797,000	+92	+7,601,000

Genetics, more than most sciences and medical disciplines, must cut across fields. Basic scientific contributions to genetics come from chemistry, statistics, psychology, molecular and cell biology. Almost any area of medicine, be it anesthesiology or cardiology, has genetic aspects. Most serious prevalent human diseases include genetic components. The major part of the genetics program continues to focus on topics not directly related to disease entities. Research on nucleic acid chemistry and metabolism and on gene function are examples. Research using lower organisms, such as bacteria, fungi, and fruit flies, continues to be extensively supported. In this respect, the program is considered a long-range resource generating concepts applicable to all genetic disease.

In the past few years, increased emphasis has been given to proposals by molecular biologists interested in the genetics of mammalian systems including man. This trend can be attributed to several recent developments: (a) improvements in technology, particularly in tissue culture and somatic cell genetics; and (b) increased interest in the capability of the molecular biologists to extend the conceptual framework of gene action, now largely based on work with lower organisms, to the more complex systems including man. An understanding of genetics is not only important in the prevention of metabolic disorders, but also in dealing with such diverse medical problems as transplantation of organs and clinical pharmacology. Numerous attempts are being made to solve the problems associated with enzyme replacement therapy, which is one of the few means currently of dealing with some genetic diseases. Another major area of study is concerned with finding out what makes genes, which are present in all the cells of the body, express themselves in only a fraction of these.

Pharmacology-Toxicology

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Pharmacology-Toxicology	355	$26,359,000	335	$26,179,000	-20	-$180,000
Budget Mechanism:						
Research Grants:						
Regular Program:						
Noncompeting	202	11,415,000	160	10,702,000	-42	-713,000
Competing	46	2,950,000	67	4,433,000	+21	+1,483,000
Subtotal, Regular	248	14,365,000	227	15,135,000	-21	+770,000
Special Programs:						
Pharmacology-Toxicology Research Centers	9	5,643,000	9	4,700,000	---	-943,000
Research Career	25	630,000	20	505,000	-5	-125,000
Subtotal, Special	34	6,273,000	29	5,205,000	-5	-1,068,000
Training Programs:						
Individual	7	99,000	20	280,000	+13	+181,000
Institutional	61	5,289,000	54	5,226,000	-7	-63,000
Research and Development Contracts	5	333,000	5	333,000	---	---
Total	355	26,359,000	335	26,179,000	-20	-180,000

The Pharmacology-Toxicology Program is a comprehensive program including clinical pharmacology, toxicology, and bio-related chemistry. The overall objective is to provide a rational basis for the safer use of presently available drugs and to contribute to the design of more effective therapeutic agents. The program has given a great deal of attention to the area of drug metabolism. A drug rarely remains unchanged in the body; the vast majority are transformed to other chemicals, which are, in some cases, inactive, but in other cases more active than the original drug. In some instances, the transformed drug is highly toxic or even carcinogenic. Growing knowledge of the metabolic pathways of drugs and the therapeutic and toxic properties of their metabolites is making it possible to synthetize specific chemical modifications to either favor or circumscribe these drug actions, with improved effectiveness and safety of drug therapy as a result.

A grantee of the program has recently discovered a new way to synthesize steroid hormones which were previously in very short supply. Since these hormones have profound physiological significance and are used widely in the treatment of inflammatory and immune diseases, and since the method has some general applicability, the design of new steroid drugs with minimal side effects may be possible. New emphasis is being placed on pediatric pharmacology. It is now widely recognized that children often do not react like little adults, and often metabolize drugs in different ways fron adults. This can have profound implications for effective and safe treatment of particularly very young children.

Another study has illustrated the need for studies in man by discovering why methyl alcohol is so toxic to man, often resulting in blindness or death, while rats or other laboratory animals are relatively unaffected. Studies have shown that this compound is metabolized differently in man and have also shown the effects of diet on susceptibility to methyl alcohol poisoning.

Clinical and Physiological Sciences

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Clinical and Physiological Sciences	211	$21,750,000	204	$20,930,000	-7	-$820,000
Budget Mechanism:						
Research Grants:						
Regular Program:						
Noncompeting	88	5,706,000	90	6,279,000	+2	+573,000
Competing	23	2,029,000	20	1,764,000	-3	-265,000
Subtotal, Regular	111	7,735,000	110	8,043,000	-1	+308,000
Special Programs:						
Anesthesiology Research Centers	5	3,190,000	4	3,000,000	-1	-190,000
Trauma and Burn Research Centers	12	4,650,000	12	4,850,000	---	+200,000
Research Career	12	325,000	17	426,000	+5	+101,000
Subtotal, Special	29	8,165,000	33	8,276,000	+4	+111,000
Training Programs:						
Individual	16	231,000	26	370,000	+10	+139,000
Institutional	55	5,619,000	35	4,241,000	-20	-1,378,000
Total	211	21,750,000	204	20,930,000	-7	-820,000

The objective of this program is to understand the biochemical and physiological changes that occur following trauma or during anesthesia. Trauma, which is a major cause of death and morbidity, sets in motion a very complex series of reactions in the body, which to date are not very well understood. Even though the initial injury may have been repaired surgically, serious complications related to nutrition, blood pressure, and infection frequently occur. Such complications are particularly marked following major burns, which also present the surgeon with the challenge of restoring an intact skin. Because of the protracted convalescence in burn patients, infection is a particularly serious problem. Institute grantees appear to have made some significant progress in this area during the past couple of years. Other grantees are developing ways to maintain caloric and nutritional support.

In the field of anesthesiology, there are several major goals. Safe anesthetic agents and safe methods of administration are being sought painstakingly by institute grantees. These studies include work on the modifying effects of various drugs and diseases on the potency and side effects of anesthetics. Another important goal of the program is to seek an understanding of the basic mechanism of pain, including chronic pain, which continues to baffle the physician. Working together with psychologists, the anesthesiologists are studying the behavioral aspects of both acute and chronic pain.

Recognizing the current shortage of well-trained investigators in the fields of anesthesiology and trauma and burn research, the Institute is offering both individual and institutional National Research Service Awards in these areas. The programs are designed to provide potential clinical scientists with a strong background in physiology and biochemistry.

Biomedical Engineering

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Biomedical Engineering..	172	$16,772,000	174	$16,811,000	+2	+$39,000
Budget Mechanism:						
Research Grants:						
Regular Program:						
Noncompeting.....	90	7,480,000	88	7,604,000	-2	+124,000
Competing.....	22	2,180,000	24	2,354,000	+2	+174,000
Subtotal, Regular.	112	9,660,000	112	9,958,000	---	+298,000
Special Programs:						
Biomedical Engineering Research Centers.....	5	2,200,000	5	2,200,000	---	---
Diagnostic Radiology Research Centers..	2	1,200,000	2	1,200,000	---	---
Research Career.....	14	343,000	13	318,000	-1	-25,000
Subtotal, Special.	21	3,743,000	20	3,718,000	-1	-25,000
Training Programs:						
Individual.....	9	128,000	20	284,000	+11	+156,000
Institutional.....	24	2,483,000	16	2,093,000	-8	-390,000
Research and Development Contracts.....	6	758,000	6	758,000	---	---
Total.....	172	16,772,000	174	16,811,000	+2	+39,000

This program encompasses both theoretical and applied aspects of biomedical engineering and seeks to apply the knowledge and technologies of the physical sciences and engineering to the development of more effective methods for the prevention, diagnosis, and treatment of disease. In the more theoretical area, studies are pursued on computer software, mathematical analysis of physiological processes, and in biometry. Another area under intense study is biomaterials, where an effort is made to develop materials which may be used for prosthetic devices, for chronic implantation. Two major problems have faced the investigators in this area: (1) the reaction of the patient's tissues to the implanted material, and (2) the gradual decay of the material itself. Utilizing advances in polymer chemistry, one of the grantees is making highly promising progress in this area. Another promising area is concerned with the development of micro-computers and micro-sensors suitable for long-term monitoring of patients. Because of their small size, these instruments are also adaptable to portable systems, giving an increased measure of flexibility to medical care. Other areas where Institute grantees are making notable progress are in the fields of ultrasound for both diagnostic and investigational purposes; the use of radioisotopes in diagnosis and physiological studies; and sophisticated engineering advances in the use of X-radiation which have made it possible to lower the radiation exposure in relation to the information obtained by the doctor. Work on automating clinical laboratory tests on blood cells is making progress, but is still in a developmental stage.

Minority Access to Research Careers

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Minority Access to Research Careers....	66	$1,706,000	74	$2,122,000	+8	+$416,000
Budget Mechanism:						
Training Programs:						
Individual.....	61	821,000	68	997,000	+7	+176,000
Institutional.....	5	885,000	6	1,125,000	+1	+240,000
Total.....	66	1,706,000	74	2,122,000	+8	+416,000

The Minority Access to Research Careers Program (MARC) is a research training program, the goal of which is to increase opportunities for students and faculty at minority institutions for advanced research training and preparation for research careers in the biomedical fields of science. A concurrent objective is to strengthen the capabilities for teaching and research in those disciplines at minority institutions.

The proportion of U.S. citizens holding doctoral degrees who are members of minority groups is strikingly lower than the percentage of minority U.S. citizens. The number of blacks and members of other minority groups currently being trained for the doctorate is correspondingly small. By contrast, the demand throughout the nation for Ph.D.s in the biomedical sciences from among blacks and other minority groups is unprecedented. Vigorous recruitment is underway throughout the government, academic institutions, hospitals, research institutions, and industry.

The MARC Faculty Fellowship Program provides opportunities for advanced research training for selected faculty members of four-year colleges, universities and health professional schools in which student enrollments are drawn substantially from ethnic minority groups. These institutions may nominate faculty members to apply for MARC Fellowships in support of a period of advanced study and research training in graduate departments and laboratories, either as candidates for the Ph.D. degree or as investigators obtaining postdoctoral research training in the biomedical sciences. These awards may be made for one to three years of support. When the period of training is completed, fellows are encouraged to return to their sponsoring schools to do research and teaching so as to inspire and assist minority students to prepare for professional careers in the biomedical sciences and in medicine.

The MARC Visiting Scientist Award allows outstanding scientist-teachers to serve in the capacity of visiting scientists at four-year colleges, universities, and health professional schools where student enrollments are drawn substantially from minority groups. The primary intent is to strengthen

research and teaching programs in the biomedical sciences for the benefit of students and faculty in these institutions by drawing upon the special talents of scientists from other institutions. Reciprocal benefits should also accrue to the MARC awardee through the added experience to be gained by involvement in innovative science education and research development programs.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivity:						
Intramural Research...	18	$467,000	18	$487,000	---	+$20,000
Total.....	18	467,000	18	487,000	---	+20,000

Intramural research supports direct training of research associates assigned to laboratories which are related to clinical pharmacology, toxicology, and bio-related chemistry. Nine appointments are made each year for a total of 18 two-year appointments.

The increase of $20,000 consists of an $18,000 program increase and $3,000 for within-grade pay increases offset by $1,000 for one less day of pay.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivity:						
Direct Operations...	108	$6,409,000	107	$7,562,000	-1	+$1,153,000
Total.....	108	6,409,000	107	7,562,000	-1	+1,153,000

This activity provides professional and supporting staff required for the scientific review and administration of the 2,656 grants and 13 contracts estimated to be funded in 1977. Approximately 2,836 grants and 13 contracts would be funded in 1978.

The increase of $1,153,000 consists of $17,000 for within-grade pay increases, $511,000 for centrally furnished services, $485,000 for program evaluation, and a program increase of $167,000 offset by $8,000 for one less day of pay and $19,000 for a decrease of one position.

One administrative position has been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivity:						
Program Management....	38	$1,293,000	38	$1,349,000	---	+$56,000
Total.....	38	1,293,000	38	1,349,000	---	+56,000

These funds provide for the support of the Institute Director and her immediate staff. They, in turn, are responsible for the overall direction, operation, planning, and development of the many Institute programs.

The increase of $56,000 consists of $10,000 for within-grade pay increases, $7,000 for the Federal Employees' Compensation Fund, $3,000 for the Federal Telecommunications System, and a program increase of $40,000 offset by $4,000 for one less day of pay.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Cellular and Molecular Basis of Disease (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$69,048,000	Indefinite	---	$75,659,000

Purpose: The purpose of the Cellular and Molecular Basis of Disease Program is to support research on the complex structure and function of human cells and their subcellular and molecular components with the expectation that such research will ultimately contribute to the control and prevention of most diseases.

Explanation: This program supports research through regular research projects, research center grants, fellowships, and research training grants.

Accomplishments in 1977: Approximately 741 regular research grants, 72 special programs, 51 individual awards, and 132 institutional awards will be funded in 1977. Such research and research training is of a fundamental multidisciplinary nature -- encompassing the disciplines of biophysics, biochemistry, microbiology, cell biology, physiology, and pathology in the study of cell membranes and cell organelles such as microtubules, myofilaments, and mitochondria, and how these function in normal growth and development and are altered in disease, injury, and the aging process. Enormous advances have been made recently in our understanding of the physiochemical structure of cell membranes, their microscopic appearance and manifold functions, including the highly selective transport of nutrients and other chemicals in and out of the cell. The base of knowledge in cell biology is being broadened by molecular studies of proteins and enzymes and their varied metabolic reactions. A highly selected group of research training centers has been funded to provide training support for new young scientists in cross-discipline fields.

Objectives, 1978: Research in cell differentiation and specialization will be emphasized. Newer instruments for investigating cell structure, such as the high voltage scanning electron microscope and a variety of spectrophotometric methods will be exploited for the study of membranes and other subcellular components. It is estimated that 868 regular research grants, 66 special programs, 68 individual awards, and 99 institutional awards would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Genetics (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$61,196,000	Indefinite	---	$68,797,000

Purpose: The purpose of the Genetics Program is to support research aimed at the prevention, therapy, and control of genetic diseases in man, including those multifactorial illnesses with a strong hereditary component.

Explanation: Activities are supported through grants, fellowships and contracts.

Accomplishments in 1977: The Genetics Program will continue to provide support for a wide spectrum of genetics research, ranging from the chemistry of genetic materials to population genetics. We expect that this research will continue to provide important concepts and methods that are basic to the study of a wide range of diseases, including cancer and heart disease.

With the release of NIH guidelines for research on DNA recombinant molecules, and the creation of an NIH "Office of Recombinant DNA Activities" (whose administrative location is within the NIGMS), the program is in an improved position to responsibly administer certain types of research in ways consistent with the safety of laboratory personnel and the general public.

The Human Mutant Cell Bank, the only major contract administered by the program, will be an increasingly effective resource for stimulating interest in, and improving the capability of scientific investigators to study problems of human genetic disease. It is estimated that 639 regular research grants, 104 special programs, 70 individual awards, 54 institutional awards, and two contracts will be supported in 1977.

Objectives, 1978: Much of the research involves simple model systems, such as fruit flies, which provide important concepts for understanding the heredity of man. Other research has provided new or improved methodology, including advances in the culture of human cells, and more refined methods for studying chromosomes.

The program will continue to seek an appropriate balance between support of fundamental "long-range" research and more applied or clinical research.

Among the categories of research which will be emphasized are those projects which will "map" the location of human genes on chromosomes. We will continue to encourage research on the poorly understood genetics of diabetes, atherosclerosis, or hypertension, each of which may represent a group of diseases. Environmental factors appear to be highly significant in the pathogenesis of these diseases. It is estimated that 738 regular research grants, 97 special programs, 83 individual awards, 41 institutional awards, and two contracts would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Pharmacology-Toxicology (Public Health Service Act, Title IV, Part F)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$26,359,000	Indefinite	---	$26,179,000

Purpose: This program embraces drug-related research from synthesis of new drugs to studies on the effects of drugs in man.

Explanation: Activities are supported through grants, fellowships, contracts and an intramural research associate program.

Accomplishments in 1977: Approximately 248 regular research grants, 34 special programs, 7 individual awards, 61 institutional awards, and five contracts will funded in 1977.

New information is being obtained on the serious allergic response to penicillin which occurs in sensitive patients. Recent work suggests that the cardiovascular system may be the primary site of allergic reactions leading to fatality and that the cardiac dysfunction can be potentiated by administration of other therapeutic drugs.

Acidosis is one of the symptoms of poisoning by various alcohols, including methanol and ethylene glycol. Formic acid has been identified as the principal metabolite of methanol in humans and other primates but not in other species which are not as susceptible to methanol poisoning. It has been shown that 4-methylpyrazole, an inhibitor of the first step of alcohol metabolism, is capable of preventing fatality in monkeys poisoned with methanol or ethylene glycol. This may develop into a clinically useful therapy for accidental poisoning by these common chemicals.

Objectives, 1978: All aspects of drug metabolism have historically been of interest to the program. It has recently been found that substances which increase the concentration of interferon (a potent anti-viral protein produced by certain cells of the body) drastically reduce the level of drug metabolizing enzymes in the liver. It will be important to learn whether viruses, vaccines, and other interferon-inducing agents in fact lower the rate of drug metabolism in man. Among the many research areas in the Pharmacology-Toxicology Program which offer opportunities for progress, emphasis will be placed upon clinical pharmacology (with special attention to pediatric pharmacology or the use of therapeutic drugs in children), pharmacogenetics, immunopharmacology, and molecular mechanisms of toxicity. It is estimated that 227 regular research grants, 29 special programs, 20 individual awards, 54 institutional awards, and five contracts would be funded in 1978.

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NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Clinical and Physiological Sciences (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$21,750,000	Indefinite	---	$20,930,000

Purpose: The purpose of the clinical and physiological sciences program is to promote and foster basic and clinical research in the physiological sciences and in certain clinical areas, particularly anesthesiology and trauma. Trauma and burn research is directed to the discovery of better ways to prevent death from injury, mitigate pain, speed recovery of patients and lessen the extent of disabilities caused by injuries.

Explanation: Activities are supported through grants, fellowships and contracts.

Accomplishments in 1977: Approximately 111 regular research grants, 29 special programs, 16 individual awards, and 55 institutional awards will be funded in 1977. The research center grants in anesthesiology and in trauma and burns support studies on the body's total response to accidental injury and surgical insult through the coordination of basic and clinical investigations. The program fosters and encourages collaborative research in cell biology, physiology, biochemistry, microbiology, pharmacology, behavioral sciences and bioengineering. In trauma, emphasis is given to research on wound healing, life-threatening sepsis, hormonal imbalance, prevention of acute starvation and rehabilitation of injured patients. A new trauma and burn research center was activated in June 1976 at the University of Utah Medical Center. The research includes studies on hepatobiliary dysfunction, gastric mucosal ischemia, effects of corticosteroids following trauma and burns and the development of instrumentation for continuously measuring oxygen consumption under these conditions.

A workshop was held recently to discuss ways to foster research and manpower training in anesthesiology. On the basis of the discussion, NIGMS is placing emphasis on support of research project grants concerned with the mode of action of anesthetics and muscle relaxants, and the basic physiologic and metabolic changes resulting from anesthesia. Individual and institutional postdoctoral fellowships are offered in trauma and burn research, and individual fellowships in anesthesiology.

Objectives, 1978: Continued emphasis will be placed on the aforementioned areas. Considerable efforts will be made to encourage high-quality research on the pathophysiology of accidental injury. Anesthesiologists will be encouraged to submit individual research project grants. Research training is being strengthened by course work and experience in basic science laboratories. It is estimated that 110 regular research grants, 33 special programs, 26 individual awards, and 35 institutional awards would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Biomedical Engineering (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$16,772,000	Indefinite	---	$16,811,000

Purpose: The purpose of the biomedical engineering program is to support the effective introduction of the principles and practices of engineering science into fundamental and applied biomedical research. In selected instances, support is provided for the development of prototype instruments and devices which will be useful in improving health care.

Explanation: This program supports research through regular research grants, special center grants, fellowships, training grants, and contracts.

Accomplishments in 1977: Approximately 112 regular research grants, 21 special programs, 9 individual awards, 24 institutional awards, and six contracts will be funded in 1977. Special emphasis will be devoted to 1) the encouragement of increased research on biomaterials, and particularly on the interactions of these substances with body fluids and tissues; and 2) the application of engineering concepts, such as control theory, to studies of physiologic processes. Continued effort will also be directed toward studies involving microelectronic instrumentation for biomedical research and patient care; ultrasonic imaging systems; application of engineering techniques to the diagnosis and treatment of critically ill patients; use of radioisotopes and infrared and laser radiation for the improvements of diagnostic radiology; and automation in the medical laboratory.

Support for predoctoral and postdoctoral research training in systems and integrative biology will continue to be funded through National Research Service Awards.

Objectives, 1978: Special emphasis will continue to be given to the fostering of a more adequate base of research in biomaterials, and will be extended to the related areas of biomechanics and prosthetics. Activities will also be pursued vigorously in each of the major research areas of the ongoing program including: mathematical analyses of biological processes, physiological systems analysis, instrumentation, computers, patient monitoring, non-invasive tissue characterization by ultrasonic and electromagnetic methods, diagnostic radiology, and automation in the medical laboratory. Predoctoral and postdoctoral research training will continue to be encouraged and supported through the use of Institutional and Individual National Research Service Awards. It is estimated that 112 regular research grants, 20 special programs, 20 individual awards, 16 institutional awards, and six contracts would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Minority Access to Research Careers (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$1,706,000	Indefinite	---	$2,122,000

Purpose: The purpose of the Minority Access to Research Careers (MARC) Program is to support research training in the biomedical sciences. The program is designed to assist minority institutions in training greater numbers of scientists and teachers in health-related fields.

Explanation: This program supports research training through individual and institutional fellowship awards.

Accomplishments in 1977: Approximately 61 individual awards and five institutional award will be funded in 1977. Special emphasis will be given to research training in the program areas of cellular and molecular basis of disease, genetics, pharmacology and toxicology, clinical and physiological sciences, and biomedical engineering. In addition, research training will be supported in the areas of cancer biology and infectious disease.

Cooperative agreements for the support of activities within the MARC Program have been arranged between the NIGMS, NCI, and NIAID. These arrangements will allow for the support of research training relevant to the missions of the named Institutes.

Objectives, 1978: We expect to launch an undergraduate program of institutional fellowships in the MARC Program. The objectives of the MARC Undergraduate Training Program are as follows: 1) to strengthen research training programs in the biomedical sciences; 2) to help develop a strong biomedical sciences curriculum; and 3) to increase the number of well prepared minority students who will compete for entry into graduate programs leading to the Ph.D degree. Emphasis will be placed on the inclusion of all eligible minority groups in the activities of the program. It is estimated that 68 individual awards and six institutional awards would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
18	$467,000	Indefinite	18	$487,000

Purpose: The purpose of the Pharmacology-Toxicology Research Associate Program is to develop leaders in pharmacological research for key positions in academic, industrial, and governmental research laboratories. The program is intended for those who have made a commitment to pharmacology or toxicology by training or research, and for those with backgrounds in clinical medicine or basic science who wish to acquire specialized experience in the field of pharmacology.

Explanation: Under this program, postdoctoral research experience is offered to promising investigators in the clinical or basic sciences. Qualified individuals receive two years of postdoctoral training in one of the intramural laboratories of the various institutes comprising the National Institutes of Health. Those who receive appointments in the Pharmacology-Toxicology Research Associate Program study principles of pharmacology and toxicology and the application of physical and chemical concepts.

Professional growth is achieved through the process of personal guidance by senior scientists, chosen by mutual selection, coupled with a variety of laboratory problems and different research approaches designed to advance both the work in progress and the competence of the prospective independent investigator.

Accomplishments in 1977: Nine Pharmacology-Toxicology Research Associates completed the first year of their research program and nine second-year associates graduated. The research opportunities available to these associates was expanded to include research in the intramural laboratories of the National Institute of Environmental Health Sciences. These additional research opportunities will help to produce pharmacologists with sophisticated training in areas related to environmental toxicants, an area of critical urgency.

Several of the outstanding young pharmacologists were recruited by NIH for additional periods, while others accepted permanent academic positions.

Objectives, 1978: The Pharmacology-Toxicology Research Associate Program will continue to select only the most outstanding candidates for admission to the program. Nine trainees will graduate from the program and nine new fellows will take up residence at the National Institutes of Health.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
108	$6,409,000	Indefinite	107	$7,562,000

Purpose: This activity provides professional and supporting staff required for guidance, surveillance, scientific direction, and administration of the individual grants operations.

Explanation: Funds are made available to provide scientific direction of grant operations and grants processing activities.

Accomplishments in 1977: This activity handles the processing of all NIGMS grants following the primary review process. In addition, it provides important aspects of program stimulation and development including scientific merit and program relevance. It is estimated 1,851 regular research grants, 260 special programs, 214 individual awards, 331 institutional awards, and 13 contracts will be funded in 1977.

Objectives, 1978: The staff would continue to provide close surveillance over the many NIGMS grants. Approximately 2,055 regular research grants, 245 special programs, 285 individual awards, 251 institutional awards, and 13 contracts would be funded in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Title IV, Part E)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
38	$1,293,000	Indefinite	38	$1,349,000

Purpose: Program Management provides for the overall leadership and staffing necessary for the administration and management of the research effort of the Institute.

Explanation: The National Institute of General Medical Sciences supports a broad base of fundamental and applied biomedical research programs aimed at the solution of certain major health problems. The Institute Director and her staff are responsible for the overall direction, operation, planning, and development of the many Institute programs.

Accomplishments in 1977: The Director and supporting professional and clerical staff provide continuing guidance and surveillance over the many programs of the Institute.

Objectives, 1978: Continued leadership will be provided for the administration and management of these programs.

WEDNESDAY, MARCH 9, 1977.

NATIONAL INSTITUTE ON AGING

WITNESSES

DR. ROBERT N. BUTLER, DIRECTOR, NATIONAL INSTITUTE ON AGING
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
DAVID L. CHICCHIRICHI, EXECUTIVE OFFICER, NATIONAL INSTITUTE ON AGING
JAMES R. WEHLING, BUDGET OFFICER, NATIONAL INSTITUTE ON AGING
MS. ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now we have the National Institute on Aging. Dr. Robert N. Butler, the Director, will make the presentation.

We have your biographical sketch, Doctor, which we will include at this point in the record.

[The biographical sketch follows:]

CURRICULUM VITAE OF ROBERT NEIL BUTLER

The National Institute on Aging (NIA) is one of 11 Institutes at the National Institutes of Health, the main biomedical research agency of the Federal Government.

Robert Neil Butler, M.D., physician, psychiatrist, gerontologist, author.
Birthdate: January 21, 1927.
Birthplace: New York, N.Y.

Author:

Books: "Human Aging" (with others) (1963; reprinted 1971, 1974); "Aging and Mental Health" (with Myrna I. Lewis), 1973; "Why Survive? Being Old in America," 1975; Pulitzer Prize, 1976; "Sex After Sixty" (with Myrna I. Lewis), 1976.

Other: Over 100 research and clinical papers in the fields of life cycle, middle age and aging, psychotherapy, confidentiality, drugs, creativity—as well as book reviews and articles for newspapers and magazines. Regularly featured column, "Public Interest Report," for the International Journal of Aging and Human Development. Chapters in "American Handbook of Psychiatry," the "Comprehensive Textbook of Psychiatry," and "Clinical Geriatrics."

Member Boards of Trustees: National Council on the Aging; National Caucus on the Black Aged; Washington School of Psychiatry; Andromeda; Legal Research and Services for the Elderly; District of Columbia Commission on Aging; and Advisory Council, Senior Medical Consultants.

Editorial board: International Journal of Aging and Human Development and Journal of Geriatric Psychiatry Geriatrics.

Honors, Awards: Pulitzer Prize, 1976; Washingtonians of the Year, 1976; Leo Laks Award, 1976; Certificate of Appreciation, Mid-Atlantic Chapter of the American Medical Writers Association, 1976; and Community Service Award, D.C. Medical Society, 1976.

Previous professional activity

Private practice: Psychiatry and psychoanalysis. Group therapy (life crises groups).

Consultative practice: Institutions, agencies, et cetera. Individual diagnostic consultations. Social, health, retirement, and research planning.

Faculty: Howard University School of Medicine (Associate clinical professor); George Washington University School of Medicine (associate clinical professor); the Washington School of Psychiatry; and Washington Psychoanalytic Institute.

Consultant: U.S. Senate Special Committee on Aging; National Institute of Mental Health; St. Elizabeths Hospital; Langley Porter Neuropsychiatric Institute (University of California); and Center for Law and Social Policy.

Research: National Institute of Mental Health, research psychiatrist, 1955–62; the Washington School of Psychiatry, research psychiatrist, 1962–76; and basic, clinical, and community studies:

(1) Psychotherapy and Psychology of Middle and Later Life
(2) Human Aging Study of NIMH, 1955–66
(3) Memoir Study of Persons of Achievement After Middle Life
(4) Community Studies

Public policy: Action research, advocacy, consultation, writing, testimony.

Television: Participant in TV documentaries; Cocreator, Lifetime magazine, 1974.

Military service: (1) U.S. Maritime Service—1944–47; Warrant Officer—Ensign.

(2) U.S. Public Health Service, 1955–62; 1976–present; senior surgeon, 1961; Inactive Reserve, 1962–76; Medical director, 1976–present.

Other professional data

Organizations: American Psychiatric Association, 1959–present (Fellow, FAPA, 1963–present); Gerontological Society, 1962–present; American Geriatrics Society (Founding Fellow), 1962–present; Washington Psychiatric Society, 1959–present; Washington School of Psychiatry, 1959–present; the Medical Society of the District of Columbia, 1965–present; Group for the Advancement of Psychiatry (GAP), 1965–present; Forum for Professionals and Executives (Founding Member), 1965–present; Washington Psychoanalytic Society, 1965–76; American Medical Association, 1955–62 (via USPHS); and Southern Medical Association, 1962–65.

Education: B.A., Columbia, 1949; M.D., Columbia University College of Physicians and Surgeons, 1953.

Residency: University of California; National Institute of Mental Health; Chestnut Lodge; Diplomate, American Board of Psychiatry and Neurology (P), 1961.

Mr. FLOOD. We also are very pleased to say that you won a Pulitzer Prize last year on your book, "Why Survive; Being Old in America." That is a great honor and we join with your colleagues in congratulating you for this great award.

Dr. BUTLER. Thank you.

Mr. FLOOD. Do you have some people you would like us to know?

Dr. BUTLER. Yes; I would like you to meet Mr. David Chicchirichi, executive officer, and Mr. James Wehling, budget officer.

Mr. FLOOD. We have your statement we will place in the record at this point.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—NATIONAL INSTITUTES OF HEALTH

STATEMENT OF THE DIRECTOR, NATIONAL INSTITUTE ON AGING

Mr. Chairman and members of the committee: This is my first appearance before your committee as the Director of the National Institute on Aging. It is both a great personal pleasure and a professional honor.

DEVELOPMENT OF THE NIA

The creation of the National Institute on Aging (NIA) is a good example of human providence. Current projections by the U.S. Bureau of Census shows that 17 percent of our American population will be over 65 years of age by the year

2030. Those youngsters who were said to have "greened" America will "gray" America. Since this figure is based on no improvements in health care. I would guess that a more accurate estimate is 20 percent, or one out of very five Americans, will be 65 and above. The social, personal, technological, and economic ramifications are staggering. Fortunately, this country has joined some seven other nations in creating major research centers to support and conduct research on aging and the needs and special problems of the aged in order to anticipate and alleviate some of the dysfunction this demographic revolution could bring.

The development of the National Institute on Aging into a viable organization has required a number of steps:

1. The initial capitalization of the Institute itself through appropriate organization and efficient transfer of preexisting programs in aging from the National Institute of Child Health and Human Development;
2. The selection of key staff;
3. The exploration and creation of populations for study, including human populations as well as various animal models;
4. The solicitation of the interest of both well-established and young scientists in the field of aging; and
5. The comprehensive development of the state of knowledge; that is, the formation of an information and data base for the emergent and growing science of gerontology and for medical perspectives on geriatrics.

KEY STAFF APPOINTMENTS

One person particularly responsible for the development of the Institute is Dr. Nathan Shock—a great pioneering gerontologist. In 1941, Dr. Shock brought to the Public Health Service his dream—a new idea—that of the importance of the science of aging. Thirty-three years later with the enactment of the Research on Aging Act of 1974 his idea came to fruition. It was a pleasure to appoint Dr. Shock the first Scientific Director of the National Institute on Aging, even though this was his last year of Federal service. He retired from this position on December 31, 1976, but I am most happy to say that he remains with us as a Scientist Emeritus, continuing to contribute to the Institute and the field of aging with his remarkable vigor, imagination, and generosity. I am also pleased to announce that I have selected a successor to Dr. Shock as Scientific Director and have filled the positions of Associate Director for Extramural and Collaborative Research and Clinical Director.

The Congress and the administration have identified coordination as a most important issue facing the field of aging. Therefore, I am presently recruiting a Deputy Director, whose principal function will be coordination with other NIH and Federal agencies. Collaboration is the most efficient way to utilize limited resources. There are many issues such as nutrition and epidemiology (the natural history of disease) which are of concern to several of the Institutes and need to be approached collaboratively.

I am also establishing a Section on Epidemiology, Demography and Biometrics and recruiting an individual to head this unit. If we are to see an improvement in the health status of our old, we must consider the incidence, prevalence, and distribution of a variety of diseases that particularly affect these people; the differential life expectancy among ethnic groups, racial groups, and between the sexes; and the antecedents of significant problems and disease states ranging from senility to functional disability.

RESEARCH PLAN ON AGING

A requirement of the Research on Aging Act of 1974, which created the NIA, was the development of an HEW-wide research plan for aging. This plan has been completed through the efforts and generosity of the American scientific community, the National Advisory Council on Aging and the NIA staff. I call this plan "Our Future Selves," to focus attention on one of the major problems of aging particularly troublesome in this country: the denial of the reality of aging and the denial of the fact that it is inevitable. The research plan is an HEW-wide plan. It is not a statement of NIA goals only. Hopefully what emerges from a reading of the plan is the notion that much remains to be done and that a unified effort based on scholarship, cooperation, and coordination will be required to realize the goals of the plan.

RESEARCH AND COST CONTAINMENT

NIA's mandate has extraordinary breadth—ranging from the biological to behaviorial sciences and investigative medicine to societal concerns, and the provision of public and scientific education programs. The need for a broad research approach is apparent when we look to the escalating and staggering costs of health care. Sixty percent of every Federal health care dollar in 1976, a total of $20 billion, was spent for the elderly, most of which was related to medicaid and medicare. In New York State alone a medicaid bed costs between $12,000 and $15,000 per year—over $1,000 a month. These staggering costs cannot be mitigated solely by alternatives to institutional care. The care provided by homemakers/home-health aides or day care centers, the use of prosthetics, and effective diagnosis and treatment prior to institutionalization shifts attention from institutional care. These alternatives do help to contain costs as well as to reduce personal and family anguish, but are appropriate only to a point.

Fundamentally, however, the ultimate service and the ultimate cost containment is research to prevent or modify the cause of the debilitating conditions of late life. A research breakthrough that would contribute to the prevention or treatment of one major dementing brain disease would do more than any "alternative to institutionalization" to reduce hospital and nursing admissions. There are now 1.2 million Americans in 23,000 nursing homes—more patients in nursing homes than there are in hospitals. If we could succeed within the next decade in keeping even 100,000 people out of nursing homes, this could mean as much as $1 billion per year in cost savings, clearly justifying our research and development investment.

SERVICE-RELATED RESEARCH

This relationship between research and cost of health care does not mean that research and service are the same. We carefully distinguish between them. Our legislative authority allows research and not service. We can, however, serve by providing the research foundation on which good service is based. For example, by examining the nutritional status and the nutritional requirements of people as they age, we would be performing service-related research. Today at lunch, some 250,000 Americans over 60 will have received a hot meal under title VII of the Older Americans Act. By cooperating with the Administration on Aging we can improve the scientific base for determining the nutritional requirements of the elderly.

PROGRAM BALANCE

My most troubling discovery upon assuming the position of Director in May was to find that less than 4 percent of our extramural grants to American universities, hospitals, and research centers were in the area of investigative medicine. Grants in this area should support the study of such matters as the postmenopausal endocrine states, benign prostatic hypertrophy (enlargement of the prostate gland), sleep disturbances, cerebral physiology, senile dementia, pharmacology, nutrition, physical fitness, and exercise physiology.

The disturbing lack of research in investigative medicine probably reflects the absence of the systematic teaching of geriatric medicine to American medical students, interns, residents, and the 330,000 practicing physicians. I am not talking about a proprietary question, namely, whether or not there should be a specialty called geriatric medicine. Rather, a body of knowledge should be available to stimulate the imagination of potential medical students and researchers. The NIA can support research training for physicians, but not clinical training. Hopefully, by pointing out the need for teaching geriatric medicine and through coordination with the Health Resources Administration, the Administration on Aging, and private foundations, it would be possible to expand teaching of physicians and other allied health professionals in geriatric medicine.

ANIMAL MODELS

One of the most interesting logistical problems faced by researchers in aging is that of an appropriate system to study. Clearly the human is not always an appropriate model of aging from birth to death. Therefore, we really need to understand a variety of different animal species as they age. There are contributions to be made from a variety of unusual sources such as the nematode

(worm), which lives only 30 days, and has an enzyme system that is of particular interest and the salmon, which dies after spawning.

In December, NIA held a conference on animal models. To my knowledge, this is the first time that students of such a wide range of different animal species were ever together. This exciting workshop marked establishment of a new body of knowledge that will characterize different animal species as they age. The genetic background, lifecycle tables, and immunological and physiological characterization are among the elements necessary for the production of such animal models. Development of these models systems is enormously important to our researchers.

ACTIVITIES OF SPECIAL INTEREST

During fiscal year 1977 there were several other items of interest. Our extramural program developed a special small grants program to help bring new scientists into aging. We have established an important contract in pharmacology and with the help of another NIH Institute, the National Institute of General Medical Sciences, we are making every effort to obtain promising research proposals from pharmacologists. The basic concepts and instruments for the study of the absorption and distribution of drugs and their reactions within the body are available to us but have not been applied systematically and comprehensively to the middle and later years. Thus, prescriptions for older people are not based on scientific guidelines. Hopefully, results from these efforts will provide the data necessary to formulate these guidelines.

The entire intramural research program at the Gerontology Research Center at Baltimore is under systematic review. We will soon have, for the first time, a Board of Scientific Counselors. Although our aging program at Baltimore is probably the world's most outstanding, we must always strive to improve and pursue promising leads.

We have planned and begun recruiting for the addition of women to the Baltimore Longitudinal Study. Longitudinal studies are absolutely essential to the understanding of physical and emotional changes with age. We also plan to tap other longitudinal studies such as the Framingham heart study and the 1,000 aviator study of the Department of the Navy.

We have held or are planning to hold a number of meetings to assess the state of the art or to focus attention on areas which we feel need further research. Among these conferences are the following:

1. Economics and Aging, chaired by Dr. Arthur Okun, former Chairman of the Council of Economic Advisers, and myself, to consider potential research questions in economics;

2. Geriatric medicine workshops with groups from various medical schools to discuss instruction and curriculum development;

3. Senile dementia, cosponsored by NIA, the National Institute of Neurological and Communicative Diseases and Stroke and the National Institute of Mental Health, to discuss aspects of senile dementia which may account not only for the entry of as many as half a million older people into nursing homes, but which is also extraordinarily devastating to human personality, memory, and identity;

4. Exercise physiology, physical fitness, and aging, sponsored by NIA in conjunction with the President's Council on Physical Fitness and Sports.

The President's budget proposes an increase for basic research supported by NIH. The NIA share of this initiative will be used in the areas of genetics, immunology and cell biology as they relate to age. This basic research is important because the study of aging involves disentangling the phenomena of normal biological aging from a variety of other factors which affect life. Diseases, social adversity, occupational hazards, personal crises, poor nutrition, and inadequate physical fitness are among those factors which masquerade as aging. As these variables are identified and accurately measured we begin to have a clearer picture of the process of aging. Once differentiated, certain of these factors will be susceptible to effective diagnosis, modification, prevention and treatment.

I am proud, as I hope you are, of the beginnings this Institute has made in dealing with a universal, complex process. The Institute plans a deliberate, reasoned approach to the study of aging, keeping in mind the many immediate problems that adversely affect older Americans and their families at the same time that we pursue untargeted research.

I hope and expect that the great amount of interest generated within and by the new NIA will result in the growth of the field of aging and in the number of investigators outside NIH, and will enhance the amount and availability of information on the subject of aging. Mr. Chairman, the 1978 budget request for the National Institute on Aging is $34,500,000, an increase of $4,500,000 over the 1977 appropriation of $30 million.

SUPPORT OF NEW RESEARCH GRANTS

Mr. FLOOD. Your overall budget request proposes a 15 percent increase in 1978.

Dr. BUTLER. Yes.

Mr. FLOOD. I notice you are planning to reduce support for new research grants. Why is that?

Dr. BUTLER. The fact is that we will have 74 fewer new awards that we can support because the commitments to grants made last year reduces the possibility of new grants in fiscal 1978.

NUMBER OF RESEARCH GRANT APPLICATIONS

Mr. FLOOD. Are you being overwhelmed with applications or are you finding it necessary to go out and stimulate these scientific communities to get applications?

Dr. BUTLER. I would say both those points are true. In many respects there has been a great deal of interest in the new Institute and we get thousands of letters from a great many people interested in the Institute, including suffering families and students interested in our programs.

We have an increased number of research proposals but at the same time we feel it is imperative to stimulate interest in certain areas, particularly pharmacology. There is so little known about the relationship between pharmacology and age that it is necessary to especially encourage applications for research in this area. We have had the support of Dr. Kirschstein in the National Institute of General Medical Sciences whom you just heard, in stimulating pharmacologists to study age-related problems.

FUNDING OF APPROVED GRANT APPLICATIONS

Mr. FLOOD. What percent of your approved applications will you actually fund in fiscal 1977?

Dr. BUTLER. In fiscal 1977 we will have a backlog of approximately $4.5 to $5 million of approved, unfunded, high-quality applications.

AREAS OF HIGH-PRIORITY RESEARCH

Mr. FLOOD. What are the high-priority areas of research that you will be supporting in 1977 and 1978?

Dr. BUTLER. For 1978 we are going to have major programs in cellular biology and immunology. As you probably know, there is a marked decline in the immune protectiveness of the body as we become older. There will also be major support in the areas of genetic causes of aging, nutrition, and, as I mentioned earlier, pharmacology.

COORDINATION WITH NIH

Mr. FLOOD. Since most of the NIH Institutes support some research which in one way or another impacts on the problems of the elderly, do the areas of research that you just mentioned overlap with the other Institutes or have you carefully attempted to fill the gaps in their research plans?

Dr. BUTLER. We are trying to make very creative use of that overlap. We recognize there are important interactions between the fundamental biological process of aging and many diseases in terms of timing and severity. We are trying to meet with Institute Directors and coordinate efforts in critical areas, for example, the study of senile dementia which accounts for too many people in nursing homes.

We are collaborating with the National Institute of Neurological Communicative Disorders and Stroke in sponsoring a conference on the causes of senile dementia which will result in recommendations for research efforts to prevent its occurrence.

Mr. FLOOD. In the material you submitted to Congress you say 60 percent of the Federal health care dollar is spent for the elderly but 2/10 of 1 percent was spent on research directly related to the aging. That seems pretty low to us. Will you explain how you arrived at that percentage?

Dr. BUTLER. As best as we are able to discover in addition to our budget for fiscal 1977 of about $30 million, approximately 30-plus million more dollars are spent within the Federal establishment directly related to research on aging for a total of about $61 million.

Research on many of the diseases associated with the later years are supported through the categorical disease institutions at NIH.

Mr. FLOOD. We have institutes studying chronic diseases that afflict the elderly plus some which study the changes in cell structure and changes in immune system at various stages of life. Maybe we need a definition of aging.

Dr. BUTLER. I think we do—and part of that definition requires better communication among the NIH Institutes. For example, osteoporosis which is the progressive softening of bone after menopause, afflicts about 14 million women. It is a type of disease that probably combines some of the effects of aging, and the effects of hormone metabolism including changes in estrogen, thyroid, parathyroid and mineral metabolism. We have to understand normal, time-related changes as well as disease, which requires us to coordinate our efforts with other researchers.

AGING RESEARCH CENTERS

Mr. FLOOD. In your opening statement you indicate that this country has joined with seven other nations in creating major research centers to conduct research on aging and special problems of the aging. Which countries are you referring to and how will you collaborate?

Dr. BUTLER. They are all industrialized countries. Japan, Israel, the Soviet Union, Rumania, France, and Holland are the six other nations that, as a consequence of the explosion in both absolute numbers and relative proportions of older people in their populations,

have made major commitments to research in the field of aging. Some other nations have not used that approach but have created chairs of geriatric medicine; the United Kingdom has created 12 and Holland has created a chair in geriatric medicine.

Mr. FLOOD. How many research centers on the aging do we have in this country and what kind of research are they conducting?

Dr. BUTLER. They vary in character. We provide support for two of the major centers. One is at Duke University which is largely performing social and behavioral research with some modest biological base but not a substantial medical base. The University of Southern California is also strongly oriented toward social and behavioral research and is also doing some research in biology. The most important of the centers supported by the Institute is the Gerontology Research Center in Baltimore, our intramural program, which is rapidly becoming the most outstanding aging research center in the world.

Mr. FLOOD. How much do you plan to spend in 1978 in support of these centers?

Dr. BUTLER. Our budget will permit us to expand support of the Gerontology Research Center by $1 million to $7 million. This increase will permit us to begin to plan for expansion or initiation of research in the areas of nutrition, the neurosciences and endocrinology, and immunology. We are not able within the limitations of the budget to move much beyond the planning phase in these particular areas.

Mr. FLOOD. Do you see a need for a large center program in the future?

Dr. BUTLER. I have wanted to move with great caution and good sense to learn from the experience of other institutes, and to try to tailor a private and public mix of funding support for these centers. It is important to look for different sources of funds so that stability is not entirely dependent on Federal dollars.

We see some evidence of this in the Davis Institute of Gerontology in Denver where the State, city and private sources have created an institute which is a very attractive model to us. We will probably have two exploratory grants up to a total of about $600,000 which will be used to determine the most effective ways of creating aging research centers. These research centers are seen as resources for training and research in aging, for development of aged animal colonies and for the study of selected human populations. The centers will also provide libraries, computer capability, and specialized equipment.

PLANS FOR THE INTRAMURAL RESEARCH PROGRAM

Mr. FLOOD. Doctor, what are your plans for the Baltimore intramural research program?

Dr. BUTLER. We are currently planning for the expansion of the longitudinal study which up to this time has comprised a sample of 650 men. The expansion will be accomplished through the addition of small numbers of women targeted around specific research interests such as osteoporosis, which I mentioned earlier, clinical immunology and certain differences in mental processes that may or may not exist between the men and women.

We are also planning for expansion of the pharmacology program and are beginning to plan to move into the neurosciences. We need to look at brain function to determine more about the blood/brain barrier which is crucial to our understanding of the many organic brain diseases which affect people as they grow older and account for the fact that we currently have more patients in nursing homes than in hospitals.

DEVELOPMENT OF PROSTHETICS

Mr. NATCHER. During the past few decades there have been many advances in industrial, astronautical, and military technology. Does the Institute have any programs which explore the possible links of technology breakthroughs as far as solution of the problems of the elderly is concerned?

Dr. BUTLER. You have asked a question that is very dear to me; namely, to see if we can collaborate with the National Aeronautics and Space Administration, the Bureau of Standards, and the Veterans' Administration to transfer the many prosthetic and advanced technological devices for use by the elderly. Examples of these devices might include sensors on the end of canes, manipulators and remote control devices. Such transfer of technology will enhance the quality of life for people in nursing homes as well as those who remain in their own homes.

We have discussed this possibility with all the groups I have mentioned. We don't have the kind of results I would like to be able to report to you. We don't have the bioengineering capacity on our own staff, but we have had meetings with the excellent bioengineers in NIH. We want to do this research.

One of the biggest problems, as I see it, is the marketing of these devices. We can bring together the medical scientists and the bioengineers to create very useful devices. However, the problem remains of marketing these devices at a cost that is within reach of the average American family and older person. We think there are solutions to that problem.

FUTURE HEALTH CARE COSTS FOR THE ELDERLY

Mr. NATCHER. If the number of the elderly in our population increases according to projections, how can this Nation continue to absorb the cost of health care for this segment of our society?

Dr. BUTLER. Well, I think the very fact that we have a National Institute on Aging should help us a great deal in containing the health care costs for the elderly. The population increase is not a matter of maybe; it is a very definite forecast, because the young people who were born in the post-World War II baby boom, barring some catastrophy or thermonuclear accident, will definitely be with us 50 years from now and will continue at minimum 17 percent of the population.

If we can enhance and invigorate the immune-protectiveness of the body which current data suggests decreases with age to 10 percent of the competence of an adolescent and if we can reinvigorate people to withstand disease as they get older, we will be making an important contribution to the reduction of the cost of health care.

We don't want to have more and more frail, dependent, ill and disabled people living longer. We want the biological vigor and health of that population to be maintained so that they can continue to contribute to their society through a variety of activities including paid work.

INFORMATION DISSEMINATION

Mr. NATCHER. What information in the field of aging is available and ready for dissemination at this time?

Dr. BUTLER. As a newcomer to NIH, I was very impressed with the Heart Institute's efforts to create a consensus in the field of hypertension. We have been giving thought to moving along the same lines with respect to that condition which is all too often and too easily called senility. We know that the confused state called senility is probably the result of maybe 100 different conditions ranging from drug overuse to aenemia. We want to try to build a consensus of data with respect to the detection, diagnosis, prevention, and treatment of the acute brain disorders of later life, manifested as intellectual confusion and memory loss.

We think this information once developed can be transferred directly and accurately to practicing physicians and to the public at large.

INSTITUTIONAL TRAINING AWARDS

Mr. NATCHER. What will be the effect of eliminating institutional awards and predoctoral support under your present training budget?

Dr. BUTLER. Under present policy, we, in fact, lose one institutional grant in the next fiscal year and are able to fund only five more individual fellowships. In an emergent, new, and exciting field such as gerontology where we are trying to attract the vigor and attention of established American scientists and bring in young scientists as well, the policy with respect to training is a serious one with which we have to contend as best we can.

Mr. NATCHER. Thank you, Doctor.

Thank you, Mr. Chairman.

Mr. FLOOD. Mr. Early?

COORDINATION WITH FEDERAL AGENCIES

Mr. EARLY. Doctor, with regard to the chairman's question in reference to your testimony on page 3, how is that coordination coming about?

Dr. BUTLER. We are currently working with the agencies within the Department of Health, Education, and Welfare that have either a service or a research relationship to the field of aging. It is important for us to have regular, systematic meetings with them to avoid duplication in our programs.

Mr. EARLY. So we fund all the agencies. Are they going to get the information in to you and are you going to have research continue from that point or how does it work?

Dr. BUTLER. Perhaps a good example would be in the area of investigative medicine. We have had very few research grants in that area. This is a new institute and we are new to it, but less than 4 percent

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of our grants have been in such research areas as sleep disturbance, dementia, and postmenopausal illness.

Thus we are collaborating with the Health Resources Administration to encourage the teaching of geriatric medicine to medical students, interns and residents, and practicing physicians, not as a new specialty but as an important body of knowledge. That is an example of an effective way we are collaborating.

Mr. EARLY. My concern is just that insofar as this is a new agency. I have no opposition to new agencies if they phase out some of the nonproductive old agencies. This doesn't phase out any. We have no recommendation for any decrease in aging, research, health, or other areas. This is an increase. I don't see where it is productive.

Dr. BUTLER. Well, part of the need for an increase in aging research is reflected in the demographic data which present the striking fact that the aged in our population will be increasing from 10 percent of the population over 65 to 17 percent by 2030.

Mr. EARLY. Your chart shows tremendous increases but your research into how we treat aging people does not affect where we go there?

Dr. BUTLER. That is correct; however, the chart does illustrate the importance of a healthy older population.

REORGANIZATION OF MEDICARE AND MEDICAID

Mr. EARLY. I read in this morning's paper that Mr. Califano was merging medicare and medicaid, et cetera. In your statement you say 60 percent of every dollar spent in health is there. What input have you had in this reorganization?

Dr. BUTLER. I have not had any personal input in this reorganization, but the reorganization makes very good sense to me. It will put in one place those programs which are related to health and health costs.

COST CONTAINMENT

Mr. EARLY. I have not seen a reorganization that did anything but spend more money in my 20 years in Government. Here is your agency and we are funding a new agency and we are reorganizing. Maybe the reorganization is going to abolish this agency we are just starting.

Dr. BUTLER. Of course, there are clear and obviously important relationships between research and health costs. Through research we may be able to contain costs in a very significant way. On the other hand, this agency created by the Secretary is regulatory in type and has a special mission which is very different from the mission and purpose of our Institute.

So while we should certainly know about the activities of other agencies, it is appropriate and understandable that there would not necessarily be the same level of coordination between this Institute and the medicare and medicaid offices as there would be between us and Federal agencies working in the field of aging.

Dr. FREDRICKSON. I would like to add a comment: The National Institute on Aging was created out of part of the National Institute for Child Health and Human Development. It was decided by the Congress that there needed to be some better emphasis, some way of bring-

ing to a focus the activities that were relative to aging—to give a new prominence to a problem which has been somewhat neglected in biomedical research and, more particularly, in the field of medicine in general.

I think what Dr. Butler is trying to do, in great part, is to provide a new focus on the fact that aging people are different, in the way in which they handle drugs, for example, and in their reaction to many diseases.

One of the great deficiencies in American medical education is this lack of people who really do have an expertise in the biological differences between aged and younger people.

Now if this Institute can give an appropriate focus to such problems, without an exaggerated attempt to simply extend the biological time of man, I think it can provide a new balance and an important new direction to research that has not been very much emphasized in the past, such as behavioral and social science research which is a relatively new aspect of biological and biomedical science.

This Institute is young. It is just beginning. But I am encouraged by the fact that I think it probably does provide a focus and that it is now taking a lead, as an agency, in attempting to introduce as much as possible, the scientific method into all the aspects of the Government related to aging.

Mr. EARLY. I agree with that. I want to assist, Dr. Butler, in any small way I can to get down that road. But we don't face up to the fiscal realities. We have to remove responsibility from other places.

I read your statement about reducing the stagnant number of people aging in nursing homes right now and what it will project in accordance with this chart.

In Massachusetts the mental health department had the same type of statistics showing us all these older people that were living in rural towns, farming, et cetera, and they brought in a whole new scheme where we uprooted them and put them into the cities, back into the mainstream. That program was a failure.

We have a very good set of statistics, but we are paying an awful price for it because these people are out on the urban streets with no place to go. I just hope that doesn't happen here. To achieve the goal of reducing the number of aged in nursing homes, if we do it just to establish statistics. I think that is a massive fraud.

Dr. BUTER. May I comment?

Mr. EARLY. Yes.

Dr. BUTLER. The alternatives to nursing home care through provision of foster care or home helpers, as they call them, is one route and that is what I think you are referring to principally.

What we are talking about is finding the causes of the many conditions that make it necessary for people to enter nursing homes such as broken hips and incorrect or excessive medication. If we can prevent people requiring nursing home care in the first place, then the expensive home support services to which you refer may never be necessary, or may be utilized to a lesser degree.

We are talking about basic prevention of the need for nursing home services through the production of new knowledge which lead to the ultimate cost containment.

Mr. EARLY. I think that is a right road to travel but I also think with regard to research we have been on the same path too long. I don't think NIH has tried enough alternate plans. The chairman is always bringing up how grants are awarded, et cetera. But with regard to the aged, I don't think we have reexamined the system for many years.

Dr. BUTLER. This is a new focus. I have found NIH extremely congenial and collegial in the establishment of the National Institute on Aging.

Mr. EARLY. We are also interested in new agencies which can be productive and not just rhetoric. We have to make some tough decisions and I hope that we will shift more responsibility to this agency, and more money, and see if they can't produce more.

Thank you.

Mr. FLOOD. Mr. Michel?

Mr. MICHEL. Thank you, Mr. Chairman.

Welcome to the subcommittee, Dr. Butler and congratulations, too, on your having won the Pulitzer Prize last year for the book, "Why Survive; Being Old in America."

Dr. BUTLER. Thank you.

SUMMARY OF "WHY SURVIVE"

Mr. MICHEL. Could you capsule what the real theme of that book was?

Dr. BUTLER. Of course, the title was meant to be ironic to get people to think about the fact that people must, do, and inevitably will survive. We have to face up to the fact that in this century we had an unexpected increase in the numbers of older people that caught us unawares. We must bring the institutions such as medical facilities, nursing homes, and work policies up to date so that all of us, not just older people today, but you and I and everyone, can expect a more decent older age.

SUMMARY OF "SEX AFTER SIXTY"

Mr. MICHEL. I note from your biography that you also authored a book last year entitled "Sex After 60". What was the nature of that book? Did you have any good suggestions? I am sorry I did not read it.

Dr. BUTLER. I commend it to anyone.

Mr. MICHEL. Whether he is 60 years old or not?

Dr. BUTLER. It is a serious, thoughtful book. Many people thought that as people grow older the human need for closeness and sexual activity automatically and inevitably declines and it does, but not to the degree to which it had been previously thought.

This book is a practical guide for people who have had heart attacks, serious arthritis and strokes, and many impacting diseases which may lead them to be fearful about the conduct of a normal human process. We address that, we hope, in a thoughtful manner.

MANDATORY RETIREMENT

Mr. MICHEL. I recently introduced legislation which would in essence prohibit mandatory retirement because I felt such requirements

did discriminate against many elderly persons who might have a number of good working years ahead of them. I think the aging process might in fact be speeded up by forced, premature retirement.

I am sure you probably have a number of thoughts on this subject. Would you mind just commenting very briefly and, if necessary, expanding on the record? I know there are all kinds of factors that come into play here. I have argued a number of years back when there were attempts to lower the retirement age, and aside from the increased burden to pay the benefits in a smaller and smaller group, that as life expectancy was increasing we probably ought to do just the reverse and think of expanding the number of work years. What is your thought on that?

Dr. BUTLER. As Dr. Fredrickson said, one of the special opportunities of this Institute is to support research in the social and behavioral aspects of aging. The impact of retirement is very profound for many people.

We also need to be prepared should legislative or judicial changes end mandatory retirement requirements by having available an adequate base of scientific knowledge for introducing flexible retirement through assessment techniques, biomedical vitality, intellectual ability, and social competence.

This is the kind of research which we do want to support and already have supported to some extent.

DIFFERENTIAL LIFE EXPECTANCY

Mr. MICHEL. What is the percentage of persons over 65? I think in your statement you say by the year 2000——

Dr. BUTLER. It is 10 percent today.

Mr. MICHEL. I have been using for the last year or so figures that would indicate today we have three people working for every one person who is retired in one form or another. If all the projections stay the same, by the year 2000 there are only going to be two people working for every one retired within those few number of years which really should cause us to do a great deal of rethinking about some of the things we legislate around here.

Now, women currently have a longer lifespan than men, but everyday we hear more about how many more women are being integrated into the work force. Have we got any indication at all that that fact will tend years ahead to narrow the gap between the life expectancy of men and women in that they will be subjected to the same kind of strains and what-not that supposedly contribute to men dying quicker than women?

Dr. BUTLER. My reading of the information so far does not speak to this being the case. The causes are probably much more complicated than that. Perhaps stress and strain bears some relationship, but even at birth the greater number of male babies compared to female babies is one indication of a different level of vigor between the two sexes. This difference is probably based on such factors as genetic programing, hormones, or diseases. Even high risk occupations contribute to the lower life expectancy of males.

We don't have any clear evidence that stress per se is the major factor accounting for this.

Mr. MICHEL. The adoption of the equal rights amendment will not change that physical difference between the sexes?

Dr. BUTLER. No. I mentioned our longitudinal study in which we plan to examine groups of women to try to understand the variety of factors inherent in this physical difference.

RESEARCH PLAN ON AGING

Mr. MICHEL. Could you summarize for us the key points in the HEW-wide research plan for aging?

Dr. BUTLER. Well, the plan is divided into three areas: biomedical research, social and behavioral research, and health service delivery.

Our concern in our Institute is primarily with the first two. We attempted to identify both short-term and long-term goals for basic and applied research. Some of the short-term goals would be in the areas of pharmacology, to understand better how drugs are absorbed and handled by the body as the person grows older; immunology, to determine how evidence from animal studies of decreasing effectiveness of the immune system with age is applicable to human beings; and neurosciences, to determine the different factors leading to the condition known as senile dementia.

Those are some of the questions that lend themselves to direct and immediate benefits to older people and their families today.

In the long term, differential life expectancy between the sexes is less likely to produce immediate results, although we need to begin our research now. We tried to very practically divide our objectives between those where we could hope to have some early information from those that would take longer.

GERIATRIC MEDICINE

Mr. MICHEL. Now your statement indicates concern that only 4 percent of your extramural grants were in the area of investigative medicine. Does that mean you are going to increase the percentage in this coming year?

Dr. BUTLER. Of course, we must and should respond to the investigator-initiated research that comes from around the country. If the research proposals in clinical investigative medicine are of high quality, they will be supported. We don't want to support poor proposals, so we won't arbitrarily support an area unless high quality proposals are submitted to us.

We are trying to stimulate the interest of the American medical community in the subject matter of aging. That doesn't only mean physicians but also individuals in departments of pharmacology, chemistry, anatomy, and pathology. We hope that investigators from these areas will produce innovative ideas for consideration by our study sections and advisory council.

Mr. MICHEL. How would you characterize the quality of the grant applications you have received?

Dr. BUTLER. They have been getting better and better. Studies of program statistics going back to when the Institute was part of the National Institute for Child Health and Human Development indi-

cate that there has been a considerable improvement in the quality and priorities in the grant applications that come to us.

Mr. MICHEL. I am glad to hear you say that. I know up here all you have to do is say aging or something for the elderly and right away you get a more receptive ear. You get an extra $10 or $50 million depending upon who is offering the amendment and what bill it is.

I got the general impression that initially as we began expanding our interest in this area, that you really didn't have to have all that good an application to get a favorable nod. I hoped they were improving in their quality and character and there is something more behind it than simply catering politically to that vast number of growing people in the aged area.

Dr. BUTLER. I don't think we would serve medical and biological research by supporting projects that are not of the highest quality.

Mr. MICHEL. Thank you.

EPIDEMIOLOGY OF AGING

Mr. FLOOD. You are asking for a unit on epidemiology, demography, and biometrics. You are justifying this on the basis that in order to measure improvement in the health status of the elderly you must consider incidence, prevalence, and distribution of diseases that affect the elderly.

Now, of course, I hope you are not going to go out and start collecting all kinds of data that is already available over at NIH. You are not going to do that, are you? When I look at the Eye Institute Information we have here, they tell me 50 percent of the people with glaucoma are over 65. What is that unit of yours going to do?

Dr. BUTLER. It has several purposes, a crucial one being coordination. It will relate to the other institutes at NIH, the National Center for Health Statistics, the Census Bureau, and the Social Security Administration so as to utilize data produced by those agencies whenever possible. We need to have one area that is devoted to consideration of age and the antecedents to the varieties of diseases affecting older people.

Mr. FLOOD. For the record you had better develop that one and show how the epidemiology unit will avail itself of the data available at each institute that you mentioned as well as the National Center for Health Statistics and, as you mentioned also, the Social Security Administration.

[The information follows:]

Although there has been considerable epidemiological and demographic data collected, there has not been a systematic analysis and interpretation of this data using the parameter of age. I have therefore, created the Office of the Associate Director for Epidemiology, Demography, and Biometry to coordinate, promote, and conduct research to isolate factors of normal aging from disease in the elderly in such areas as differential life expectancy, nutrition, osteoporosis, immunology and endocrinology. Investigations will cover both biomedical and psychosocial aspects of aging. Important research questions have been identified for investigation including the following:

What are the precursors of various chronic diseases (Alzheimer's disease/senile dementia and hardening of the arteries) in the elderly?

How do endocrine and immune functions relate to morbidity and mortality?

What are the antecedents of differential life expectancy among racial and ethnic groups and between the sexes?

What can we learn from studying the effects of retirement, relocation, bereavement, and economic loss in cohorts of elderly persons?

The research will coordinate the use of date which has been or will be collected primarily by the National Center for Health Statistics, U.S. Bureau of the Census, the Social Security Administration, the World Health Organization and the other institutes at NIH to prevent duplication of effort and to facilitate dissemination of information to the research community and to the public. The research findings of this office will be used to develop new knowledge and research leads, to assist in establishing program priorities and to improve research study design within the intramural and extramural programs of the National Institute on Aging. The office will serve as a focal point for information on longitudinal studies supported by public and private institutions to ensure maximum benefit from existing data collections. Efforts will also be made to exploit the resources already created by former longitudinal studies such as the Framingham Study and the Thousand Aviator Study.

Two positions have been assigned to this function initially. A biostatician, a demographer, and a statistical clerk would provide additional necessary expertise.

Dr. BUTLER. The executive staff has been developing a status report about the Institute as of the end of these first 9 months I have been Director. We have been looking at its early capitalization, and I can provide that report for the record.

[The information follows:]

THE NATIONAL INSTITUTE ON AGING

A REPORT TO THE DIRECTOR

INTRODUCTION

As you near completion of your first year as director of the Institute, it is an appropriate time to consider some of the accomplishments, failures, problems and opportunities that have and will face this Institute during the recent past and the foreseeable future. As you have requested, this brief report highlights the primary factors that characterize the current status of an Institute with a broad mandate in an exciting field. The report deals primarily with the administrative environment within which we function but includes an assessment of programmatic resources that have been made available to carry out the broad legislative mandate of the Research on Aging Act of 1974. This assessment is important because the establishment of this Institute has led to a surge of public interest and rising expectations that have exceeded the capacity of our new organization.

ORGANIZATIONAL SETTING

In creating the National Institute on Aging, Congress showed that it understood a critical national need, the need to find new knowledge about the aging process and so find new ways of preventing, modifying, or even reversing various aspects of that process--particularly its deleterious effects and the accompanying diseases and disabilities. The Congress also reaffirmed its confidence in the National Institute of Health by placing the National Institute on Aging within this research agency of rare excellence. Our warm reception by the community at the National Institutes of Health, and more practically, the collaboration agreed upon by the Institutes for research projects of mutual interest and benefit has been most helpful. The jointly sponsored conferences that have been held during the past year lay the groundwork for mutually supported substantive research programs in the future.

DEVELOPMENT OF THE INSTITUTE

The core programs of the National Institute on Aging, consisting of approximately $16 million and 173 positions, were transferred from the National Institute of Child Health and Human Development. These programs were the intramural research program with 158 positions, the extramural program with 10 positions, and 5 positions for administration of the Institute including the program direction, administrative, budget, personnel management, planning and program analysis functions. The FY 1976 appropriation bill included 20 additional positions and an increase in funds of $3.3 million. Nine of the 20 positions are being used to strengthen the programmatic and administrative management of the grants and contracts program. Most of the remaining eleven are being used for key staff such as a deputy director, an epidemiologist, a scientific director, an information officer, a budget officer and the executive officer. The FY 1977 appropriation included 7 positions and an increase of $10.7 million. Five of these positions are being used in the intramural program for an expansion of the Baltimore Longitudinal Study to include women and 2 positions

were used in support of the grant and contract programs. Thus, the Institute has available in FY 1977 200 budgeted positions and $30.0 million. All of these positions either are filled or active recruitment is underway.

THE IMPACT OF A GROWING NUMBER OF ELDERLY

The social context within which the Institute must operate is characterized by major demographic changes. The number of elderly in this nation has increased and will continue to increase dramatically. These changes have not been anticipated, and, as they continue, our Institute must try to minimize the number of frail and dependent elderly by helping people retain the health of their middle years. This action is critical to containing the extraordinary costs associated with the diseases and disabilities of late life. A research program that includes initiatives that were not a part of the aging program previously supported as a part of the National Institute of Child Health and Human Development is required.

PROGRAM BALANCE

The programs that the Institute has continued to support or develop within available funds and manpower leave certain critical areas either under represented or unrepresented. Many of these areas involve research that has potential for reducing family anguish, reducing health care costs and/or addresses major clinical problems.

The problem of senile dementia is a case in point. Each of us fears loss of mental ability with age. Perhaps as many as 50% of the 1.2 million people in nursing homes are there because of impaired mental capacity. Our Institute should give high priority to reducing the need for costly institutional care and the family anguish that accompanies senile dementia. Currently, however, our intramural research program has no neurosciences component to address this problem. Our best estimate is that 12 professional, 10 support positions, and annual funds of $1.5 million are needed to conduct an effective program.

Understanding the effects of drugs in the elderly is another important area. The often unexpected effects of drugs, either singly or in combination, in the elderly leads to falls and fractures or confusional episodes often diagnosed as senility. Although we have one contract in this area we do not have an expert in pharmacology on our staff to conduct or monitor a program in geriatric pharmacology. Four professional positions, four support positions, and initial funds of $2.0 million are recommended for this function.

The application of advanced technology to the problems of the elderly holds great promise. Various prosthetic devices may reduce significantly the dependence of the elderly on expensive forms of health care, either in the home or in an institution. The Institute does not have a research

bioengineer and 2 support staff required to develop an effective program with the National Aeronautics and Space Administration or the National Bureau of Standards. We need this expertise, and initial funding of perhaps $2.0 million. It is difficult to provide an accurate estimate without staff knowledgeable in this area.

Nutrition is another important area. There has been no systematic survey of the nutritional status of this nation's elderly. Much can be learned about changing nutritional requirements with age and about the metabolism of nutrients in the elderly. To begin a research program in this area will require 5 professional and 8 support positions. This program can take advantage of the current longitudinal study, particularly as women are added to this study. Funding of $.6 million for intramural research and $2.0 million for grant and contract support is recommended.

The implications of a large number of elderly in our society are most apparent when one thinks of mandatory retirement and the ratio between working people and those dependent on them. A psychosocial expertise that focuses on retirement and its impact has immediate importance. This field is one, in particular, that has been lacking in support in the past and requires remedial action as soon as possible. A psychologist, a sociologist and one support person would initiate positive action if provided with a budget of $1.0 million.

CONCLUSION

The Institute has laid much of the groundwork for an expanded program by developing a core staff, by reviewing its current programs for weaknesses and gaps and by developing palns for some of the more critical areas that have been identified. It is clear that, to meet its broad mandate, the Institute requires the expertise, the supporting staff and other resources required to launch programs into areas that have not been adequately supported in the past.

BALTIMORE LONGITUDINAL STUDY

Mr. FLOOD. Last year the committee provided funds to your Institute for the purpose of adding women to the longitudinal study. Has this been done?

Dr. BUTLER. We have created the early designs for the addition of female subjects and will begin with the addition of the wives of the men who have been part of the original longitudinal study.

Mr. FLOOD. It has been going on?

Dr. BUTLER. We are beginning to recruit two senior scientists for this project, one in the field of endocrinology, an area which is clearly of importance in distinguishing the biological difference between the sexes, and one in heart disease because of the high incidence of heart disease in men.

Mr. FLOOD. How many women in total will be included in this longitudinal study?

Dr. BUTLER. We are going to begin slowly, probably with samples of 50 each. Over the next several years we will not be likely to have more than 200 women added to this study.

Mr. FLOOD. What are some of the more important findings of the longitudinal study in men? I am thinking about good health, longevity, diet, exercise, and life style, and so on.

What are a couple of the most important things?

Dr. BUTLER. It has been very important to develop baseline data, so we can understand and compare diseases. For instance, sometimes we may diagnose as disease something that is a normal decrement of age. We need to have techniques for measuring kidney clearance. A nomogram which shows the filtration rate and function of the kidney has been one result of the male longitudinal study.

The glucose tolerance work is another finding of the longitudinal study. This enormous collection of information regarding normal rates and types of change in glucose metabolism with age has been very important. We hope soon to have a full report of this research.

NUTRITION AND AGING

Mr. FLOOD. Last year we talked at some length about one of your grantees studying diet and age. Of course, that intrigued everybody all over the room. Can you give us a little update? What activities are you planning in this area of nutrition and aging?

Dr. BUTLER. We are not in a position to move at this time because of a lack of resources in personnel in nutrition, but we are beginning the planning in any case. We don't know the nutritional requirements that change with age. We don't have adequate information about the nutritional status of older Americans. We don't know about the differences and needs of trace elements. We know from some animal studies that protein restriction relates to longevity, but does that occur in the older animal and will it ocur in the human as they grow older?

So we have at least four questions in the area of nutrition to explore.

Mr. FLOOD. What work is being done to explore the progressive mental deficiency of the elderly?

Dr. BUTLER. Memory is a pervasive problem among older people and has been rarely studied in terms of a longitudinal progression. We have studies of visual retention which deemphasizes the importance of words and language and provides a more effective way of examining the loss of memory.

These studies have shown the changes do not occur as early as has been thought, and when they do occur, are more related to diseases than normal aging. When memory loss occurs, cues can be built to help the individuals overcome the loss through the use of auditory pathways.

A principle that has been operative in our laboratories is to look not only at the decrement but also to search for ways of overcoming the decrement.

SENILE DEMENTIA

Mr. FLOOD. What is the research all through NIH regarding senile dementia?

Dr. BUTLER. The National Institute of Neurological Communicative Disorders and Stroke, the National Institute of Mental Health, and the National Institute on Aging support no more than 17 research grants in senile dementia.

Mr. FLOOD. Is there any breakthrough on the horizon?

Dr. BUTLER. There have been promising leads, including some interesting information regarding the presence of aluminum in the plaques which are characteristic of Alzheimer's disease, a condition which is probably the same as senile dementia. There has been work connected with autoimmune mechanisms. It is for that reason we are collaborating with other institutes.

Mr. FLOOD. We seldom ask questions like this, but could NIH be doing more in the area of senile dementia if funds were available?

Dr. BUTLER. Yes; we feel there are enough promising leads from four or five different schools of thought that would produce important research in diagnosis and causation of senile dementia. There is some question as to whether senile dementia is one condition or a variety of different states.

Mr. FLOOD. What progress are you making with your biofeedback technique? That is supposedly to help the elderly control hypertension and other ailments.

Dr. BUTLER. One condition, fecal incontinence, has been controlled. This is a serious problem which afflicts people in nursing homes. We are collaborating with the Veterans' Administration in testing this technique on a larger group of people.

INSTITUTIONALIZATION OF THE ELDERLY

Mr. FLOOD. You point out in your statement the high cost of institutionalizing the elderly. We have heard it said quite a good deal that many people at a nursing home simply don't belong there, but they are there because of misdiagnosis.

What about that?

Dr. BUTLER. We have an estimate, which probably requires reexamination, that up to as much as 13 percent of the older population in

nursing homes is misdiagnosed as having senility. If the cause of that intellectual confusion had been effectively treated, they would probably not have entered nursing homes.

Mr. FLOOD. What is the Public Health Service doing to help the practicing physician better understand the particular medical problems of the elderly?

Dr. BUTLER. As I indicated earlier, I am pleased to say we have been meeting with representatives of the Health Resources Administration which is part of the Public Health Service, and are planning a conference to bring together representatives of medical schools for discussions of the transfer of information. We also have had a series of workshops on this subject, the first of which was through the American Geriatrics Society. We are organizing another such meeting to discuss the incorporation of the body of knowledge related to the change in human physiology with age in the curriculums of medical schools.

SLOWING THE AGING PROCESS

Mr. FLOOD. You know, Doctor, it is very difficult to talk about your Institute at all without having someone right away ask, are there any forthcoming breakthroughs now regarding the slowing down of the aging process? Do you have anything to say about that?

Dr. BUTLER. Well, I am always hesitant to be too extravagant in those areas. Certainly simple matters, exercise and nutrition, do seem to bear upon the reduction of morbidity and the enhancement of the quality of life in older people. There is some data from human and animal work. If we are able to extrapolate the animal data on the immune system to humans, then certainly there would be an increased capacity to reduce infection and reduce morbidity in the later years.

COORDINATION AT NIH

Mr. FLOOD. Before I finished my questions with you, I am impressed by one sentence in the opening statement, "Collaboration is the most effective way to utilize limited resources."

I couldn't have said that one better myself. That is quite a statement. That is the message that this committee has been trying to get across to NIH for years and years. So I am very happy that you agree. I hope all your colleagues at NIH understand it and see it your way.

Thank you very much.

[The following questions were submitted by Members of the Subcommittee with the request that they be answered for the record.]

MR. STOKES

RACIAL AND ETHNIC FACTORS IN LIFE EXPECTANCY

Mr. STOKES. Dr. Butler on page 3 of your testimony you indicate that in order to see an improvement in the health status of the elderly we must consider "the differential life expectancy among ethnic groups." Dr. Butler are you saying that certain ethnic groups evince a propensity for diminishing longevity?

ANSWER. Yes, Mr. Congressman, ethnic groups in this country have a life expectancy which is below average.

Mr. STOKES. What specific ethnic groups are you referring to?

ANSWER. The ethnic groups which have lower than average life expectancy are Blacks, native American Indians and Spanish speaking Americans. Among the Asian American population, some groups such as Japanese, have life expectancies equal to that of white people, while other groups such as Filipinos have lower life expectancies. When our Epidemiology, Demography, and Biometry unit is established, the Institute will undertake studies in collaboration with the Census Bureau to unravel the racial and ethnic factors of life expectancy. We plan to look not only at the health problems, but also at the strengths of ethnic cultures such as family structure which help the elderly cope with their environment.

Mr. STOKES. Dr. Butler are you familiar with the findings of the vital statistics report of the National Center for Health Statistics which indicate that the life expectancy for the white population was 73.2 years and for the minorities it was 67.9 years?

ANSWER. I am familiar with these statistics.

Mr. STOKES. Dr. Butler do you agree with these findings and if so how does the National Institute on Aging plan to address the problem of the diminishing longevity of the minority aged?

ANSWER. At this time we are planning research on the social and biomedical causes and effects of differential life expectancy.

Mr. STOKES. Specifically what policies, programs and studies do you plan to pursue to correct this serious life expectancy differential?

ANSWER. We are now planning a workshop with representatives of ethnic minorities, Blacks, Spanish-speaking, Asian Americans and Native Americans to identify in depth areas of biomedical and psychosocial research of importance to the health of ethnic groups which the Institute would be able to support. We are working with the National Caucus on the Black Aged to stimulate interest and participation of minorities in health research. The Institute has already identified certain broad areas of research that pertain to the needs of minority groups and, as a result, will soon publish a request for applications for research in order to stimulate research projects aimed at understanding the racial, ethnic and socioeconomic factors affecting life expectancy. In addition, we are attempting to increase the opportunities for minority researchers in the field of aging through cooperation with the Minority Biomedical Support program of the Division of Research Resources and through discussions with the Administration on Aging and the National Institute of Mental Health. As findings become available, we intend to disseminate the information to the research community and the public.

MR. CONTE

FOREIGN AGING RESEARCH CENTERS

Mr. CONTE. What other nations have created major research centers to support and conduct research on aging? Are you involved in any cooperative efforts with these other countries' centers?

ANSWER. The nations which have created aging research centers in addition to the United States are Japan, Israel, the Soviet Union, Romania, France, and Holland, all industrialized countries. These nations, as a consequence of the explosion in both absolute numbers and relative proportions of older people in their populations, have made major commitments to research in the field of aging. Some other nations have created chairs of geriatric medicine, among them, the United Kingdom, Sweden, and Holland.

We are not currently involved in direct cooperative research efforts with these foreign centers. But we do maintain a close relationship through correspondence and communicate our research findings to each other. Through the World Health Organization, the Institute engages in international activities in the field of aging by lending personnel for short periods of time for work in the field of aging.

RESEARCH PLAN ON AGING

Mr. CONTE. Has the research plan for aging been completed? Could its major recommendations be placed in the record?

ANSWER. Yes, the plan has been completed. We would be pleased to submit the major recommendations of this plan for the record.

Summary Statement of the Research Plan on Aging

The research plan on aging, entitled "Our Future Selves" adressed itself to three areas: biomedical research, social and behavioral research, and health service delivery. It recommends a well-planned and carefully coordinated application of the pertinent scientific disciplines—genetics, biochemistry, epidemiology, demography, scoiology, psychology, anthropology, economics, political science, and others. With this discipline oriented approach, the methods of many sciences can be applied to a common problem and a cadre of highly trained researchers created, having as its central focus the problems of aging and the aged.

A number of initial, highly selected research priorities can be emphasized which include both short-term and long-term goals for basic and applied research. We now have an opportunity to extend our knowledge and to design effective programs to deal with many of the issues that concern aging and the aged. In some cases, we can move ahead fairly rapidly, with applicable returns on our research investment possible within 5 years; for other issues, their very complexity mandates a longer, more sustained effort, although significant improvement in our understanding is possible within several years.

Some of these issues are listed below, both those amenable to a short effort of about 5 years and those requiring a long-term investment:

BIOMEDICAL ISSUES

Short term

The decline in immunological competence with aging, and its implications.

Variations in the process of aging and the patterns of disease among the aged of different ethnic, racial, and cultural groups and between the sexes.

The interaction of aging and its accompanying diseases with such external factors as nutrition, physical fitness, and response to medicines.

Collaborative studies with other Institutes of the NIH and with other DHEW agencies of diseases more common to the aged—for example, diabetes mellitus, senile dementia (or mental deterioration), atherosclerosis, and osteoporosis.

Effective diagnosis and management of the reversible forms of senility.

Long term

The criteria for health and successful aging.

The mutually interacting influences of aging and disease.

Influence of cultural background on successful aging.

Personal and economic costs of major diseases in old age.

Prosthetic technology as an aid to the maintenance of an independent life.

BEHAVIORAL AND SOCIAL ISSUES

Short term

The social costs, system costs, and socioeconomic impact of an increased population of the elderly on communties, public and private services, and the elderly.

Flexible retirement policies, their advantages and disadvantages to the society at large and to the aged.

Occupational and social roles for older people.

Adjustments to crises of the lifecycle.

Support of income maintenance programs.

Long term

Relationships among family structure and support, lifestyles, and patterns of aging.

Middle age as a transition to old age.

Personality changes during life, from young adult to very old age.

Improvement and maintenance of memory.

The year 2000: the meaning and impact of the new age structure on American society.

ISSUES IN HUMAN SERVICES AND DELIVERY

Short term

Integrated services for the elderly.

Ready access by the elderly to prosthetic aids.

Structural and fiscal basis for improvements in medicare.

Self-care and its relationship to preventive medicine.

Living arrangements for the elderly.

Long term

The family as a health and social service delivery system.
Research base for care of the aged under a national health insurance system.
Educational opportunities for the aged.
The environment for long-term care.
Costs of health care in old age.

RESEARCH RESOURCES

Short term

Expanded training in geriatrics and gerontology.
Availability of animal and human populations for aging studies.

Long term

Information systems and research evaluation.
University based and regional centers for research on aging and the problems of the aged.

FUNDING OF COMPETING AND NONCOMPETING

Mr. CONTE. What accounts for your large increase in requested funds for noncompeting projects and the decrease in new regular projects?

ANSWER. A relatively large number of new research grants were awarded in 1977. These projects in addition to other commitments will be funded as noncompeting in 1978. As a result of these other commitments we have less money available to fund new research grants in 1978.

SENILE DEMENTIA

Mr. CONTE. Can you tell me about some of the work you are doing on what is often described as "senile dementia"? Is anything being done in the connection between malnutrition and the acceleration of the aging of mental processes?

ANSWER. We are currently collaborating with the National Institute of Mental Health and the National Institute of Neurological and Communicative Disorders and Stroke to develop a research program on senile dementia. There have been some promising leads in recent research on Alzheimer's disease, a condition which is probably the same as senile dementia. There has also been some work on the relationship between the immune system and senile dementia.

The relationship of nutrition to aging of the mental processes is a research area of great importance and one in which our efforts are restricted at present by a lack of resources. The Institute conducts nutrition research in order to better understand the nutritional requirements of the elderly and the relationships between nutrition and age. Specific research projects seek to identify the effect of age on nutritional status in a population where food intake is not markedly influenced by economic needs. Other studies attempt to relate nutritional status to a variety of physical and biochemical variables influenced by age. Research also attempts to identify the biological mechanism by which lifespan is increased by caloric and/or protein restriction.

We still need to gain basic knowledge about the nutritional status of the elderly, the impact of direct infusion of nutrients such as protein supplements before surgery, the effect of high starch and high sugar diets, the interactions of nutrients and medication, and the elderly's need for vitamins, trace elements, fats, carbohydrates and protein. In addition, there is need for research on the psychological influences on eating habits. We know that the symptoms of senility in some elderly people are caused by anemia resulting from poor nutrition. Apathy, loneliness, and depression may contribute to poor eating habits.

RESEARCH PLAN ON AGING

Mr. CONTE. What immediate steps will you be taking to implement the aging research plan?

ANSWER. To the extent resources permit, our budget does in fact reflect the recommendations of this plan. We are currently evaluating our intramural and extramural efforts in the two areas of the departmentwide plan of primary concern to this Institute, specifically, the areas of biomedical research and social and behavioral research. We will continue our efforts in these areas as well as planning for or implementing activities in pharmacology, immunology, senile dementia, epidemiology and differential life expectancy, and nutrition.

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AGED ANIMAL MODELS

Mr. CONTE. What is being done to increase the availability of aged animals for your research studies?

ANSWER. A major part of our program is the development of animal models with known genetic background. A rat is considered aged at 28 months, a dog at 10 to 12 years. It therefore requires considerable leadtime to produce animals useful for aging research. We must do preliminary studies of pathology, anatomy and genetics to determine what strains of animals are best suited for research aimed at understanding the human aging process. After selecting the strains it is necessary to breed and rear the animals in controlled laboratory environments. Because different models are often required for each human characteristic or disease studied, development of these models is a constant effort. To help contain the cost of animal models, we are also conducting research on simpler organisms such as cell lines; nematodes (worms), which live about 30 days; and salmon which age quickly after spawning.

BALTIMORE LONGITUDINAL STUDY

Mr. CONTE. Can you tell me more about the Baltimore Longitudinal Study? How long has it been going on? What has been learned from it? What do you anticipate learning from it?

ANSWER. The Baltimore Longitudinal Study was begun in 1959 and is currently composed of 650 men. The basic purpose of the longitudinal study is to develop baseline data for describing the normal process of aging. Using the baseline data, we can then more accurately diagnose disease states and conduct research on treatment and prevention of disease in the elderly. One recent achievement of the longitudinal study is the development of a nomogram which shows the relationship of age to the filtration rate of the kidney and which is of practical use to physicians in diagnosing abnormal kidney function.

We have also studied the change with age in glucose tolerance. This information is helpful in containing the cost of health care by providing guidelines for determining whether an elderly patient is diabetic or is exhibiting a normal, age-related decrement in glucose tolerance. Biofeedback techniques have been developed for controlling hypertension and fecal incontinence and will soon be tested in collaboration with the Veterans' Administration.

The elderly sometimes experience a loss of memory. In the longitudinal study we are developing methods to promote learning and memory in the elderly by teaching the use of mnemonic techniques.

Past accomplishments of the longitudinal study include studies which showed that if a person stopped smoking, the lungs would be virtually as healthy after two years as the lungs of a person who had never smoked. The longitudinal study has also been concerned with the effect of alcohol on the aged, cardiovascular function, and exercise as a method of improving health.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Amounts Available for Obligation 1/

	1977	1978
Appropriation.....	$30,000,000	$34,500,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $10,000; 1978 - $20,000.

National Institute on Aging

Budget Mechanism

	1977 Estimate			1978 Request		
	No.	FTE 1/	Amount	No.	FTE 1/	Amount
Research grants:						
Regular program:						
Noncompeting projects..	76	---	$8,886,000	195	---	$13,891,000
Competing renewals.....	20	---	1,630,000	15	---	1,271,000
New.....	131	---	6,943,000	57	---	4,896,000
Supplemental.....	(7)	---	85,000	(7)	---	87,000
Subtotal.....	227	---	17,564,000	267	---	20,145,000
Special programs:						
Special center program.	---	---	---	2	---	600,000
Res. career dev. awards	4	---	88,000	6	---	140,000
Subtotal.....	4	---	88,000	8	---	740,000
Total, research grants.....	231	---	17,652,000	275	---	20,885,000
Training programs:						
Indiv. - Non-competing...	16	16	236,000	13	13	194,000
New.....	12	12	180,000	20	20	300,000
Subtotal.....	28	28	416,000	33	33	494,000
Inst'l. - Non-competing..	9	73	1,090,000	11	104	1,496,000
Competing.....	---	---	---	---	---	---
New.....	3	40	694,000	---	---	---
Subtotal.....	12	113	1,784,000	11	104	1,496,000
Total, training program....	40	141	2,200,000	44	137	1,990,000
Research and dev. contracts	19	---	1,917,000	20	---	2,058,000
Intramural research.....	---	---	6,266,000	---	---	7,270,000
Direct operations.....	---	---	1,418,000	---	---	1,729,000
Program management.....	---	---	547,000	---	---	568,000
Total, NIA.....	290	141	30,000,000	339	137	34,500,000

1/ Full-time equivalent.

DHEW - National Institutes of Health

CROSSWALK - 1977 Column of 1978 Justification

INSTITUTE: National Institute on Aging

Mechanism / Program	Research Grants						Laboratory and Clinical Research	Research and Development Contracts	Direct Operations	Program Mgmt.	Total
	Regular Program		Specials		Training Programs						
	Non-competing	Competing	Multi-disciplinary Centers	Other	Indiv.	Institution.					
1. Aging.....	$8,886,000	$8,678,000	---	$88,000	$416,000	$1,784,000		$1,917,000			$21,769,000
2. Intramural research							$6,266,000				6,266,000
3. Direct operations									$1,418,000		1,418,000
4. Program management										$547,000	547,000
Total obligations	8,886,000	8,678,000	---	88,000	416,000	1,784,000	6,266,000	1,917,000	1,418,000	547,000	30,000,000

DHEW - National Institutes of Health

CROSSWALK - 1978 Column of 1978 Justification

INSTITUTE: National Institute on Aging

Mechanism / Program	Research Grants						Laboratory and Clinical Research	Research and Development Contracts	Direct Operations	Program Mgmt.	Total
	Regular Program		Specials		Training Programs						
	Non-competing	Competing	Multi-disciplinary Centers	Other	Indiv.	Institution.					
1. Aging.....	$13,891,000	$6,254,000	$600,000	$140,000	$494,000	$1,496,000		$2,058,000			$24,933,000
2. Intramural research							$7,270,000				7,270,000
3. Direct operations.									$1,729,000		1,729,000
4. Program management										$568,000	568,000
Total obligations.	13,891,000	6,254,000	600,000	140,000	494,000	1,496,000	7,270,000	2,058,000	1,729,000	568,000	34,500,000

Summary of Changes

1977 Estimated obligations	$30,000,000
1978 Estimated obligations	34,500,000
Net change	+4,500,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Annualization of 1977 position increase	---	$70,000	---	$+83,000
2. Within-grade grade pay increases	---	67,000	---	+33,000
3. Wage board pay increases	---	156,000	---	+2,000
4. Federal Employees Compensation Fund	---	5,000	---	+7,000
5. NIH service and supply fund increase	---	300,000	---	+30,000
6. Federal Telecommunications System charges	---	---	---	+2,000
7. Gerontology Research Center maintenance contract	---	830,000	---	+36,000
8. Payment for centrally furnished services (Standard level user charge)	---	869,000	---	+58,000
	---	(129,000)	---	(+4,000)
Subtotal	---	---	---	+251,000
B. Program:				
1. Research grants				
a. Noncompeting continuations	---	8,972,000	---	+8,719,000
b. Competing	---	8,678,000	---	+6,906,000
2. Individual training:				
a. Noncompeting continuations	---	236,000	---	+180,000
b. Competing	---	180,000	---	+300,000
3. Institutional training:				
a. Noncompeting continuations	---	1,090,000	---	+580,000
4. Research contracts:				
a. Renewal	---	818,000	---	+1,010,000
b. New	---	1,099,000	---	+400,000
5. Intramural research	163	6,266,000	---	+862,000
6. Direct operations	21	1,418,000	---	+220,000
7. Program management	16	547,000	---	+18,000
Subtotal	200	---	---	+19,195,000
Total, increases	---	---	---	+19,446,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Decreases:				
A. Built-in:				
1. One day less pay.....	---	$4,480,000	---	$-15,000
B. Program:				
1. Research grants				
a. Noncompeting completed.....	---	8,972,000	---	-3,714,000
b. Competing completed or converted to noncompeting.....	---	8,678,000	---	-8,678,000
2. Individual training				
a. Noncompeting completed.....	---	236,000	---	-222,000
b. New converted to noncompeting.....	---	180,000	---	-180,000
3. Institutional training				
a. Noncompeting completed.....	---	1,090,000	---	-174,000
b. New converted to noncompeting.....	---	694,000	---	-694,000
4. Research contracts				
a. Renewal completed..	---	818,000	---	-170,000
b. New converted to renewal.....	---	1,099,000	---	-1,099,000
Subtotal.....	---	---	---	-14,931,000
Total, decreases...	---	---	---	-14,946,000
Total, net change..	---	---	---	+4,500,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
86	Aging.....	---	$21,769,000	---	$24,933,000	---	$+3,164,000
88	Intramural research.....	163	6,266,000	163	7,270,000	---	+1,004,000
	Standard level user charge...		(107,000)		(112,000)		(+5,000)
89	Direct operations	21	1,418,000	21	1,729,000	---	+311,000
	Standard level user charge...		(22,000)		(21,000)		(-1,000)
90	Program mgmt....	16	547,000	16	568,000	---	+21,000
	Total obligations.....	200	30,000,000	200	34,500,000	---	+4,500,000
	Standard level user charge...		(129,000)		(133,000)		(+4,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	200	200	---
Full-time equivalent of all other positions	28	28	---
Average number of all employees	219	219	---
Personnel compensation:			
Permanent positions	$3,548,000	$3,641,000	$+93,000
Positions other than permanent	273,000	298,000	+25,000
Other personnel compensation	78,000	85,000	+7,000
Subtotal, personnel compensation	3,899,000	4,024,000	+125,000
Personnel benefits	581,000	590,000	+9,000
Travel and transportation of persons	95,000	127,000	+32,000
Transportation of things	22,000	17,000	-5,000
Rent, communications, and utilities	110,000	132,000	+22,000
Printing and reproduction	37,000	44,000	+7,000
Other services:			
Res. & develop. contracts	1,917,000	2,058,000	+141,000
Payment for centrally furnished services	869,000	927,000	+58,000
Other	1,498,000	2,344,000	+846,000
Supplies and materials	761,000	913,000	+152,000
Equipment	359,000	449,000	+90,000
Grants, subsidies and contributions	19,852,000	22,875,000	+3,023,000
Total, obligations by object	30,000,000	34,500,000	+4,500,000

Significant Items in House and Senate
Appropriation Committee Reports

Item	Action taken or to be taken
1977 House Report	
1. The Committee directs that some of the increased funds and staff be used to include women in the Baltimore Longitudinal Study.	1. Four positions and approximately $300,000 are being used to plan for the addition of women to the Baltimore Longitudinal Study.

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act Section 301 - Research and Investigations, in general...	Indefinite	---
Public Health Service Act Title IV, Part H -- National Institute on Aging..	Indefinite	$33,025,000 2/
Title, IV, Part I -- National Research Serv. Awards	1/	1,475,000 3/

1/ Authorization expires September 30, 1977; extension legislation is pending.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $515,000 for old training programs.

National Institute on Aging

COMPARABLE 1/

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1975 2/.....	$14,728,000	$14,922,000 3/	$16,622,000	$15,822,000
1976.....	16,290,000	15,626,000 4/	20,626,000 4/	19,388,000 5/
1977.....	26,220,000	29,200,000	31,200,000	30,000,000
1978.....	34,500,000			

NOTES:

1/ The figures presented in this table have been adjusted to reflect the transfer of major functions. This permits a more objective comparision of the amount contained in the budget year with amounts in prior years.

2/ Comparable amounts for aging (previously included within NICHD) for 1974 and previous fiscal years are not available due to the change in the budget activity structure from a mechanistic presentation to a programmatic presentation.

3/ Excludes amounts for research and development contracts which were not considered by the House due to the lack of authorizing legislation.

4/ Excludes fellowships and training grants not considered due to pending legislation ($1,762,000).

5/ Includes $1,762,000 for training programs authorized by the continuing resolution.

National Institute on Aging

ACTUAL

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1976 1/	$16,190,000	$15,526,000 1/	$20,526,000 1/	$19,288,000 2/
1977	26,220,000	29,200,000	31,200,000	30,000,000
1978	34,500,000			

NOTES:

1/ Excludes fellowships and training grants not considered due to pending legislation ($1,762,000).

2/ Includes $1,762,000 for training programs authorized by the continuing resolution.

Justification

National Institute on Aging

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Aging.....	---	$21,769,000	---	$24,933,000	---	$+3,164,000
Intramural research.	163	6,266,000	163	7,270,000	---	+1,004,000
Direct operations...	21	1,418,000	21	1,729,000	---	+311,000
Program management..	16	547,000	16	568,000	---	+21,000
Total obligations...	200	30,000,000	200	34,500,000	---	+4,500,000

General Statement

The National Institute on Aging (NIA), established to coordinate, conduct and promote research into the biomedical, behavioral, social and economic aspects of aging, will be in the third year of operation as an independent Institute in fiscal year 1978.

In accordance with its directive from Congress, the Institute has accomplished the following:

1) Appointed its first Director and begun development of essential staff resources for conducting expanded programs;
2) Prepared and transmitted to Congress a comprehensive research plan entitled Our Future Selves: A Research Plan Toward Understanding Aging for the Department of Health, Education, and Welfare.
3) Launched a special research grant program to attract new investigators into the field of aging;
4) Designed a program to incorporate women into the Baltimore Longitudinal Study,
5) Begun expansion of research grant support into sparsely funded areas such as clinical research and research on the behavioral and social aspects of aging;
6) Initiated steps to insure coordination with other agencies concerned with research on aging within the National Institutes of Health, the Department and elsewhere within the Federal Government.
7) Initiated an analysis of currently available data on drug-drug interactions in middle-aged and older adults.
8) Continued to develop animal models of known genetic background suitable for aging research.

These efforts are the first steps necessary to address the quality of life for elderly Americans.

The vast increase in the absolute number and relative proportion of older people in our society illustrates the need for a strong aging research program. Individuals over 65 comprised 3% of the population in 1900, nearly 10% by 1972, and are projected to comprise approximately 20% by the year 2020. Approximately 3 million Americans were over 65 in 1900, 20 million by 1972, and 43 million may have passed this milestone and remained alive in the year 2020. These age-structure relationships will bring many changes in our society. Anticipating and understanding these changes may help alleviate some of the dysfunction and discomfort that could result.

Aging research may also assist in containment of spiraling health care costs for the elderly. In 1975, the Federal Government spent approximately $17 billion or 60 per cent of its health care dollars, for the elderly. Only two-tenths of one per cent of this amount was spent on research directly related to aging within the Department of Health, Education, and Welfare. More adequately financed research programs that lead to improvements in the health status of older Americans could have a direct impact on expenditures for such programs as health insurance for the elderly and the financing of nursing home care. Many of the programs conducted by the NIA will therefore have cost containment as a major theme.

The 1978 request continues the emphasis of the 1977 President's Budget, that is, to support high quality biological research while at the same time expanding the Institute's efforts in clinical, biological, and societal aspects of aging. Among the specific programs proposed for FY 1978 and described in the following material, are: the addition of women to the Baltimore Longitudinal Study at the Gerontology Research Center (GRC); continued refinement of the biofeedback technique for controlling blood pressure and fecal incontinence; increased studies on how people can care for themselves and modify habits they wish to change; expansion of research on the decline of the immune system with age; continued studies of the cellular changes that produce physiological decline; initiation of studies within the intramural program of those phenomena commonly known as senile dementia, sponsoring state of the art conferences on several subjects of immediate concern, and preparation of several informal fact sheets for the public based on what we already know about issues of importance to the elderly.

Aging

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Research grants:						
Regular	227	$17,564,000	267	$20,145,000	+40	$+2,581,000
Special	4	88,000	8	740,000	+4	+652,000
Total, research grants.	231	17,652,000	275	20,885,000	+44	+3,233,000
Training:						
Individual awards	28	416,000	33	494,000	+5	+78,000
Institutional awards.	12	1,784,000	11	1,496,000	-1	-288,000
Total, training	40	2,200,000	44	1,990,000	+4	-210,000
Research and development contracts	19	1,917,000	20	2,058,000	+1	+141,000
Total, aging activity..	290	21,769,000	339	24,933,000	+49	+3,164,000

Introduction: The aging activity supports a nationwide research effort at universities, medical schools, hospitals and other institutions that attempts to understand biomedical, behavioral and social aging processes so that the debilitating effects of age can be delayed or avoided.

Program plans for 1978: In 1978, the Institute will continue the expansion of programs begun in 1977 in a few critical areas.

Relatively meager resources are directed toward clinical research on aging in the United States today. With the exception of the Institute's Gerontology Research Center in Baltimore, there are virtually no aging research centers with a significant clinical component. Therefore, the NIA is requesting funds to award two exploratory grants to determine the feasibility of establishing university-based and medical school-affiliated aging research centers that would provide the focus for attracting the resources and the many disciplines required to perform effective high quality aging research. This program will seek to develop interest in clinical research on aging in order to bring geriatric medicine into established practice, thereby reducing the need for exclusive commitment of Federal support for research centers.

As grant-supported research on aging grows, it is necessary to develop and make available appropriate new animal models for study. Because of the expense and lead time needed to produce them, older research animals of known genetic makeup are not available in numbers or locations sufficient to support an expanded research program. In 1978, therefore, the Institute proposes to expand production capacity and the availability of animals utilizing the research contract and interagency agreement mechanisms.

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A high priority for the Institute is the development of research related to individualized preventive medicine and self-care. Emphasis will be placed on the individual's responsibility for achieving better health status. Research will be conducted in the behavioral and social sciences to develop methods for self-care and to determine whether a patient's knowledge of self-care methods leads to better utilization of the health services system. Research on life patterns and their implications for health status in the later years is an important aspect of these studies.

The effectiveness of the immune system declines rapidly with increasing age, which makes older people much more susceptible to infectious diseases and other challenges with which the immune system normally copes. Characteristic of this decline are lower levels of antibodies in the blood, gradual decline in the activity of bone marrow stem cells and an increase in the population of cells known to interfere with the disease fighting activities of the body's immune cells. Most of this decline is associated with a decrease in cell responsiveness. Research aimed at understanding further the reasons for the decline and how it might be slowed will be expanded in 1978.

Attempts to ameliorate the deterioration of age related human function may ultimately depend upon mechanisms of the aging process that operate at the molecular and cellular levels. Therefore, studies of the biological basis of senescence, that is, studies of the cellular changes that produce the progressive physiological decline, will be continued and expanded. It is these studies that will eventually provide a comprehensive understanding of senescence in all tissues and organs of the body.

Genetic mechanisms not only control the development of the human body but also the minute-to-minute cellular functions of each individual. These genetic mechanisms which have as their molecular basis nucleic acids and enzymes are thought by many scientists to control aging either by direct action or by the loss of certain vital abilities during the development of the individual. Therefore, the program on genetic mechanisms intrinsic to aging will be expanded.

Some exploration will also be conducted in endocrinology and epidemiology.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural research	163	$6,266,000	163	$7,270,000	---	$+1,004,000

Introduction: The intramural program conducts research that has as its objective the improvement of the physical and mental health of older citizens in a way that will allow them to remain active and productive members of their families and communities. The entire program is presently located in Baltimore, Maryland and is known as the Gerontology Research Center.

Program plans, 1978: The intramural research effort is divided into four primary program areas: clinical physiology, behavioral science, cellular and comparative physiology, and molecular aging. In 1978, these programs will receive additional funds to expand existing projects and to replace completed projects with new studies.

A continuing concern for the intramural program is the quantity and quality of its aging animal holding facility. The high cost and inadequate supply of aging animals suitable for research purposes make it imperative that the intramural program continually improve its existing facility. This course of action is wise not only from a research standpoint but is also required by the Animal Welfare Act of 1970 and DHEW policy statement on animal welfare. The intramural program will therefore take steps to meet more completely these requirements.

The clinical physiology program which has overall responsibility for the Baltimore Longitudinal Study will add a modest number of groups of female subjects targeted for special studies to the existing all male study population of 650. The behavioral science program will continue testing the applicability of the biofeedback technique in broader institutional settings. Studies show that the time delay to respond to a signal because of the occurrence of a prior signal, called the psychological refractory period, which is considered to reflect the capacity of the brain to process information, is prolonged in sixty-year-old men and is longer still in men in their seventies. Further studies in 1978 will show whether the psychological refractory period can be used as an index of age-associated change in the ability to acquire and use information. The molecular aging program using recently developed techniques will expand studies of control mechanisms that affect such vital bodily processes as kidney function and heart function. FY 1978 will also see the inauguration of a broad-based capability for examining alterations in neurobiological competence with age. These efforts will be especially focused on defining neuroanatomical, neurophysiological and neuropsychological predictors of the devastating intellectual decline in mental acuity, displayed by a small but significant proportion of our older citizens, and usually described under the rubric of "senile dementia."

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct operations....	21	$1,418,000	21	$1,729,000	---	$+311,000

Introduction: This activity provides for the professional and administrative review, approval and monitoring of grants and contracts, facility support costs and related general expense items essential to all of the Institute's research programs. Among these items are the activities of the National Council on Aging.

Program plans, 1978: During fiscal year 1978, the Institute will provide the essential support services required to begin implementing the aging research plan. Efforts will be made to strengthen the professional and administrative review and approval functions of the Institute to handle the increasing workload. In line with the Institute's mandate from Congress, an expanded effort will provide for more effective dissemination of research information. Particular emphasis will be given to development of the Information Office to enable dissemination of results from research supported by the Institute and the initiation of health education programs. Informational materials to be developed will emphasize the need for research on aging, as this need is not entirely recognized or understood by all those interested in aging and the aged. Informal fact sheets are also planned on areas of general interest to the public such as research on senility, retirement, immunologic aspects of aging, grief as a part of aging, the medical aspects and social implications of the longer life expectancy for women, drug-drug and drug-age interactions, and self-care habits for the old.

In 1977, the Institute jointly sponsored a conference on senile dementia with the National Institute of Mental Health and the National Institute of Neurological and Communicative Disorders and Stroke. Similar conference activity is planned for 1978 in such areas as mammalian models relevant to the process of aging, cognitive psychology of aging and immunology and aging.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program management.....	16	$547,000	16	$568,000	---	$+21,000

Introduction: This activity provides the resources necessary to carry out the overall management and scientific direction of the Institute. Among the functions performed are financial, personnel, and space management; program planning; coordination of all the Institute's activities; the review of current and proposed programs; and the funding of personnel costs associated with the dissemination of research information.

Program plans for 1978: This activity will continue to provide for the overall management and scientific direction of the Institute's programs. Efforts in 1978 will be aimed at implementing the aging research plan and providing for the efficient management of an expanded program. One important program management task is to address the issue of program balance between the basic biological research supported by the Institute, and clinical, behavioral and social research programs. Another task is to insure coordination of NIA programs with other Federal agencies that have an interest in aging research. In 1977, coordination efforts were expanded by gaining representation for the Director, NIA on the Federal Council on Aging; by continuing frequent contacts with the Veterans Administration; by initiating contacts with the National Aeronautics and Space Administration on development of prosthetics for the elderly; by sharing support for the Committee on Mental Health and Illness of the Elderly with the National Institute of Mental Health and the Administration on Aging; and by establishing the Interagency Consultants for Research Planning in Aging, DHEW. Expansion of these kinds of activities will have high priority in 1978.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Program Purpose and Accomplishments

Activity: Aging (Public Health Service Act, Title IV, Part H and I)

1977 Appropriation		1978		
No.	Amount	Authorization	No.	Budget Estimate Amount
290	$21,769,000	1/	339	$24,933,000

Purpose: The Aging activity supports a nationwide research effort of comprehensive and systematic studies of biomedical, behavioral and social aspects of aging in an effort to ameliorate or prevent the debilitating effects of aging.

Explanation: The aging activity includes those projects conducted in non-Federal facilities through grant awards to individual investigators; through fellowship awards directly to promising young researchers and to institutions that have designed particular research training programs; and through research contracts which allow the Institute to fill specific gaps.

Accomplishments in 1977: Because research on humans or human materials is not always possible, experimental systems for the study of senescence have been greatly refined and expanded. Colonies of healthy and extremely well-characterized mice and rats are now maintained and available for use by scientists to study aging processes. To continue and advance studies of aging of human cells in tissue, a new cell line has been established, characterized, and stored, frozen in liquid nitrogen. These studies yield findings that can be checked against the findings made in the longitudinal studies of humans that the Institute supports. The majority of the chemical processes that maintain life functions are controlled by enzymes. Recent studies have shown that with increasing age enzymatic molecules are altered and carry out their functions less well. This leads to a less effective performance of their vital functions in the maintenance of living individuals.

Objectives for 1978: The Institute will continue the expansion of programs begun in 1977 in a few critical areas. Two exploratory grants will be awarded to determine the feasibility of establishing university based and medical school-affiliated aging research centers. This program will seek to develop interest in clinical research on aging in order to bring geriatric medicine into established practice, thereby reducing the need for an exclusive commitment of Federal grant support. The Institute proposes to increase the availability of aged animals utilizing the research contract and interagency agreement mechanisms. Research related to the ways the individual can care for himself during his later years, is also important. Studies of the cellular changes that produce progressive physiological decline will be continued and expanded. It is these studies that will eventually provide a comprehensive understanding of senescence in all tissues and organs of the body.

1/ Title IV Part H - Indefinite; Title IV Part I - Legislation pending.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act, Title IV, Part H)

1977 Appropriation		1978		
Pos.	Amount	Authorization	Budget Estimate Pos.	Amount
163	$6,266,000	Indefinite	163	$7,270,000

Purpose: This activity supports the intramural research program of the Institute.

Explanation: The intramural research activities of the Institute are carried out in the Gerontology Research Center located in Baltimore, Maryland. Basic research is conducted in order to obtain a fundamental knowledge of the aging process and to seek ways to improve the physical and mental health of our older citizens in a way that will allow them to remain active and productive members of their families and communities.

Accomplishments in 1977: Research advances made by NIA scientists are providing the basic knowledge about aging that can eventually be used to guarantee a healthy and productive later life for all people. The Baltimore Longitudinal Study of Aging has continued to provide the primary resource for studies in men. A small number of female research subjects are being added to the Baltimore Longitudinal Study to provide information on sex differences. Efforts have continued not only to provide basic data on age changes in individuals but also to probe into underlying mechanisms of these changes. Analysis of these studies during 1977 showed that alcohol presents a greater potential risk to older people since they experience greater performance problems, but are less aware of their impairment than the young. An ongoing study using echocardiography to measure the aged heart shows that while older hearts are thicker and fill more slowly than those of young men, there are no functional impairments in older hearts either at rest or in response to rapid changes from rest to moderate workload.

Objectives for 1978: Basic research will continue in the four primary program areas of clinical physiology, behavioral science, cellular and comparative physiology and molecular aging. Because research on aging requires experimental animals of known genetic background some of the funds for this activity will be used to renovate animal quarters, modernize caging, and improve animal husbandry. Studies show that the time delay to respond to a signal because of the occurence of a prior signal, called the psychological refractory period, which is considered to reflect the capacity of the brain to process information, is prolonged in sixty-year-old men and is longer still in men in their seventies. Further studies will show whether the psychological refractory period can be used as an index of age-associated change in the ability to acquire and use information.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Title IV, Part H)

1977 Appropriation Pos.	1977 Appropriation Amount	1978 Authorization	1978 Budget Estimate Pos.	1978 Budget Estimate Amount
21	$1,418,000	Indefinite	21	$1,729,000

Purpose: This activity administers the grants and contracts program of the Institute as well as providing support for the National Advisory Council on Aging for review of grant applications.

Explanation: This activity provides the funds for the review and approval of grants, facility support costs and related administrative and general expense items essential to the research program.

Accomplishments in 1977: During fiscal year 1977 the Institute will fund 231 research grants, 40 fellowships and training grants and 19 research and development contracts. Workshops and conferences are planned or have been held on such topics as: exercise and physical fitness for the elderly; economic issues of aging such as the increase in the proportion of the elderly in our population, retirement, Social Security, and income and expenditures of the elderly; the use of human and animal autopsies as a methodology in aging research; and the protection of the elderly as human research subjects. The Institute is continuing to identify other Federal agencies and private groups with interests in the needs of the aged to coordinate research efforts and to disseminate information.

Objectives for 1978: The Institute will provide support services to begin implementation of the aging research plan. Efforts will be made to improve the grants management functions of the Institute to handle the increasing workload. Particular emphasis will be given to development of the Information Office to enable the dissemination of results from research supported by the Institute and the initiation of health education programs. Informational materials to be developed will emphasize the need for research on aging, as this need is not entirely recognized or understood by all those interested in aging and the aged. Informal fact sheets are also planned on areas of general interest to the public, such as research on senility, retirement, immunologic aspects of aging, grief as a part of aging, the medical aspects and social implications of the longer life expectancy for women, drug-drug and drug-age interactions, and self-care habits for the old. State of the art conferences in such areas as mammalian models relevant to the process of aging, cognitive psychology of aging, and immunology and aging are planned.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Title IV, Part H)

1977 Appropriation		1978		
Pos.	Amount	Authorization	Budget Estimate Pos.	Amount
16	$547,000	Indefinite	16	$568,000

Purpose: This activity provides the Institute with such essential managerial functions as intergovernmental coordination; scientific direction; program planning; public and scientific information dissemination; and administrative, budget and personnel management.

Explanation: The salaries and expenses of the Institute's Director and his supporting staff are paid from this activity.

Accomplishments in 1977: In 1977, several efforts at coordination with other Fed ral agencies interested in aging research were begun. These activities were meetings between the NIA Director and each of the other Institute directors at the National Institutes of Health; a conference on senile dementia jointly sponsored by the NIA, the National Institute of Mental Health, and the National Institute for Neurological and Communicative Disorders and Stroke; representation for the Director, NIA on the Federal Council on Aging; and contacts with the National Aeronautics and Space Administration on the development of prosthetics for the elderly. Other accomplishments included the recruitment of key staff members and completion of a comprehensive aging research plan for the Department of Health, Education and Welfare.

Objectives for 1978: The program management staff will continue to monitor the development of the Institute to achieve an effective organization for the support and conduct of expanded research programs on aging. Emphasis will be placed on achieving balance among the disciplines of biological, clinical, social and behavioral research currently supported by the Institute.

WEDNESDAY, MARCH 9, 1977.

NATIONAL EYE INSTITUTE

WITNESSES

DR. CARL KUPFER, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. WILLIAM F. RAUB, ASSOCIATE DIRECTOR, NATIONAL EYE INSTITUTE
EDWARD H. McMANUS, EXECUTIVE OFFICER, NATIONAL EYE INSTITUTE
FRANCINE V. LITTLE, BUDGET OFFICER, NATIONAL EYE INSTITUTE
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now we have the National Eye Institute.

The presentation will be made by Dr. Carl Kupfer, the Director.

We have your biographical sketch, Doctor, which we will place in the record at this point.

[The biographical sketch follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, NATIONAL INSTITUTES OF HEALTH—BIOGRAPHICAL SKETCH

Name: Carl Kupfer, M.D.
Position: Director, National Eye Institute.
Birthplace and date: New York, N.Y., February 9, 1928.
Education: A.B., Yale University, 1948; M.D., the Johns Hopkins Medical School, 1952.
Experience, present: Director, National Eye Institute, National Institutes of Health.
1966–70: Professor and chairman in Ophthalmology, University of Washington School of Medicine.
1962–66: Assistant professor in Ophthalmology, Harvard Medical School.
1960–62: Instructor in Ophthalmology, Harvard Medical School.
1958–60: Research fellow in Ophthalmology. Harvard Medical School.
1957–58: Research fellow in Optholmology, Wilmer Eye Institute, the Johns Hopkins Medical School; laboratory assistant, biostatistics, the Johns Hopkins Medical School.
1953–54: Laboratory assistant, biostatistics, the Johns Hopkins Medical School.
1952–54: Internship and assistant residency, Wilmer Eye Institute, the Johns Hopkins Hospital.
Association memberships: American Physiological Society, Association for Research in Vision and Ophthalmology, American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, and Pan American Ophthalmological Society.
Publications: Author or coauthor of over 60 publications in clinical ophthalmology and the anatomy, physiology and biochemistry of the visual system.

Mr. FLOOD. Do you have some people with you that you would like us to meet?

Dr. KUPFER. On my right is Dr. William Raub, Associate Director of Extramural and Collaborative programs, on my immediate left is Mr. Edward McManus, Executive Officer, and to his left is Ms. Francine Little, Budget Officer.

Mr. FLOOD. All right, we will place your statement in the record at this point, Doctor.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
National Institutes of Health

Statement by Director, National Eye Institute

on

"National Eye Institute"

Mr. Chairman and Members of the Committee:

Every year nearly 4 million new cases of eye disease occur in the United States. These necessitate more than 31 million yearly visits to doctors for professional treatment or care. Each year an estimated 567,000 people are discharged from short-stay hospitals with an eye disease or injury listed as their main diagnosis. The annual cost of such care, when added to the economic costs of blindness, exceeds $5 billion. Moreover, a 1976 Gallup Poll has reconfirmed the findings of an earlier survey that Americans fear blindness more than any other affliction, except cancer. Research supported by the National Eye Institute is directed toward reducing these numbers by improving our ability to prevent, diagnose, and treat blinding and disabling eye diseases.

Diabetes and the Eye

Diabetic retinopathy is a major cause of blindness which I have often discussed with this committee. In two generations, this disease has risen from obscurity to become a major threat to the sight of thousands of Americans and to millions of people throughout the world. It now accounts for 20 percent of annual new cases of blindness among people between the ages of 45 and 74.

In 1972, the National Eye Institute began a nationwide study of the treatment of diabetic retinopathy. Its purpose was to determine whether photocoagulation--treatment with powerful, intense beams of focused light--can reduce the rate of blindness from this disease.

Organizing such a study proved to be a complex undertaking because there are few precedents for large-scale, controlled, clinical trials, especially to evaluate surgical procedures. In fact, in eye research, nothing of this magnitude had ever been attempted. Even before the first patient could be enrolled, new methods of acquiring and evaluating clinical data had to be developed and tested. However, by June 1975, over 1,700 patients had been enrolled at 15 clinical centers throughout the United States.

This effort has paid off handsomely. Last April, after only two years of patient follow-up in the Diabetic Retinopathy Study (DRS), the first conclusive evidence was reported that photocoagulation can reduce the risk of blindness in proliferative diabetic retinopathy. For this reason, the National Eye Institute took immediate action to disseminate the Study's findings to ophthalmologists and other health professionals throughout the United States and to the general public. As a result, these findings have had a major influence on eye care and vision research, one that goes far beyond their immediate relevance to the more than 300,000 people who are at the greatest risk of blindness from diabetic retinopathy.

Ophthalmologists now know that there is a treatment they can recommend with confidence to their diabetic retinopathy patients who face the threat of blindness. Primary care physicians and optometrists who treat diabetic patients now have added reason to be alert to signs of eye problems and to refer to ophthalmologists patients who may benefit from photocoagulation treatment. Hospitals and other health facilities which may have been reluctant in the past to invest in photocoagulation equipment for lack of specific information on its cost/effectiveness now have solid evidence upon which to make their decisions. In South Dakota, for example, the decision to install the first argon laser in that State was directly influenced by the DRS findings. Patients who previously had to go to Omaha, Nebraska, or Rochester, Minnesota, can now be treated closer to home with consequent savings in time and money.

The Study also has general implications for the future of vision research. Its success has generated considerable enthusiasm for additional clinical trials in diabetic retinopathy and other important eye disorders. The Diabetic Retinopathy Vitrectomy Study, the initial plans for which I reported last year, is one of these. The purpose of this new trial is to determine whether surgical removal of the vitreous in diabetic retinopathy patients who have already lost most of their vision from hemorrhage within the eye should be performed earlier than is now customary. Earlier treatment may increase the chances that good vision can be restored to such people, but it may also entail increased risk. This is why a carefully controlled and monitored study is necessary. I

am happy to report that this Study is now underway: thirteen clinics throughout the United States are participating, and most of them are already enrolling patients.

The success of the Diabetic Retinopathy Study has also given great impetus to research in the general field of diabetes. It has shown that a major complication of this disease can be treated with a high rate of success, raising hope that other disabling and life-threatening complications of diabetes can be avoided. Furthermore, it has provided new techniques for systematic study of the natural history of the disease and improved methods for scientifically evaluating the usefulness of treatments that may be developed in the future.

Yet, our very success in treating diabetic retinopathy underscores the great need for finding means of preventing this disease. Photocoagulation is not uniformly effective. Though it can significantly reduce the chance of blindness occurring, it does not cure the disease. Furthermore, treatment is expensive and time-consuming for the patient.

Studies now underway are therefore seeking to find out just how diabetes damages the eye. Important progress has already been made; for example, investigators working at the National Eye Institute have succeeded in growing retinal capillaries in tissue culture. With this technique, experiments can now be performed which are aimed at improving our understanding of how diabetes damages the small blood vessels in the retina, and possibly the small vessels in other tissues such as that of the kidney. There is already evidence from such studies that the enzyme

aldose reductase which, as I have reported previously, has been implicated in the formation of diabetic cataract, may also play a role in damaging retinal capillaries.

In research on diabetic cataract itself, attention is now focused on a class of organic compounds called flavonoids, some of which have been found to be powerful inhibitors of aldose reductase. NEI intramural scientists have found that one flavonoid more effectively delayed the onset of cataract formation in laboratory animals than any other compound previously tested. Other flavonoids are now being examined in hope of finding even more potent enzyme inhibitors. Since flavonoids are relatively harmless, further research may lead to their eventual clinical use.

During the coming year, such studies will continue and expand. Plans will be developed for additional clinical trials, including one to test the possibility of using photocoagulation earlier in the course of diabetic retinopathy in hope of improving its rate of blindness prevention. The search will continue for a substance in the eye which may promote the growth of abnormal retinal blood vessels in diabetic retinopathy. If such a substance can be found and isolated, it is possible that means for interfering its action can also be developed.

In order to encourage expanded research in the ocular aspects of diabetes which responds to the intent of the Congress, the National Eye Institute has recently made a special announcement to the scientific community expressing its great interest in supporting specific kinds of studies in this field and inviting research grant applications.

Corneal Diseases

Corneal diseases are the most common eye disorders and account for substantial economic loss in terms of expenditures for medical care and days lost from work. Corneal disorders necessitate over 10 million office visits for professional eye care each year.

Last year, I told the committee of NEI's role in supporting the development of a new drug to treat herpes simplex infection of the cornea, one of the most serious and widespread eye infections. I am pleased to report that clinical testing of this new drug--now called vidarabine--substantiated its safety and effectiveness. It has just been approved by the Food and Drug Administration for use in general ophthalmic practice. Vidarabine is expected to provide a long-needed alternative to the only other drug useful in treating herpes virus infections of the eye, idoxuridine (IDU). It will be especially valuable for treating patients who either do not respond to IDU or in whom that drug produces undesirable side effects. Because there are still no effective means for treating deep-seated and recurrent herpes virus infections, the National Eye Institute has given high priority to continued research on anti-herpes drugs.

The development of an important new research tool, the specular microscope, has provided major new opportunities in corneal research. This instrument makes it possible to study corneal cells in the intact, living human eye. It has already shown that the cells which form the inner layer of the cornea, the endothelium, reproduce either very slowly or not at all.

Thus, once this layer is damaged, it does not heal easily. The endothelium can in fact be easily damaged by disease and various surgical procedures and is affected by aging. Damage to this cell layer almost always is the cause of failure in corneal transplantation. Specular microscopy provides a means for assessing the suitability of corneal donor tissue prior to transplantation and for checking the status of the endotheliun following eye surgery.

There is reason to believe that the technique may also be useful in studying other cell layers of the eye including those of the lens and retina. If so, microscopy will be a valuable aid to the diagnosis and clinical assessment of many eye disorders.

Cataract

Cataract affects more than 3 million Americans. Despite the fact that about 300,000 operations to remove cataracts are performed each year, more than 45,000 people are blind from this disease at any given time. This is why the National Eye Institute emphasizes research on the prevention of cataract.

Cataract research in the United States is carried out by a few highly productive teams of scientists. Although geographically dispersed, these groups have excellent communications and informal working relationships. In fact, they are a model of cooperative scientific effort. The time is ripe to capitalize on these fortunate circumstances and provide these investigators with centralized resources which will enable them to take advantage of important new research opportunities.

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To this end, a Cooperative Cataract Research Group has been formed. This group has prepared a plan for concerted research in this field which will be guided by the priorities set forth in the National Advisory Eye Council's vision research program plan. In particular, the Cooperative Group will concentrate on studies of human senile cataract. Such research has been impeded in the past by the lack of standardized classification criteria and by the limited availability of human lenses for laboratory study.

When compared with the potential gains to be realized, the investment required for this effort is quite modest and, in general, can be effected by supplementing existing research grants. During the coming year, the Cooperative Group will develop a uniform system for classifying cataracts and begin designing instruments which will be used to characterize different types of excised human senile cataracts at various stages in their development. This will lead to more efficient methods for collecting and distributing human lenses to research scientists and permit precise correlation of clinical observations with laboratory findings.

Although the NEI has chosen to concentrate its support of cataract research on prevention of this disease, we are still very interested in new developments in cataract surgery, particularly in the long-term safety of such procedures. The technique of implanting in the eye at the time of surgery a small plastic lens which eliminates the need for wearing special eyeglasses or contact lenses has become widespread in the past few years. An estimated 10,000 such lenses will be inserted

during 1977. Although this number represents only about 3 percent of all cataract operations, there is every reason to believe that the number of lens implants will expand rapidly in the future.

Although the visual advantages of an implanted lens to the cataract patient are undeniable, the long-term risks of this procedure in comparison to cataract surgery without implantation have not been adequately assessed. Nor is there much data concerning the characteristics which define those patients who are most likely to benefit from lens implantation. For this reason, the National Eye Institute is developing plans, in consultation with the National Advisory Eye Council and leading ophthalmic surgeons, to initiate a study of lens implantation which can provide useful information to ophthalmologists who perform this procedure and to their patients. Although the design of such a study must be scientifically sound, it must also reflect the realities of current ophthalmic practice. Because this procedure is already being widely performed and many cataract patients now actually demand lens implantation, it is important for us to undertake this study as soon as possible.

Research Workshops

The 1975 report of the National Advisory Eye Council, Vision Research Program Planning, recommended that the National Eye Institute periodically hold conferences to bring together people with diverse backgrounds and interests to focus attention on selected areas of research where special needs and opportunities exist.

One such meeting was held to foster increased application of well-established laboratory tests of visual function and performance to the clinical diagnosis of various types of eye problems, particularly those involving the retina and higher centers in the visual nervous system. This meeting was very successful in generating several excellent proposals for effecting this transfer, and we have already solicited research center and project grant applications to test their feasibility.

A second workshop, on low vision, will be held in late Spring. Its purpose will be to assess research needs and opportunities in the rehabilitation of the millions of people who, though not legally blind, suffer from various degrees of visual impairment. The functional needs and capabilities of such individuals have never been satisfactorily assessed, nor has there been adequate evaluation of the utility and practicality of most of the devices now available to aid them. We hope that this workshop, which will include experts in eye care, rehabilitation, special education, and other fields, will be the first in a series of special efforts to stimulate research which can benefit visually handicapped people.

Research Centers

Although NEI's primary method for supporting vision research is the individual project grant, the full range of NIH support mechanisms are used where circumstances warrant. For instance, the NEI reserves research contracts for specific purposes, namely the support of multi-center clinical trials and development of specialized research resources.

Research center grants are also used in special situations where this approach seems advantageous.

In particular, the Core Center Grant is used in settings where there are already a number of high quality vision research projects supported by the NEI. The core grant can provide centralized services and facilities which can help strengthen the overall research environment, help unify discrete efforts into a cohesive whole, and thereby create opportunities for further progress.

Specialized Clinical Research Center Grants are intended to foster the application of scientific methods to research involving human patients. A key objective is to increase collaboration between laboratory and clinical investigators. The application to clinical diagnosis of visual function tests developed in the laboratory, which I mentioned before, is one example of the type of project that could be supported by this mechanism. Study of the natural history of disorders such as senile macular degeneration is another.

During the coming year, we expect to support approximately 17 Core Center Grants and 8 Specialized Clinical Research Center Grants. In general, the NEI uses research center grants to support environments where a full range of studies can be carried out, from basic laboratory research to applied studies of technology transfer, and the full range of support mechanisms--research grants, fellowships, and research contracts--may be brought to bear on vital problems in vision research.

Dissemination of Information

In addition to the extensive information dissemination activities associated with the announcement of results from the Diabetic Retinopathy Study, the National Eye Institute engaged in a number of other public information and education projects during the past year. Many of these were related to NIH and HEW Bicentennial activities. Others called attention to worldwide problems of blindness and possible approaches to their solution in conjunction with the new International Agency for the Prevention of Blindness and the World Health Organization in support of the 1976 World Health Day theme "Foresight Prevents Blindness." In other areas, messages on the prevention and treatment of eye disorders were disseminated via radio spot announcements and a series of weekly newspaper columns. We distributed over 44,000 publications on eye disorders and research and responded to more than 3,000 public inquires. Assistance was provided to a great number of news media representatives for the preparation of stories, articles, or programs dealing with vision and eye research. Included among our plans for the coming year are a consumer booklet on eye care and eyeglasses, at least two major professional journal editorials on advances in eye care and vision research, and efforts in support of a nationwide glaucoma screening program being planned by the National Society for the Prevention of Blindness.

Program Planning

As I informed the committee last year, the National Advisory Eye Council is updating and expanding its 1975 vision research program plan. This effort is now well along, and a three-volume report is expected to be published in June of this year. This second report is expected to provide guidance to the National Eye Institute in setting research priorities for the next five years.

In conclusion, Mr. Chairman, to support the activities I have discussed, as well as others designed to prevent and alleviate blindness and visual disability, the National Eye Institute's budget request for FY 1978 is $64,981,000.

FISCAL YEAR 1977 BUDGET

Mr. FLOOD. For fiscal year 1977 the Congress added $17 million to your budget?

Dr. KUPFER. Yes, sir.

Mr. FLOOD. How is that additional money being used and which programs have you strengthened with that money?

Dr. KUPFER. The major portion of funds received in fiscal year 1977 have been directed toward the area of diabetes. As you know, this is probably the leading cause of new adult blindness in the United States, and a major public health problem. There are a number of eye problems that occur in the diabetic which interfere considerably with the quality of life. As the diabetic lives on the average longer and longer, these complications are occurring more frequently. Diabetic retinopathy is one example, an increased rate of cataract development is another.

We have devoted a considerable amount of the increased funds to basic research on diabetes-related eye problems as well as clinical research to preserve the vision of patents suffering from diabetic retinopathy.

FUNDING RATE OF RESEARCH GRANTS

Mr. FLOOD. What percentage of your approved grant aplications will you fund at the $64 million level?

Dr. KUPFER. We will fund approximately 55 percent of our approved grants in fiscal year 1977.

FISCAL YEAR 1978 FUNDING

Mr. FLOOD. If this committee wanted to provide your Institute with an increase in 1978 similar to the 1977 increase, could you effectively use that amount of money to support high quality research?

Dr. KUPFER. Yes. We have seen a marked increase in the number of excellent research grant applications coming into the National Eye Institute. As a matter of fact, in 1977 it is estimated that approximately 460 grant applications will come in, and in 1978 we project that there may be in excess of 500 new grant applications.

PROGRAM EMPHASIS WITH INCREASED FUNDING

Mr. FLOOD. In what program areas would you invest an increase of $17 million?

Dr. KUPFER. The increase would be invested in several program areas. I think that the single most important program is in the area of retinal and choroidal diseases because these disorders account for more than 30 percent of all visual disability, because there are some exciting new opportunities in the field, and because these are diseases which affect people of all ages.

There are also some unique opportunities in the area of cataract research that we would want to expand. As you know, we have been very interested in the effect that diabetes has in speeding up the development of senile cataract.

I think it very appropriate to indicate, as a followup to testimony from the Institute on Aging, that the development of cataract is a sign of aging that we are very concerned with slowing down. We have developed some very exciting techniques in the laboratory to slow the development of diabetic cataracts and these are almost at a stage where they can be tested in patients.

PHOTOCOAGULATION IN DIABETIC RETINOPATHY

Mr. FLOOD. Is photocoagulation accepted as an effective procedure for treating diabetic retinopathy or is that still, as it was last time we talked about it, very experimental?

Dr. KUPFER. Sir, I think that as far as the visual research community was concerned, one of the most exciting things that happened last year was the evidence that emerged from our collaborative clinical trial on the use of photocoagulation in treating diabetic retinopathy. The evidence demonstrated that this technique is beneficial in reducing the development of blindness in patients with diabetes who have adverse changes in their retina.

This is one of the most significant clinical trials in medicine in terms of the magnitude of the beneficial effects of treatment. It is also significant in terms of its acceptance by the ophthalmic community.

Mr. FLOOD. As always in things like this, are there any adverse side effects associated with this procedure such as retinal degeneration?

Dr. KUPFER. There are two adverse side effects which I will mention to you. I would hasten to add that they are very much overshadowed by the beneficial effects.

The first adverse side effect is that there is a transitory decrease in visual acuity, but for most cases this is usually fully restored by 1 or 2 years after the treatment. This is not a significant decrease in that it represents the loss of ability to see the smallest line on the visual acuity chart that the patient would see prior to treatment.

The second adverse effect that has been noted is a small to moderate decrease in the side vision of some of these patients. I would add that the technique of photocoagulation is evolving to the point where these two adverse effects could be eliminated.

Mr. FLOOD. How long do you think it is going to be before this procedure is commonly accepted in all of our medical centers?

Dr. KUPFER. It is now commonly accepted. As a matter of fact, we heard recently that in one of the Western States a hospital which had not been certain about investing in the necessary equipment, which costs in excess of $30,000, has proceeded on the basis of the results of these studies, and has invested in a photocoagulator.

COSTS ASSOCIATED WITH PHOTOCOAGULATION

Mr. FLOOD. Is the procedure going to be so expensive to perform that it is going to be beyond the reach of the average taxpayer?

Dr. KUPFER. No, sir. The following combine to make it relatively inexpensive: (1) it is a relatively simple procedure in the sense that it can be done in an outpatient setting—it does not require hospitalization, and (2) it usually takes from 1 to 2 hours to perform, with the possibility of a second treatment being necessary.

COST OF TREATMENT PROCEDURES

Mr. FLOOD. Since we mentioned that, generally how carefully do you consider the cost of any procedures?

Dr. KUPFER. We are very concerned with cost. As a matter of fact, we are now in a position to increase the number of procedures that are done in an outpatient setting.

Mr. FLOOD. That is one of the factors examined when you have a development of procedures, isn't it?

Dr. KUPFER. Definitely, sir. For instance, one of the things we are trying to do is to slow down the costs of the development of cataracts. We have looked at information that tells us that if we can slow down the development of a cataract by 10 years, we will reduce by almost half the number of people requiring surgery to remove the cataract.

DIABETIC CATARACTS

Mr. FLOOD. What is the status of your work on diabetic cataracts? As I recall, we talked about the development of very powerful drugs to slow down the development of cataracts. Are you still in the clinical trial stage on this or what?

Dr. KUPFER. As I discussed last year, we do have some very powerful inhibitors of the enzyme that is related to the development of diabetic cataracts. This past year has been spent in increasing the effectiveness of these drugs. We now have a group of drugs which we think are not only very powerful but seem to be acceptable to the body.

CATARACT DRUGS

Mr. FLOOD. If these drugs you are talking about are approved by FDA and widely used, would it eliminate the need for surgery?

Dr. KUPFER. Not altogether, but we hope that by slowing down the development of cataract in patients with diabetes, that fewer of them will actually need surgery.

CAUSE OF CATARACT

Mr. FLOOD. Do your researchers have any idea of the causes of cataracts? We often hear some people speculate that the concentrations of calcium cause cataracts.

Dr. KUPFER. Yes, sir, you are quite right on that. There is a hypothesis that the development of a cataract is related to the fact that with age the proteins in the lens begin to clump together. When the size of these clumps reaches a certain level, light can no longer be transmitted through the lens in an orderly manner. There is some evidence to suggest that this clumping is related to the increased levels of calcium in the lens.

This awareness now opens the possibility of testing this hypothesis experimentally.

CLINICAL TRIALS

Mr. FLOOD. Again, on the clinical trials, what is the status of clinical trials on the drug ARA–AMP in treating the disease.

Dr. KUPFER. This drug is used in treating herpes simplex viral infection of the cornea. The trials have been completed, and the drug has been approved for general use by the FDA, ARA–AMP, now called vidarabine, is the second drug to be developed for the specific treatment of viral disease.

CORNEAL TRANSPLANTATION

Mr. FLOOD. Are you making any progress in reducing the rate of rejection in the corneal transplants?

Dr. KUPFER. This, of course, is part of an overall problem in transplantation immunology. Even though corneal transplantation has been comparatively more successful than transplantations of most other tissues, we are still very anxious to improve the success rate, particularly in diseases which have not responded as well as others to this procedure.

This is a very high priority research area which will be coordinated among many Institutes at NIH.

CORNEAL DISEASE

Mr. FLOOD. What kind of work are you now supporting in the whole area of corneal disease and what do you plan to support in 1978?

Dr. KUPFER. We are focusing on three areas of corneal disease. We are very much concerned with the control of the herpes simplex infection—the common virus that causes fever blisters. Herpes is the main cause of serious eye infections in the United States. Research will continue on the development of new drugs to improve the treatment of this disease and prevent its recurrence. The second main area of corneal research is transplantation immunology. The third is the development of means to reverse ulceration of the cornea. This is a biochemical problem.

Mr. FLOOD. Mr. Early?

CATERACTS

Mr. EARLY. In response to the chairman's question, you said if you can delay the development of cataracts by 10 years, you can reduce the rate of eye surgery 50 percent.

Dr. KUPFER. Approximately 45 percent, yes, sir.

Mr. EARLY. Could you elaborate?

Dr. KUPFER. Yes, sir. There are approximately 350 to 400,000 cataract extractions performed in the United States each year. Of course, the reason for the cataract surgery is that an individual's visual acuity is reduced to the point he or she no longer has useful vision. If we can delay the development of the cataract by 10 years, so that the average age at which the cataract would interfere with vision would be advanced by 10 years, then only about 55 percent of the people who are presently being operated on would need surgery.

Mr. EARLY. Do you think you have enough research money in that area?

Dr. KUPFER. Cataract research is one area in which effort has been extremely well-organized. Cataract researchers throughout the United

States has formed a collaborative group in which they exchange information in a very free-flowing fashion. I think this organizational capability allows for the most effective use of the funds provided by the National Eye Institute.

I also think that whenever there are very good research ideas to be tested, the rate with which the research would proceed would always be greater if more resources were available.

ANIMAL MODELS

Mr. EARLY. I notice in your last testimony on the aging, you suggested that there was not enough animal research being done with regard to their unique problems. How does this relate to eye research?

Dr. KUPFER. Do you mean animal models?

Mr. EARLY. Yes.

Dr. KUPFER. Development of animal models, as you might imagine, is a very desirable goal in any research situation. In the case of diseases of the eye, we, I think, have been limited as much as any other research area. For instance, we do not have a good model for diabetic retinopathy, or for macular degeneration, which is probably the main cause of blindness, and a devastating problem for the older age group. On the other hand, we have put some resources into developing animal models of certain retinal degenerations. We do not have a model for glaucoma as it exists in humans, but we do have a model to study the effects on increased pressure in the eye on the function of the optic nerve.

So it is, if you will, a mixed bag in terms of animal models.

Mr. EARLY. Dr. Fredrickson, do we have the cooperation of the Institute with regard to the veterinary research, aging, and the eye?

Dr. FREDRICKSON. Yes, we do, I think, very well. We have a Division of Research Services, which you do not ordinarily hear about during the hearings, that has the staff of about 17 veterinarians who have central responsibilities. They also maintain a genetic breeding bank where 150 rare lines are maintained.

So we provide centrally, and coordinate quite effectively, the veterinary support for all the Institutes.

Mr. EARLY. So with the cooperation or the communication, they would be looking into the eye of the aged, et cetera?

Dr. FREDRICKSON. The Division of Research Services would be very helpful in setting up animal models or maintaining them if they were developed by the Institute through its own activities.

Mr. FLOOD. Mr. Conte?

FISCAL YEAR 1977 BUDGET

Mr. CONTE. Dr. Kupfer, last year we appropriated $64 million for the Institute.

Dr. KUPFER. Yes, sir.

Mr. CONTE. I offered an amendment to increase the amount proposed by the administration at that time. I felt the budget request did not even take care of the amount of inflation that had taken place during the 12-month period. I think the National Eye Institute is an outstanding Institute which has done a tremendous job.

Dr. KUPFER. Thank you.

Mr. CONTE. You point out in your statement some of the breakthroughs that you have made. Now this year you are asking for $64,981,000 which is a $981,000 increase. That doesn't even cover the inflationary spiral, does it? Do you think that this is going to be a sufficient amount of money to enable you to do everything you want to do everything you want to do in the National Eye Institute?

Dr. KUPFER. Sir, as you pointed out, there was a significant increase in funding for fiscal year 1977. I would say that new programs that were started, and expanded programs that have been put into effect in 1977 will be maintained in 1978.

PROFESSIONAL JUDGEMENT BUDGET

Mr. CONTE. What did the National Eye Institute originally ask for?

Dr. KUPFER. Sir, I think the figure was approximately $70 million.

CATARACTS

Mr. CONTE. Congressman Early asked you about your cataract program. Has there been any work done on what actually causes the cataract condition?

Dr. KUPFER. As you know, sir, there are three types of cataracts that we are concerned with. There is the congenital cataract which interfers with vision in the newborn and young persons. There is the senile cataract, which affects people in the older age groups, and then there is the cataract related to a number of diseases, the most important one being diabetes.

We have been moving ahead on all three fronts. For the first time we have been able to successfully take the lens from a child at the time of surgery and grow this lens in tissue culture so we can study what defect exists in the lens and learn more about the mechanism for the development of congenital cataract.

DIABETIC CATARACTS

In the case of diabetic cataract, there have been major advances along the lines of knowing what the basis of the diabetic process is in hastening the cataractous process and even more important, developing drugs which slow that process down in animals made diabetic.

Fortunately, these drugs turn out to be very potent and yet at the same time not apparently dangerous to man or animals. Therefore, I think we are on the verge of conducting clinical trials to see whether these drugs will be effective in people with diabetes.

LENS IMPLANTATION

Mr. CONTE. How widely used is the lens implantation procedure at the present time?

Dr. KUPFER. There probably are between 350,000 and 400,000 cataract extractions done each year in the United States. It is estimated about 30,000 of these involve intraocular lens implantations, or approximately 10 percent.

Mr. CONTE. The Joslin Clinic is doing a lot of work on this in Boston, isn't it?

Dr. KUPFER. Yes, there are a number of institutions in Boston, Joslin Clinic, the Massachusetts Eye and Ear Infirmary.

Mr. CONTE. Mr. Chairman, I will not take the time now to ask further questions. I will submit the rest for the record.

DIABETIC RETINOPATHY VITRECTOMY CLINICAL TRIAL

Mr. FLOOD. Have you started your vitrectomy clinical trials and if so, how many clinics are involved in that?

Dr. KUPFER. Yes, sir, we began the recruitment of patients this past October. There are 13 clinics involved.

Mr. FLOOD. How long will it take to complete this trial and how much will the total cost be?

Dr. KUPFER. The total cost will be approximately $1 million per year and it is programed for approximately 5 years. Of course, the first stage will be the recruitment of an adequate number of patients to give us definitive results.

CLINICAL TRIALS

Mr. FLOOD. You have talked about several of these clinical trials so far. How many are you supporting throughout your Institute and in what areas?

Dr. KUPFER. As you know, we have primarily focused our contract program on the support of clinical trials. At the present time we have two multi-center clinical trials. We have the diabetic retinopathy photocoagulation clinical trial, and now we have begun the diabetic retinopathy vitrectomy clinical trial.

Mr. FLOOD. For the record, please give to the committee a list of your clinical trials at current status and the estimated data completion and the estimated cost to complete each one.

Dr. KUPFER. Yes, sir, we will be happy to.

[The information follows:]

CURRENT STATUS OF NATIONAL EYE INSTITUTE CLINICAL TRIALS

(Dollars in Thousands)

Contract-Supported Clinical Trials:	1977 Estimated Costs	Estimated Date of Completion	Estimated Additional Costs through Completion	Status
Diabetic Retinopathy Vitrectomy Study	$527	1982	$2,495	Has 13 participating clinics, one coordinating center, one reading center. Patient enrollment will total 800.
Diabetic Retinopathy Study	965	1981	7,015	Has 15 participating clinics, one coordinating center, one reading center. Patient enrollment totals 1,758.
Expanded Diabetic Retinopathy Study	700	1983	8,500	It is estimated that this trial will have approximately 20 participating clinics, one coordinating center, one reading center and 3,000 patients.
Intraocular Lens Implants	--	1981	4,473	Trial presently in planning stage, expect to recruit approximately 500 patients in first year.

CURRENT STATUS OF NATIONAL EYE INSTITUTE CLINICAL TRIALS
(In Thousands of Dollars)

Research Grant Supported Clinical Trials

Program	Institution	Estimated Current Support
Retinal & Choroidal Diseases	Johns Hopkins University Hospital	$200
Retinal & Choroidal Diseases	Mayo Foundation	75
Retinal & Choroidal Diseases	Pennsylvania Hopsital	122
Retinal & Choroidal Diseases	Johns Hopkins University Hospital	35 1/
Retinal & Choroidal Diseases	University of California, Los Angeles	109
Glaucoma	University of California, San Diego	130
Glaucoma	University of Illinois	37 1/
Sensory-Motor Disorders & Rehabilitation	University of California, Berkeley	22 1/
Total, estimated		$730

1/ Represents planning stage only for development of protocols and testing of forms.

GLAUCOMA

Mr. FLOOD. Another area the committee is interested in, of course, is research in the treatment of glaucoma. We have not had much chance to talk about that. What looks promising in this area and how are you going to support that in 1978?

Dr. KUPFER. We are primarily concerned with two areas in glaucoma research. The first is directed toward the relationship of the increased pressure in the eye and its ability to damage the function of the eye. There are many people who have elevated pressure in the eye. We call them ocular hypertensive patients. Yet only a certain number of these individuals will actually have damage to their eye resulting in blindness. Much of our effort is directed toward trying to identify the patients who have elevated pressure and are at high risk to developing impaired visual function.

Mr. FLOOD. Do you have any new diagnostic test now for detecting the early onset of glaucoma? We talked about a blood test being under study. What is the status there? Is that widely used? What will that cost?

Dr. KUPFER. There is a blood test which fortunately is used rather extensively for a variety of reasons. It consists of the typing of lymphocytes, the so-called HLA antigens present on human lymphocytes. There have been preliminary reports in the literature that the person with elevated intraocular pressure who will go on to develop glaucoma has a different blood typing than the individual whose eye can tolerate the elevated pressure without damage. This, along with a variety of other tests is being used to differentiate these two groups.

Mr. FLOOD. What is it going to cost the glaucoma patients annually in the treatment of that disease? Most people, as you say, are over the age of 65 and that makes the cost a very, very real burden in this problem.

Dr. KUPFER. You are quite right. I think this is why it is so important to try to differentiate between the people who may have elevated pressure and will never get into trouble and the people who have elevated pressure and will get into trouble.

The first group will not need the same careful surveillance and therefore their medical care will be much less than the second group who are at high risk.

Mr. FLOOD. Is there any way to reduce the cost of the treatment of glaucoma?

Dr. KUPFER. I think the best way, of course, is to identify the individuals who need not be seen as frequently by the ophthalmologist and need not receive drug treatment. In this manner, the cost would be much less.

Mr. FLOOD. Since we say over half the people affected with glaucoma are over 65, are you planning any collaborative research with the Aging Institute on this disease?

Dr. KUPFER. We have not discussed the area of glaucoma as much as we have discussed cataract. There appears to be a stronger correlation between the development of cataract and aging.

I might add to our discussion on glaucoma that in trying to reduce the cost of glaucoma, our main emphasis will be on reducing the cost of surgical treatment, that is, to reduce the number of people who must have surgery and therefore incur additional costs.

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In our intramural program in Bethesda we have recently built a Q-switched laser, a special type of laser used to make a new opening for fluid to leave the eye. We will begin to see whether this instrument can be used on an outpatient basis to treat chronic glaucoma. If this turns out to be successful, there will be a major reduction in the economic impact of glaucoma.

LENS IMPLANTS

Mr. FLOOD. Have you made a determination as to whether the artificial lens implants are of greater benefit than the conventional cataract surgery?

Dr. KUPFER. We are very anxious to make that determination, Mr. Chairman. As a matter of fact, one of the activities that will be taking place in fiscal 1978 will be the design of a clinical trial to answer this very question, whether the benefits of intraocular lenses may outweigh the problems that they may create.

DISSEMINATION OF INFORMATION

Mr. FLOOD. What steps are you taking to educate the public about eye diseases?

Dr. KUPFER. We have a very active public information program. As you know, we have disseminated widely the results of the diabetic retinopathy study on the use of photocoagulation; we have distributed over 44,000 publications and we have cooperated with other countries in international programs on the prevention of blindness. The World Health Organization had as their World Health Day theme this past year, "Foresight Prevents Blindness." We have been very active in the dissemination of information throughout the United States in association with that activity.

Mr. FLOOD. Thank you very much.

EFFECTS OF REDUCTION IN FUNDING

Mr. CONTE. Mr. Chairman, may I go back to my question about the appropriation request? You can elaborate for the record or not, as you wish.

You said you asked for $70 million. The figure we have before us from OMB is $64.9 million. My question would be: Are there any major areas of research which you would like to fund but will be unable to do so because of having $5.2 million less than you need?

Dr. KUPFER. As you know, sir, approximately two years ago the National Advisory Eye Council brought forth the program planning report and at that time the projected budget to take advantage of all the research opportunities and respond to the needs for 1978 was approximately $112 million.

The National Advisory Eye Council has just completed a second cycle on their program planning report. The preliminary estimates are approximately $118 million. That is the level that the Advisory Council feels would be necessary to take advantage of all the research opportunities that exist in which there is a high probability for success.

Ms. WORMSER. Mr. Conte, I might add to that. The request that was transmitted to the Department by the Public Health Service for the Eye Institute was $57 million. I think that the difference that has been discussed here was part of the internal distribution of funds within the Public Health Service and perhaps within NIH.

Mr. CONTE. Where does the $70 million come from then? Can you clarify that?

Ms. WORMSER. I believe that was the request that the Eye Institute made initially in the development of the NIH budget to NIH.

Mr. CONTE. That is what I asked. That was my original question. My followup question is: They must have had a reason for submitting a budget of $70 million. Now they wind up with a budget of $64.9 million, which falls some $5.1 million short of what they requested. So they had to cut out some program. They didn't just go and take a figure out of the dark and say we want $70 million. They must have had a budget there.

As a result of that cut they are going to have to cut back some programs. I would just like to know what those programs are and where you are going to have to tighten up your belts. I think that is a fair question.

Dr. KUPFER. Mr. Conte, let me go back to a comment I made earlier. I do want to repeat that with the significant increase in funding that we received in 1977 that there is no doubt that we can maintain that momentum in 1978.

On the other hand, there are no additional resources for new programs. I think it might be appropriate to mention briefly some of those new opportunities.

I think the first is that we do have the opportunity now to apply many of the techniques learned in the laboratory to the study of retinal disease that have not been done in a systematic way before. Since retinal disease accounts for more than 30 percent of all visual disability and blindness, this would be an extremely high priority area.

We held a workshop last October on improving the diagnosis of retinal disorders by bringing together the laboratory researcher and clinician to facilitate the application of experimental testing procedures to clinical problems. I think we have significant opportunities ready to be exploited in this area.

A second area of opportunity is in cataract research. We have brought about a cooperative program among approximately 20 cataract researchers for exchange of information and for focusing research on the human lens and human cataract development. There is no doubt that some of these research opportunities are ripe for exploitation at the present time.

So I would say that this is a major area of exploitation.

The third area is glaucoma where there is great opportunity to test new drugs and the hypothesis of whether one can differentiate the person with increased pressure who does not lose vision from the person with increased pressure who does lose vision. This, I think, will await additional resources.

Mr. CONTE. That's the answer I was looking for. I, for one, will do all I can to see that those funds and programs are put in the bill.

Thank you.

Mr. NATCHER [presiding]. From time to time during the past several months, we have been reading articles to the effect that the use of marihuana has a tendency to relieve pressure as far as the eye is concerned.

Dr. KUPFER. Yes, sir.

Mr. NATCHER. Is there any truth to that?

Dr. KUPFER. There is no doubt that when marihuana is administered, either smoking or intravenously, it does produce a fall in intraocular pressure. I think the question that is absolutely essential to answer is: Does this fall in pressure last for a reasonable length of time so that marihuana can be effective and practical in the treatment of a person with glaucoma?

Mr. NATCHER. Have you said that to anyone in the National Institute so that it could be publicized? Some people believe that that is going to convince a lot of boys and girls that they ought to continue with marihuana. The last part of your statement is real good. Are you all saying that?

Dr. KUPFER. As a matter of fact, we have begun discussions with the National Institute on Drug Abuse concerning how best to answer the question I raised. I think we do have the wherewithal to focus on this area.

Mr. NATCHER. All right, thank you very much.

The committee will adjourn until 2.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

DIABETIC RETINOPATHY

Mr. CONTE. Would you explain how the photocoagulation treatment for diabetic retinopathy works? How effective is it? Do you have any information on how widely used this treatment procedure is now?

ANSWER. The exact mechanism of action of photocoagulation therapy in diabetic retinopathy is presently unknown. At least part of the effect may be due to the destruction of new blood vessels by direct treatment. But we know that after photocoagulation in a scatter pattern covering a large portion of the retina, new vessels not directly treated will also regress or disappear, in particular, those on the surface of the optic nerve head. There are several hypotheses as to why this might occur. One of these is that photocoagulation destroys sick retina that is producing a substance that calls forth the growth of new blood vessels. Loss of this stimulus causes the vessels to regress. Another hypothesis is that photocoagulation somehow allows the retina to utilize the oxygen and other nutrients of the choroidal circulation which, according to our present knowledge, is spared from the effects of diabetes. This might be accomplished by destroying localized areas of pigment epithelium, the natural barrier between the retina and choroid, or by causing thinning of the retina, bringing the inner layers of the retina closer to the choroidal circulation, or a combination of both. In any event, photocoagulation is effective in reducing the rate of severe visual loss in eyes with proliferative diabetic retinopathy as shown by the diabetic retinopathy study where eligible patients had a 61 percent decrease in severe visual loss over a 2-year followup period. Photocoagulation for treatment of diabetic retinopathy is being widely used in the medical community. It is available at most large medical centers and most physicians specializing in the treatment of retinal diseases have ready access to the necessary equipment. The diabetic retinopathy study has shown the efficacy of this treatment, and has stimulated introduction of this technique into areas where it was previously unavailable.

DIABETES

Mr. CONTE. In your recent invitation for applications in the field of ocular aspects of diabetes, what specific kinds of studies were you looking for?

ANSWER. The NEI's request for research grant applications on the ocular complications of diabetes focused on laboratory and clinical studies relevant to not only diabetic retinopathy but also the specific types of cataracts, glaucoma, optic nerve abnormalities, and disorders of eye movement which are known to be the result of diabetes. In particular, the announcement identified the following topics: "(1) vasoproliferative and inhibitory factors; (2) vascular and retinal metabolism; (3) retinal and choroidal blood flow; (4) blood rheology and clotting factors; (5) physical chemistry, biochemistry, and physiology of the vitreous in maintenance of blood-retinal barriers and vitreous and retinal metabolism and structure; (6) immunology of vitreous and retina in relation to diabetic retinopathy; (7) neovascular glaucoma and other ocular complications of neovascularization; (8) etiology and treatment of sugar cataract; and (9) pathogenesis and possibilities for treatment of diabetic optic neuropathology and oculomotor disorders."

CORNEAL DISEASES

Mr. CONTE. Is any work being done on possible ways to promote the growth and reproduction of cells in the inner layer of the cornea?

ANSWER. Yes, Dr. Jules Baum and his coworkers at Tufts University School of Medicine in Boston have successfully cultured rabbit endothelial cells in vitro. Such cultures maintain their shape and are capable of synthesizing a basal membrane composed of collagen which resembles Descemet's membrane, the support matrix for such cells in the living cornea. Dr. David Whikehart of the Laboratory of Vision Research of the National Eye Institute has also succeeded in tissue culturing the inner layer of the cornea and is studying certain enzymes which may be important in the regulation of the transport of metal ions into this cell layer.

NEW RESEARCH GRANT REDUCTION

Mr. CONTE. Could you explain the reduction in the number of your new regular grants?

ANSWER. The reduction in the number of new regular research grants occurred because of the relatively stable level of funding assigned to the National Eye Institute for fiscal year 1978. You will note that noncompeting requirements increased in 1978. This increase is based on our current grants portfolio. In addition, increases were made in the direct operating areas of the Institute to accommodate increased costs of conducting business. The balance of funds available were placed in the new regular research grants line.

PROGRAM DECREASES

Mr. CONTE. Why are you reducing the level of support for retinal and choroidal diseases? Why the reduction in support for corneal diseases?

ANSWER. The funds available were first distributed to those areas where a commitment to support existed. The balance of the funds were distributed in an attempt to equalize the share of new moneys each of the five research programs would receive. Due to the variation of funds in the committed or noncompeting components, some programs gained in total support—others, particularly the two you mention, show a decrease. We would state here also that even though decreases are proposed for the two programs, they have not in the eyes of the Institute, decreased in their importance.

PERCENT OF EYEGLASSES WORN BY POPULATION

Mr. MICHEL. What percentage of our population now wears glasses?

ANSWER. It is estimated that 94,000,000 people—or almost half the population of this country—wear glasses or contact lenses to improve their vision.

Mr. MICHEL. Is this percentage increasing or decreasing?

ANSWER. It is reasonable to assume that this percentage is increasing for a number of reasons. One is the increasing portion of our population which is over age 45, the time in life when most of us find we need to wear glasses even if we have not had to wear them previously. Also, improved literacy, a shift to occupations which require better vision, the increasing number of people operating motor vehicles, and improved access to health care services have also, no doubt, contributed to increasing eyeglass or contact lens wear.

Mr. MICHEL. There have been some Senate hearings on the cost and quality of glasses. This may be a little out of your field, but do you have any opinions on whether Americans are being overcharged for glasses, or whether they are receiving the proper quality of glasses?

ANSWER. For a definitive answer to that question I would certainly defer to those who have investigated this matter thoroughly and who are well-acquainted with the pertinent facts. However, I am aware that data has been presented to the Federal Trade Commission, to the Congress, and in the news media which purport to show a wide variation in the prices charged for eyeglasses throughout the United States. Although it is certainly possible that if in fact such a variation exists it may in some instances be due to overcharging, other possible contributing factors need to be considered. For instance, eyeglass prescriptions vary greatly, some being more complex and therefore more costly to fill than others. Considerable variations exist in the quality of materials and construction of eyeglass frames. Also, a given patient may have unique problems and requirements which make a successful eyeglass fitting a more difficult and time consuming, and therefore more expensive, process. Other factors which must be considered are variations in a practitioner's operating and overhead costs and the variation in professional fees normally charged by different providers of eyeglasses.

With regard to quality, I think that Americans can assure the quality of the eyeglasses they purchase by having their prescription filled by a qualified and reputable practitioner. There are various sources for such information within the community including local eye care professional societies and organizations and Better Business Bureaus. The opinion of one's family doctor, as well as of relatives, friends, and neighbors may also be helpful. Once the glasses are made their quality can be checked with the practitioner who prescribed them if that individual is different from the one who made them. If this is not the case, they can be checked by a second disinterested party. Of course, one simple test of quality is how well the glasses feel to the person who wears them and how well that individual is able to see with them on.

DIABETIC RETINOPATHY

Mr. MICHEL. Why has diabetic retinopathy become an increasing problem over the past couple of generations, or was it simply undiagnosed before?

ANSWER. Diabetes has been known to cause specific changes in the retina of the eye for more than a century. However, since the longer a person lives with diabetes, the greater his or her chance of developing retinopathy, it was not until after the introduction of insulin in the 1930's and of other improvements in the treatment of diabetes which led to increased longevity of people with this disease that diabetic retinopathy became a major public health problem. Another factor in the increased incidence of this eye disease is that because the tendency to diabetes is at least in part inherited, as more diabetics are able to lead relatively normal lives which permit them to marry and have children, the number of individuals with diabetes is increasing. A third factor is that diabetics today are more likely to be under medical care, and physicians, because of greater awareness of the eye complications of the disease are more inclined to include an eye examination as part of the routine care of their diabetic patients.

Mr. MICHEL. To what degree does the new photocoagulation procedure reduce blindness from diabetic retinopathy. Are any figures or estimates available?

ANSWER. The diabetic retinopathy study has demonstrated that photocoagulation is of benefit in decreasing or delaying the occurrence of severe visual loss in patients with proliferative diabetic retinopathy. Visual loss is defined here as visual acuity of less than or equal to 5/200 at two or more complete consecutive follow-up visits. In the stages of proliferative diabetic retinopathy that were tested in the study, the 2-year rate of severe visual loss was reduced from 16.3 percent in untreated eyes to 6.4 percent in treated eyes, a reduction of 61 percent.

COOPERATIVE CATARACT RESEARCH GROUP

Mr. MICHEL. Your statement also indicates that a Cooperative Cataract Research Group has been formed. How many researchers are involved in this group?

ANSWER. There are 16 researchers involved in the Cooperative Cataract Research Group.

Mr. MICHEL. How much in the way of funds are being allocated to this Group;

ANSWER. It is estimated that in 1977, $1,522,267 will be allocated to the Cooperative Cataract Research Group.

LENS IMPLANTATION

Mr. MICHEL. When do you expect to get the study on lens implantation underway, and how long is it expected to take?

ANSWER. The statistical study of existing registries of data on lens implant cases is expected to begin during fiscal year 1977 and will require approximately 18 months. In parallel with that study, planning for a multi-center clinical trial will continue. If such a controlled study is judged to be feasible, it will commence in fiscal year 1978.

RESEARCH GRANT FUNDING

Mr. MICHEL. What percentage of the grant applications in your area received this year are being funded, and, second, what percentage of those applications approved by the study sections are being funded?

ANSWER. Approximately 48 percent of competing grant applications received will be paid in fiscal year 1977. Applications approved by the study sections are being funded at the rate of 55 percent.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Amounts Available for Obligation

	1977	1978
Appropriation	$64,000,000	$64,981,000

National Eye Institute

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	NUMBER	FTE[1]	AMOUNT	NUMBER	FTE[1]	AMOUNT
Grants						
Regular						
Noncompeting	411		$27,082,000	486		$34,769,000
Competing	115		6,684,000	51		3,648,000
New	136		9,238,000	68		4,952,000
Supplemental	(8)		100,000	(8)		100,000
Subtotal	662		43,104,000	605		43,469,000
Special						
Academic Investigator Awards	11		300,000	11		300,000
Research Career Program	25		620,000	25		620,000
Core and Specialized Clinical Research Centers	10		2,000,000	10		2,000,000
Subtotal	46		2,920,000	46		2,920,000
Total Grants	708		46,024,000	651		46,389,000
Training Program						
Individual						
Noncompeting	70	70	1,053,000	128	128	1,923,000
New	80	80	1,200,000	22	22	330,000
Institutional						
Noncompeting	32	118	2,387,000	26	101	1,890,000
Total Training	182	268	4,640,000	176	251	4,143,000
Research and Development Contracts	55		3,522,000	61		3,822,000
Intramural Laboratory and Clinical Research	89		7,098,000	89		7,737,000
Direct Operations	36		1,740,000	36		1,933,000
Program Management	27		976,000	26		957,000
Institute Total	152		64,000,000	151		64,981,000

[1] FTE - Full-time equivalent

DHEW - National Institutes of Health

National Eye Institute

1977 Column of 1978 Justification

Crosswalk
(In Thousands)

	MECHANISM										
	Research Grants										
			Special Programs								
Program	Noncompeting	Competing	Multi-disciplinary Centers	Other	Training Indiv.	Training Instit.	Research and Development Contracts	Intramural Labs and Clinical Research	Direct Operations	Program Management	Program Total
Retinal & Choroidal Diseases	9,692	7,068	840	489	939	694	3,403				23,125
Corneal Diseases	4,455	1,723	210	100	671	399	28				7,586
Cataract	2,650	2,172	302	73	147	180	--				5,524
Glaucoma	3,901	2,469	342	85	387	417	91				7,692
Sensory-Motor Disorders & Rehabilitation	6,384	2,590	306	173	109	697	--				10,259
Intramural Laboratory & Clinical Research								7,098			7,098
Direct Operations									1,740		1,740
Program Management										976	976
Total	27,082	16,022	2,000	920	2,253	2,387	3,522	7,098	1,740	976	64,000

DHEW - National Institutes of Health

National Eye Institute

1978 Column of 1978 Justification

Crosswalk
(In Thousands)

Program	MECHANISM										
	Research Grants										
			Special Programs								
	Noncompeting	Competing	Multi disciplinary Centers	Other	Training Indiv.	Training Instit.	Research and Development Contracts	Intramural Labs and Clinical Research	Direct Operations	Program Management	Program Total
Retinal & Choroidal Diseases	13,326	3,316	840	489	939	288	3,703				22,901
Corneal Diseases	4,473	1,279	210	100	671	276	28				7,037
Cataract	4,001	921	302	73	147	205	--				5,649
Glaucoma	5,720	1,516	342	85	387	453	91				8,594
Sensory-Motor Disorders & Rehabilitation	7,249	1,668	306	173	109	668	--				10,173
Intramural Laboratory & Clinical Research								7,737			7,737
Direct Operations									1,933		1,933
Program Management										957	957
Total	34,769	8,700	2,000	920	2,253	1,890	3,822	7,737	1,933	957	64,981

Summary of Changes

1977 Appropriation	$64,000,000
1978 Estimated Obligations	$64,981,000
Net Change	+$ 981,000

	1977 Pos.	1977 Amount	Change Pos.	Change Amount
Increases:				
A. Built-in				
1. Within grade pay increase	--	5,000	--	+45,000
2. FTS rate increase	--	22,000	--	+3,000
3. Wage board increase	--	25,000	--	+9,000
4. Federal Employees' Compensation Fund payments increase	--	7,000	--	+2,000
5. Service & Supply cost increase	--	35,000	--	+16,000
6. Payment for centrally furnished services	--	3,926,000	--	+62,000
(Standard Level User Charges)		(93,000)	--	(+9,000)
Subtotal	--	--	--	+$137,000
B. Program				
1. Research grants				
a. Noncompeting continuations	--	26,957,000	--	+16,022,000
b. Competing (new continuations and supplementals)	--	16,022,000	--	+8,700,000
c. Special: Scientific Evaluation	--	125,000	--	+13,000
2. Training programs				
a. Individuals				
1. Noncompeting continuations	--	1,053,000	--	+1,200,000
2. Research and Development Contracts	--	3,522,000	--	+300,000
Total increases	--	--	--	+$26,372,000
Decreases:				
A. Built-in				
1. One less day of pay	--	3,412,000	--	-13,000
2. Decrease of one (1) position	152	3,412,000	-1	-19,000
Subtotal	--	--	-1	-32,000
B. Program				
1. Research grants				
a. Noncompeting completed or converted to competing status	--	26,957,000	--	-8,510,000
b. Competing completed or converted to noncompeting	--	16,022,000	--	-16,022,000
2. Training				
a. Institutionals				
1. Noncompeting continuations	--	2,387,000	--	-497,000
b. Individuals				
1. Competing (new continuations and supplementals)	--	1,200,000	--	-330,000
Total Decreases	--	--	--	-$25,391,000
Total, Net Change	--	--	--	+$ 981,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase Decrease Pos.	Increase Decrease Amount
109	Retinal & Choroidal Diseases	--	$23,125,000	--	$22,901,000	--	-$224,000
111	Corneal Diseases	--	7,586,000	--	7,037,000	--	- 549,000
113	Cataract	--	5,524,000	--	5,649,000	--	+ 125,000
115	Glaucoma	--	7,692,000	--	8,594,000	--	+ 902,000
117	Sensory-Motor Disorders & Rehabilitation	--	10,259,000	--	10,173,000	--	- 86,000
119	Intramural Laboratory & Clinical Research	89	7,098,000	89	7,737,000	--	+ 639,000
	(Standard Level Users Charge)		(47,000)		(58,000)		(+ 11,000)
121	Direct Operations	36	1,740,000	36	1,933,000	--	+ 193,000
	(Standard Level Users Charge)		(46,000)		(44,000)		(- 2,000)
122	Program Management	27	976,000	26	957,000	-1	- 19,000
	Total Obligations	152	64,000,000	151	64,981,000	-1	+ 981,000
	(Standard Level Users Charge)		(+93,000)		(+102,000)		(+ 9,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	152	151	-1
Full-time equivalent of all other positions	6	4	-2
Average number of all employees	140	142	+2
Personnel compensation:			
Permanent positions	$ 2,790,000	$ 2,772,000	-$ 18,000
Positions other than permanent	193,000	193,000	--
Other personnel compensation	61,000	61,000	--
Subtotal, personnel compensation	3,044,000	3,026,000	- 18,000
Personnel benefits	368,000	367,000	- 1,000
Travel and transportation of persons	140,000	157,000	+ 17,000
Transportation of things	32,000	35,000	+ 3,000
Rent, communications and utilities	160,000	170,000	+ 10,000
Printing and reproduction	30,000	40,000	+ 10,000
Other Services:			
Project contracts	3,522,000	3,822,000	+ 300,000
Payment for centrally furnished services	3,926,000	3,988,000	+ 62,000
Other	1,464,000	2,131,000	+ 667,000
Supplies and materials	350,000	388,000	+ 38,000
Equipment	300,000	325,000	+ 25,000
Grants, subsidies and contributions	50,664,000	50,532,000	- 132,000
Total, obligations by object	64,000,000	64,981,000	+ 981,000

AUTHORIZING LEGISLATION

Legislation	1978 Authorized	1978 Appropriation Requested
Public Health Service Act Section 301 -- Research and Investigations in General	Indefinite	
Title IV, Part F -- National Eye Institute	Indefinite	$61,528,000 2/
Title IV, Part I -- National Research Service Awards Act	1/	3,453,000 3/

1/ Authorization expires September 30, 1977, extension legislation is pending.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $690,000 for old training program.

National Eye Institute

Comparable *

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$22,073,000	$22,073,000	$23,330,000	$22,652,000
1971	24,325,000	29,217,000	29,217,000	29,435,000
1972	31,258,000	34,437,000	38,404,000	35,670,000
1973	33,797,000	36,809,000	43,247,000	36,809,000 1/
1974	32,092,000	36,631,000	46,631,000	39,998,000 2/
1975	39,947,000	38,878,000 3/	50,000,000	44,040,000
1976	39,201,000	42,608,000 4/	50,000,000 4/	50,285,000 5/
1977	46,950,000	56,270,000	70,000,000	64,000,000
1978	64,981,000			

1/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

3/ Excludes Research and Development contracts not considered by House due to lack of authorizing legislation.

4/ Excludes fellowships and training grants not considered due to pending legislation ($4,647,000).

5/ Includes $4,647,000 for training programs authorized by the continuing resolution.

*"The figures presented in this Table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes".

National Eye Institute

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1970	$23,685,000	$23,685,000	$25,000,000	$22,828,000
1971	25,686,000	30,986,000	30,986,000	30,032,000
1972	32,639,000	36,022,000	40,187,000	37,132,500
1973	37,384,000	38,562,000	45,000,000	38,562,000 1/
1974	32,092,000	36,631,000	46,631,000	41,177,000 2/
1975	39,947,000	38,878,000 3/	50,000,000	44,133,000
1976	39,201,000	42,608,000 4/	50,000,000 4/	50,212,000 5/
1977	46,950,000	56,270,000	70,000,000	64,000,000
1978	64,981,000			

1/ Note: This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

3/ Excludes Research and Development contracts not considered by House due to lack of authorizing legislation.

4/ Excludes fellowships and training grants not considered due to pending legislation ($4,647,000).

5/ Includes $4,647,000 for training programs authorized by the continuing resolution.

Justification

National Eye Institute

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Retinal & Choroidal Diseases	--	$23,125,000	--	$22,901,000	--	-$224,000
Corneal Diseases	--	7,586,000	--	7,037,000	--	- 549,000
Cataract	--	5,524,000	--	5,649,000	--	+ 125,000
Glaucoma	--	7,692,000	--	8,594,000	--	+ 902,000
Sensory-Motor Disorders & Rehabilitation	--	10,259,000	--	10,173,000	--	- 86,000
Intramural Laboratory & Clinical Research	89	7,098,000	89	7,737,000	--	+ 639,000
Direct Operations	36	1,740,000	36	1,933,000	--	+ 193,000
Program Management	27	976,000	26	957,000	-1	- 19,000
Total	152	64,000,000	151	64,981,000	-1	+ 981,000

General Statement

Introduction

The National Eye Institute has the primary responsibility for supporting the pursuit of new knowledge about the eye and visual system and advancing the sciences related to vision in order to further progress against blindness and visual disability. Working to this end, the National Eye Institute supports, through grants, traineeships, and contracts to medical schools and other research institutions, research and research training aimed at improving the prevention, diagnosis, and treatment of vision disorders; conducts laboratory and clinical research in its own facilities, and fosters statistical and epidemiological studies of visual disorders in human populations; fosters research on the rehabilitation of the visually handicapped; encourages the application of research findings to clinical practice; heightens public awareness of vision problems; and cooperates with voluntary organizations which engage in related activities. The National Eye Institute provides about 70% of the total national support for vision research.

Significance of the Problem

At least 10 million persons--1 of every 20 in the United States--suffer from some type of significant, uncorrectable, impairment of vision. Fifteen percent of these, 1.5 million people, are unable to see well enough to read

ordinary newsprint with either eye, even with the aid of eyeglasses; five percent, approximately half a million, are classified as "legally" blind. The economic costs of professional eye care and indirect costs associated with loss of earnings from eye disorders exceed $5 billion annually. These costs do not include the 258 million dollars that came directly out of the federal treasury for such items as supplemental security income for the blind and compensation for blind and visually impaired veterans. Among the chronic diseases that restrict the ability of Americans to lead normal, productive lives, visual impairment ranks third after heart disease and arthritis. A 1976 Gallup Poll has reconfirmed the findings of an earlier survey that Americans fear blindness more than any other affliction, save cancer.

An estimated 5.7 million new cases of eye disease and injury occur each year. The most common of these conditions are ocular inflammations, cataract, retinal disorders, strabismus, glaucoma, and corneal ulcers and opacities. Of the leading causes of visual impairment, disorders of the retina, including senile macular degeneration and diabetic retinopathy, are the most common. The next most common ones are cataract, glaucoma, optic nerve disease, and inflammatory disorders of the eye.

There are an estimated 31 million visits annually for professional eye treatment or care. An estimated 567,000 persons are discharged from short-stay hospitals with an eye disease or injury as the first listed diagnosis. Approximately one-half of these discharges are for cataract surgery.

These statistics tell only part of the story, because they cannot convey the hardship and mental anguish of those persons who are deprived of normal vision and who have to survive and function in our highly complex, technical, and dynamic society.

Overview

Probably no single event has more dramatically symbolized the emergence of vision research into the mainstream of modern medicine than the announcement last April of the first results from the NEI-supported collaborative Diabetic Retinopathy clinical trial. After only two years of patient follow-up, impressive evidence was compiled that treatment with powerful beams of focused light (photocoagulation) could effectively reduce the rate of occurrence of severe visual loss from diabetic retinopathy, one of the primary causes of new blindness in the United States.

The success of this trial is largely due to the dedication of its participating investigators and to the resources and leadership provided by the National Eye Institute. There is every indication that it will stand as a landmark in vision research. Yet, the study must be viewed from a perspective which looks back 120 years to the first recorded description of specific changes in the retina of patients with diabetes mellitus.

The history of research in diabetic retinopathy illustrates the full spectrum of biomedical investigation: clinical observation, laboratory study, clinical research, and finally translation of this information into new methods of patient care. For any given line of inquiry, of course, the time and course from initial discovery through development, application and effective transfer into the health care system will vary considerably. A crucial question, therefore, is what role the federal government can play, in this case the NEI, in affecting the rate of discovery in the visual sciences, charting the course of research and fostering its broad application and transfer into the health care milieu. In an effort to address this need on a sound scientific basis, the NEI has embarked on an extensive program planning effort resulting in the publication in 1975 of the "Vision Research Program Planning Report of the National Advisory Eye Council" and a new planning report that will be made available in the Spring of 1977. This latest plan will examine and analyze evidence of the progress that has been made

toward achieving those goals put forth in the earlier planning efforts and will present a new assessment of major vision research needs and opportunities.

Research programs of the Institute are currently grouped under five major research headings: Retinal and choroidal diseases, corneal diseases, cataract, glaucoma, and sensory-motor disorders and rehabilitation. Specific objectives are delineated under the appropriate program activity.

Retinal and Choroidal Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part F and I

	1977 Appropriation		1978 Estimate		Increase Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	149	$ 9,692,000	185	$13,326,000	+36	+$3,634,000
Competing	111	7,068,000	46	3,316,000	-65	- 3,752,000
Specials:						
Core and Specialized Clinical Research Centers	4	840,000	4	840,000	--	--
Research Career Awards	10	249,000	10	249,000	--	--
Academic Investigator Awards	9	240,000	9	240,000	--	--
Subtotal	283	18,089,000	254	17,971,000	-29	- 118,000
Training Programs:						
Individual	62	939,000	62	939,000	--	--
Institutional	9	694,000	5	288,000	-4	- 406,000
Research & Development Contracts	55	3,403,000	59	3,703,000	+4	+ 300,000
Total		$23,125,000		$22,901,000		-$ 224,000

Introduction

Diabetic retinopathy, macular degeneration, retinitis pigmentosa, and other retinal degenerative diseases are primary causes of more than one third of all blindness in this country. These diseases, which can neither be prevented nor cured, are considered by ophthalmologists to be the most difficult to treat and most in need of further laboratory and clinical research. An estimated 15,000 people become blind each year from retinal and choroidal diseases, which already accounts for 32% of all blindness in the U. S.

Financing

This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Program Plans for 1978

Studies will focus on blindness and other visual disabilities associated with diabetes, with emphasis placed on clinical trials of new therapies, clinical research in natural history, genetics and treatment of diabetic retinopathy and the formation of abnormal new blood vessels in the retina. Related research on blood flow and other factors will be supported on other types of circulatory abnormalities and vascular disorders in the eye which contribute to newly recorded blindness, such as those associated with hypertension, arteriosclerosis, sickle cell disease, and vascular occlusion disorders. Improved technology for noninvasive study of the retina will be further utilized as a means of differentiating various types of disorders of the retinal region most useful in bright light vision, the macula. In addition, a knowledge of the genetic patterns of various types of macular degeneration will be pursued. Increased emphasis will be placed on gaining more knowledge of retinal cell biology and organization, particularly with respect to how the light sensitive components (the rods and cones) are produced and how they are related to the retinal pigment epithelium in health and disease. Study of the vitreous body, a transparent gel in the back part of the eye, will be expanded, with emphasis on defining the extent and origin of tissue reactions within the vitreous to provide information on which to base a more rational design of treatment for diseases involving this tissue. Studies will also be continued on the development of vitreous substitutes, both solid and gaseous, for use in the surgical treatment of retinal detachment. Other studies will focus on the vulnerability of retinal cells to nutritional deficiencies, drugs, and poisonous substances; and on the structure and chemical composition of the rod or cone cell membrane and its role in transfering light energy into a visual impulse.

Under the requested level approximately 254 research grants, of which 46 are new and competing will be awarded to address the needs and opportunities presented above. In addition, 5 institutional, 62 individual traineeships, and 59 research contracts will be awarded.

Corneal Diseases

Authorizing Legislation: Public Health Service Act, Title IV, Part F and I

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	67	$4,455,000	63	$4,473,000	-4	+$ 18,000
Competing	27	1,723,000	17	1,279,000	-10	- 444,000
Specials:						
Core and Specialized Clinical Research Centers	1	210,000	1	210,000	--	--
Research Career Awards	4	100,000	4	100,000	--	--
Academic Investigator Awards	--	--	--	--	--	--
Subtotal	99	6,488,000	85	6,062,000	-14	- 426,000
Training Programs:						
Individual	45	671,000	45	671,000	--	--
Institutional	6	399,000	4	276,000	-2	- 123,000
Research & Development Contracts	1	28,000	1	28,000	--	--
Total		$7,586,000		$7,037,000		-$549,000

Introduction

Corneal diseases include disorders caused by infectious agents such as viruses and bacteria, congenital and developmental influences, and degenerative processes. An estimated 21,000 Americans are blind from corneal disease, accounting for about 6% of all blindness in this country. Although the incidence of blindness from corneal diseases in the United States is less than other kinds of ocular disease, they have a high rate of incidence worldwide and account for more ocular pain than any other visual disorder. Annually, there are approximately 10 million office visits for professional eye care for corneal problems other than refractive errors.

Financing

This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also, institutional and individual traineeships are awarded under authority of the National Research

Service Awards Act.

Program Plans for 1978

Continuing immunologic studies will be pursued with the goal of reducing the significant rejection rate accompanying corneal grafts; trials of new antiviral drugs useful in treating herpes simplex infections and the definition of the host factors responsible for the primary acquisition of the herpes virus and the recurrence of infections will be studied; studies to determine the value and importance of soft contact lens and their use in the treatment of corneal diseases will be pursued; and, further improvement of special microscopes and other instrumentation useful in corneal diagnosis will be studied to make these instruments simple and convenient for routine use in clinics.

Under the requested level approximately 85 research grants, of which 17 are new and competing will be awarded to address the needs and opportunities presented above. In addition, 4 institutional, 45 individual traineeships and one research contract will be awarded.

Cataract

Authorizing Legislation: Public Health Service Act, Title IV, Part F and I

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	40	$2,650,000	57	$4,001,000	+17	+$1,351,000
Competing	34	2,172,000	13	921,000	-21	- 1,251,000
Specials:						
Core and Specialized Clinical Research Centers	1	302,000	1	302,000	--	--
Research Career Awards	3	73,000	3	73,000	--	--
Academic Investigator Awards	--	--	--	--	--	--
Subtotal	78	5,197,000	74	5,297,000	-4	+ 100,000
Training Programs:						
Individual	10	147,000	10	147,000	--	--
Institutional	2	180,000	2	205,000	--	+ 25,000
Research & Development Contracts	--	--	--	--	--	--
Total		$5,524,000		$5,649,000		+$ 125,000

Introduction

Cataract is a cloudiness of the normally clear lens which obstructs vision by disrupting the passage of light to the retina. This disease is a major cause of visual disability and blindness throughout the world. In the United States alone, one sixth of all visual impairments is due to cataract. Of the approximate 3,013,000 Americans with cataracts, 64,000 are legally blind. Although the surgical removal of the cloudy lens is a successful surgical procedure, cataracts are still responsible for 14% of all blindness.

Financing

This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also, institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Program Plans for 1978

Studies aimed at ultimately yielding a means of preventing or retarding the development of cataract will continue, for in order to prevent a disease one must understand its causes. In senile cataract, there are almost certainly a number of contributory causes, which are superimposed on normal aging processes. The prevention of senile cataract therefore requires a much improved understanding of the structure of the human lens, of its metabolic processes and the changes induced in it by increasing age and external influences. Continuing studies will therefore focus on protein changes in the lens and the role of protein aggregation in the development of cataract. Fundamental studies will also seek adequate animal models for explaining the mechanism of cataract formation, in order to relate these findings to understanding the etiology of human senile cataract.

In the area of sugar cataracts, studies will continue to focus on the enzyme inhibitors recently developed in order to determine whether such inhibitors will help to prevent cataract in humans suffering from defects in sugar metabolism, such as diabetes.

Most importantly, the major national collaborative research effort in human cataract research initiated in FY 1977 will continue in FY 1978. Research advances in this program and the relative cohesiveness of the national effort in this area should permit a more coordinated approach to the solution of the human cataract problem by collaboration among over 20 research centers including the intramural program of the NEI. Special arrangements for the swift interchange of research information will be supported.

Additionally, the Institute will provide centralized research resources for this area of research and establish a focal point within the Institute to coordinate and assist in accelerating the national cataract research effort.

Under the requested level approximately 74 research grants, of which 13 are new and competing will be awarded to address the needs and opportunities presented above. In addition, 2 institutional and 10 individual traineeships will be awarded.

Glaucoma

Authorizing Legislation: Public Health Service Act, Title IV, Part F and I

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	59	$3,901,000	80	$5,720,000	+21	+$1,819,000
Competing	39	2,469,000	20	1,516,000	-19	- 953,000
Specials:						
Core and Specialized Clinical Research Centers	2	342,000	2	342,000	--	--
Research Career Awards	1	25,000	1	25,000	--	--
Academic Investigator Awards	2	60,000	2	60,000	--	--
Subtotal	103	6,797,000	105	7,663,000	+2	+ 866,000
Training Programs:						
Individual	26	387,000	26	387,000	--	--
Institutional	6	417,000	6	453,000	--	+ 36,000
Research & Development Contracts	1	91,000	1	91,000	--	--
Total		$7,692,000		$8,594,000		+$ 902,000

Introduction

Glaucoma is one of the leading causes of visual disability in the Nation. It is responsible for twelve percent of all blindness in the United States and 14% of all new cases of blindness. Eye surgery for glaucoma represents about 3 percent of all eye surgery, and the cost for one year of this surgery has been estimated to be $8,758,000. However, a large majority of patients with glaucoma are treated by means of eyedrops and other medications rather than by surgery. In the United States, the cost for one year for one type of eyedrop used in the treatment of glaucoma was $29,000,000. Thus, besides being a widespread and often serious eye disease, glaucoma is a costly one.

Financing

This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research

Service Awards Act.

Program Plans for 1978

Continued support will be given to understanding how changes in blood circulation of the eye leads to increases in intraocular pressure which often result in damage to the optic nerve. A number of treatment methods for this disease will be tested to determine the most effective mode of correcting such ocular circulatory disturbances before impaired vision results. Research designed to identify more accurately the individuals at risk to closed-angle glaucoma will also receive emphasis. Additional emphasis will be given to study of the cell biology of the ciliary body (that portion of the eye which produces aqueous humor) and its growth in an artificial medium, and of the trabecular meshwork (a pore-like structure through which the aqueous humor percolates to the outflow channels).

Under the requested level approximately 105 research grants, of which 20 are new and competing will be awarded to address the needs and opportunities presented above.

In addition, 6 institutional and 26 individual traineeships will be awarded.

Sensory-Motor Disorders and Rehabilitation

Authorizing Legislation: Public Health Service Act, Title IV, Part F and I

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	96	$ 6,384,000	101	$ 7,249,000	+5	+$865,000
Competing	40	2,590,000	23	1,668,000	-17	- 922,000
Specials:						
Core and Specialized Clinical Research Centers	2	306,000	2	306,000	--	--
Research Career Awards	7	173,000	7	173,000	--	--
Academic Investigator Awards	--	--	--	--	--	--
Subtotal	145	9,453,000	133	9,396,000	-12	- 57,000
Training Programs:						
Individual	7	109,000	7	109,000	--	--
Institutional	9	697,000	9	668,000	--	- 29,000
Research & Development Contracts	--	--	--	--	--	--
Total		$10,259,000		$10,173,000		-$ 86,000

Introduction

Research pertaining to sensory and motor disorders of the visual system includes investigations related to the optical properties of the eye, visual sensory and perceptual functions, disorders of eye movements and methods of rehabilitation necessitated by severe vision impairment or blindness. The complex sensory-motor system responsible for vision constitutes the largest single sensory input to the central nervous system, interacts with the higher centers of perception, and influences the full spectrum of information gathering, throught process, and action.

Sensory and motor disorders of vision may be either congenital or acquired and account for 16% of all blindness. Research into the visual system in health and disease is hoped to improve the diagnosis and treatment of strabismus (crosseye), amblyopia (decreased vision apparently caused by abnormal development of the visual nervous system), and other sensory and motor problems, such as improper convergence and accommodation. A total of 37,000 Americans are blind

from optic nerve atrophy and myopia alone (9.2% of all legal blindness) and each year 3,000 more people are blinded by these disorders.

Laboratory and clinical research is being supported to elucidate the brain's role in interpreting the pattern of nerve impulses received from the optic nerve and in feeding essential information back to the ocular muscles. These studies are exploring the development of visual abilities in the infant as well as normal visual function in the adult. In many cases, early detection of sensory-motor disorders may permit successful treatment and prevention of blindness, and research is being pursued to make this possible.

Within recent years a wide array of tests developed in basic vision science laboratories for the noninvasive but highly precise movement of visual function in humans have matured to the point where they are ready for application in clinical research. These tests have substantial promise of advancing our detailed understanding of the natural history of diabetic retinopathy, senile macular degeneration, and other common disorders of the visual system and of eventually becoming routine diagnostic tools for retinal disease and lesions of the visual nervous system. During FY 1977, a workshop to discuss how to encourage the transfer of these recent findings was organized by the NEI. A workshop to discuss low vision and rehabilitation will be held during FY 1977.

Financing

This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Program Plans for 1978

Studies of congenital, developmental and degenerative abnormalities, i. e., strabismus and amblyopia, will continue to pursue information on early growth patterns and development of visual pathways. Research on strabismus surgery and on neuromuscular abnormalities would continue. Other studies will further concentrate on psychophysical functions, dyslexia and oculomotor control.

Under the requested level approximately 133 research grants, of which 23 are new and competing will be awarded to address the needs and opportunities presented above. In addition, 9 institutional and 7 individual traineeships will be awarded.

Intramural Laboratory and Clinical Research

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Laboratory & Clinical Research	89	$7,098,000	89	$7,737,000	--	+$639,000

Introduction

The Intramural Laboratory and Clinical Research program of the National Eye Institute is focused on developing new and improved techniques for the prevention, diagnosis, and treatment of vision disorders. Activities of this area are carried out under the Office of the Scientific Director, the Clinical Branch, which translates research findings into practical applications and the Laboratory of Vision Research which conducts basic research that will provide better insight into disease processes and the function of visual systems. Also included in this program area is the Office of Biometry, Epidemiology and Field Studies which conducts research and provides statistical and epidemiological support in the incidence and prevalence of visual disorders.

One important advance during 1977 was the demonstration that in experimental diabetes the treatment of the diabetic animal with aldose reductase inhibitor effectively delayed the onset of the cataract. This was the first demonstration that the course of diabetic cataracts in the intact animals could be altered. Studies are underway to improve the delivery of the inhibitors in eye drops.

Other advances in cataract research have been made. It now looks possible to grow human lens cells in artificial medium. Thus it is now feasible to establish cell lines of the lens epithelium. This new development may provide insight into the causes of congenital cataracts.

Program Plans for 1978

Investigations planned in the Clinical Branch will aggressively explore the disease conditions that are the major contributors to blindness and debilitation. The glaucoma research program will study the natural history of patients with ocular hypertension (elevated eye pressure without loss of vision) and the effects of medical treatment upon this disease. Other studies will continue to explore various pharmacological and surgical modalities to identify the most effective method of controlling glaucoma. The research program studying retinal degeneration and genetically determined ocular diseases will take advantage of new diagnostic tests to help categorize and classify an array of these diseases. A continued effort will be made to identify specific defects in ocular degenerative diseases. The diabetic retinopathy research program will continue efforts to establish the mechanism by which new blood vessels grow in the retina. Control of this process could be an important treatment for the prevention of blindness from diabetes.

The Laboratory of Vision Research will continue to develop areas of research that foster better understanding of the basis for disease processes and visual function. Research on retinitis pigmentosa (night blindness) will be expanded to capitalize on emerging research opportunities. In patients with retinitis pigmentosa one particular receptor of retinol (the alcohol form of Vitamin A)

in the retina is apparently missing. Further experiments will be conducted to determine whether this loss in retinol receptor is responsible for the disease or whether it is a consequence of the disease. In addition the study of retinitis pigmentosa will also be undertaken in animal models. Studies will continue on diabetic cataracts in order to improve the delivery of the aldose reductase inhibitors in the form of eye drops.

The Office of Biometry, Epidemiology and Field Studies will continue to give special emphasis to epidemiological studies. These studies include the identification of risk factors associated with eye disease, clinical trials to measure the effectiveness of alternative treatment modalities, and research into biostatistical methodology as applied to vision research. This Office will continue to play an active role in stimulating efforts to establish additional clinical trials and natural history and case control studies, as well as other forms of epidemiological vision research.

Direct Operations

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations	36	$1,740,000	36	$1,933,000	--	+$193,000

Introduction

The direct operations activity of the National Eye Institute provides support for the overall administrative management and scientific direction of the Institute's grants and contracts programs. Over 564 grant applications and 55 contract awards were administered by this activity. Included here is the Office of the Associate Director for Extramural and Collaborative Programs (ECP). The Office of Scientific Information (located under the ECP) developed a computer based information system for use by Institute staff in capturing data in regards to grant and contract information.

Program Plans for 1978

The Office of Extramural and Collaborative Programs will continue to provide leadership in devising the most feasible funding guidelines for the Institute's grants programs. Clinical trials, both multi-center, utilizing the contracts mechanism and single-clinic trials utilizing the grants mechanism, will be developed to determine their effectiveness in producing research results. It is expected that over 620 grant applications and 61 contracts will be administered in FY 1978. A large effort will be expended during this time period to explain the new program planning report and insure its acceptance and implementation by the vision research community.

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Program Management

Authorizing Legislation: Public Health Service Act, Title IV, Part F

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management	27	$976,000	26	$957,000	-1	-$19,000

Introduction

This activity is the focal point from which decisions are made regarding the overall scientific and administrative direction of Institute programs.

During FY 1977, the Office of the Director, aware of the potential gains from fostering increased cooperation among the world's scientists in solving common problems of blindness and visual disability, expanded its international activities. The following agreements, which range from broadly-based and long-term formal cooperative research agreements between the U. S. and other countries to conferences and workshops focused on specific disease problems are: (1) U. S. - U. S. S. R. Collaborations - to conduct research on retinal degenerations (including retinitis pigmentosa), cataract and glaucoma; (2) U. S. - Japan Cooperative Agreement - whereby interested scientists in both the U. S. and Japan can select a research area in which they wish to work and then procede to make tentative arrangements to collaborate with an investigator of their choice; and (3) Workshop on Vitamin A in the Treatment of Xerophthalmia and Keratomalacia - these diseases affect the cornea and are a leading cause of blindness and visual impairment worldwide. The workshop was mandated to identify important research opportunities in the field.

Program Plans for 1978

During FY 1978, this Office will continue its program planning efforts initiated in FY 1975 through its Office of Program Planning and Scientific Reports by following-up and widely disseminating the second Vision Research Program Planning Report which is due for release in the Spring of 1977. Additionally, this Office will continue its program of public information and scientific reporting on the results of research in vision.

Funds are also provided here for salaries and other expenses incurred by the Office of Administrative Management and the Office of the Director.

One administrative position has been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Retinal and Choroidal Diseases
(Public Health Service Act, Title IV, Part F and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$23,125,000	1/	--	$22,901,000

Purpose: The retina program supports research to acquire knowledge of how the retina functions normally as well as studies to advance understanding of how the retina is damaged by disease; applied studies to develop methods of prevention, early detection, and treatment of retinal disease; and development of animal models of various retinal diseases to facilitate laboratory and clinical research.

Explanation: This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Accomplishments in 1977: Most of the blindness caused by retinal vascular disease is associated with diabetes. Significant progress has been made in this area through the National Eye Institute support of a multicenter randomized clinical trial to establish the efficacy of photocoagulation in the treatment, alleviation, and prevention of diabetic retinopathy. This study has shown that the risk of blindness caused by retinal vessel abnormalities associated with diabetes mellitus can be significantly reduced in this disease.

Another cause of blindness in diabetic retinopathy is vitreous hemorrhage. Removal of blood-filled vitreous (vitrectomy) has been shown to be of some benefit to individuals who have had severe bleeding into the vitreous for at least one year. The National Eye Institute has initiated another multicenter randomized clinical trial to evaluate the effects of vitrectomy performed in the first six months after vitreous hemorrhage as compared to the present practice of waiting one year after vitreous hemorrhage to remove the diseased vitreous. This study will determine the value of early intervention in the improvement of vision in diabetic retinopathy.

Objectives, 1978: Additional research will be supported in the area of circulatory abnormalities and vascular disorders, such as hypertension, arteriosclerosis, sickle cell disease, and vascular occlusion disorders, which contribute to newly recorded blindness. Other studies will focus on blindness associated with diabetes, with emphasis placed on clinical research in natural history, genetics and treatment of diabetic retinopathy and the formation of new blood vessels in the retina. In addition, a knowledge of the genetic patterns of various types of macular degeneration will be pursued. Increased emphasis will be placed on gaining more knowledge of retinal cell biology, particularly in the area of photoreceptor (rods and cones) production and rod outer segment removal by the pigment epithelium cells. Other studies will focus on the vitreous body and its reaction to other tissues, the development of vitreous substitutes, and the vulnerability of retinal cells to nutritional deficiencies, drugs, and poisonous substances.

1/ Title IV, Part F - Indefinite; Title IV, Part I - Legislation pending

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Corneal Diseases
(Public Health Service Act, Title IV, Parts F and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$7,586,000	1/	--	$7,037,000

Purpose: Corneal disease research is aimed at reducing the impact of corneal diseases through methods of treatment, prevention, and diagnosis.

Explanation: This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Accomplishments in 1977: The basis of corneal transparency is an active area of research. Significant progress has been made in the past few years in developing techniques to study the thin flattened cells that line the cornea (the endothelium) and its supporting framework (the stroma) in order to characterize the nutrients required for maintaining the endothelium. Advances have been made in (1) understanding cornea metabolism; (2) the area of corneal tissue transplantation by the development of a media which allows for longer storage of these tissues; (3) the development of sophisticated instrumentation which allows for direct visualization in human patients of the cells which line the posterior surface of the cornea.

One additional important area of research is that of herpes simplex infection of the cornea, one of the most painful ocular viral diseases. Its importance stems not only from the frequency of initial attacks, but also from the likelihood of its recurrence with progressive scarring, pain, and reduction in vision. Vision research scientists have been seeking means to control and treat this infection, and a number of drugs have been found that reduce the severe visual effects associated with the infection.

Objectives, 1978: Continuing immunologic studies will be pursued in order to address the significant rejection rate accompanying corneal grafts; trials of new antiviral drugs useful in treating herpes simplex and the definition of the host factors responsible for the primary acquisition of the herpes virus will be studied; studies to determine the value and importance of soft contact lens and their use in the treatment of corneal diseases will be pursued; and, further improvement of instrumentation useful in corneal diagnosis will be studied to make these instruments simple and convenient for routine use in clinics.

1/ Title IV, Part F - Indefinite; Title IV, Part I - Legislation pending

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Cataract
(Public Health Service Act, Title IV, Parts F and I)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$5,524,000	1/	--	$5,649,000

Purpose: Cataract research attempts to identify the causes of cataract and develop methods for its prevention and improved treatment.

Explanation: This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Accomplishments in 1977: As a result of recent major developments in the field of protein biochemistry, studies have shown that the clouding which occurs in senile cataracts may be the result of an age-dependent clumping of the structural proteins of the lens.

Another major advance in cataract research has come recently through studies of laboratory animals. It is known that in sugar cataract, such as occur in patients with diabetes or galactosemia, specific chemical defects related to enzyme activity trigger the formation of lens opacities. Enzyme inhibitors have been developed which can delay the formation of these cataracts in animals.

During FY 1977, a Cooperative Cataract Research Group (a consortium of leading investigators in the cataract area) will begin a large scale, coordinated study of the human lens in health and disease. This collaborative effort gives promise of building the base of knowledge needed to develop drugs and other therapies to retard -- or prevent -- the formation of cataracts and thereby reduce the need for corrective surgery, which is estimated to cost approximately $750 million annually.

Objectives, 1978: Studies will continue which will ultimately yield a means of preventing or retarding the development of cataract. In senile cataract, there are almost certainly a number of contributory causes, which are superimposed on normal aging processes. The prevention of senile cataract therefore requires a much improved understanding of the structure of the human lens, of its metabolic processes and the changes induced in it by increasing age and external influences. Continuing studies will therefore focus on protein changes in the lens and the role of protein aggregation in the development of cataract. Fundamental studies will also seek adequate animal models for explaining the mechanism of cataract formation, in order to relate these findings to understanding the etiology of human senile cataract.

Most importantly, the major national collaborative research effort in human cataract research initiated in FY 1977 will continue in FY 1978. Research advances in this program and the relative cohesiveness of the national effort in this area should permit a more coordinated approach to the solution of the human cataract problem by collaboration among over 20 research centers including the intramural program of the NEI.

1/ Title IV, Part F - Indefinite; Title IV, Part I - Legislation pending

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Glaucoma
(Public Health Service Act, Title IV, Parts F and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$7,692,000	1/	--	$8,594,000

Purpose: Glaucoma research studies the cause of glaucoma, development of techniques for prevention and early detection of glaucomatous disease, and improved methods of treatment.

Explanation: This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Accomplishments in 1977: Much of the research in glaucoma is concerned with the biochemical and pharmacological factors involved in the production of aqueous humor (a clear fluid in the front portion of the eye) and in its secretion from the eye. This work has lead to improved treatments with a reduction of side effects, and a better understanding of the effects of various drugs. While still under debate, the use of delta-9-tetrahydro-cannabinol, a marijuana derivative, has been shown to lower intraocular pressure for short periods.

In cases where intraocular pressures are not controllable, surgery may be performed successfully. Progress in the use of lasers for the treatment of glaucoma now make possible a rapid and simple operation with a minimum of patient discomfort.

In many cases the present diagnosis and detection procedures are successful only after nonreversible damage has occurred. More highly refined methods of measuring the contours of the optic nerve (photogrammetric techniques) are beginning to allow for evaluation of the optic nerve head to detect minute and early changes that may be prerequisite to the beginning of glaucoma.

Objectives, 1978: Continued support will be given to understanding how changes in blood circulation of the eye leads to increases in intraocular pressure which often result in damage to the optic nerve. A number of treatment methods for this disease will be tested to determine the most effective mode of correcting such ocular circulatory disturbances before impaired vision result. Research designed to identify more accurately the individuals at risk to closed-angle glaucoma will also receive emphasis. Additional emphasis will be given to study of the cell biology of the ciliary body (that portion of the eye which produces aqueous humor) and its growth in an artificial medium, and of the trabecular meshwork (a pore-like structure through which the aqueous humor percolates to the outflow channels).

1/ Title IV, Part F - Indefinite; Title IV, Part I - Legislation pending

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Sensory-Motor Disorders and Rehabilitation
(Public Health Service Act, Title IV, Parts F and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$10,259,000	1/	--	$10,173,000

Purpose: The sensory-motor program supports laboratory and clinical studies on the development and function of those activities of the brain and the eye muscles that make vision possible. The goal of these efforts is a better understanding of the causes of low vision and blindness which cannot be traced to specific dysfunctions of the eye itself.

Explanation: This program is funded through the award of research grants and contracts, complemented by an intramural research program. Also institutional and individual traineeships are awarded under authority of the National Research Service Awards Act.

Accomplishments in 1977: Much knowledge has recently been gained about the anatomical and functional changes that occur in the visual nervous system of cats and monkeys deprived of light stimulation in one eye or with experimental misalignment of the eyes. In such animals, the critical periods for the development of amblyopia have been determined with accuracy. Experiments are underway to determine the degree to which these changes may be reversed at a later time. Very recent findings show that functional changes resulting from stimulus deprivation can sometimes be reversed by drugs that block inhibition in the central nervous system. These findings suggest the possibility of using pharmacological methods for correcting developmental abnormalities in the visual system.

Several psychophysical tests developed in the laboratory have potential for application to the diagnosis of retinal diseases and lesions of the visual nervous system. During FY 1977, a workshop to discuss how to encourage the transfer of these recent findings was organized by the NEI. A workshop to discuss low vision and rehabilitation will be held during FY 1977.

Objectives, 1978: Studies of congenital, developmental and degenerative abnormalities, i. e., amblyopia, will continue to pursue information on early growth patterns and development of visual pathways. Research on strabismus surgery and on neuromuscular abnormalities would continue. Other studies will further concentrate on psychophysical functions, dyslexia and oculomotor control.

1/ Title IV, Part F - Indefinite; Title IV, Part I - Legislation pending

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Intramural Laboratory and Clinical Research
(Public Health Service Act, Title IV, Part F)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
89	$7,098,000	Indefinite	89	$7,737,000

Purpose: The Intramural Laboratory and Clinical Research program of the National Eye Institute is focused on developing new and improved techniques for the prevention, diagnosis, and treatment of vision disorders. Also included here is the Office of Biometry, Epidemiology and Field Studies, which conducts epidemiological and statistical studies in conjunction with collaborative investigations of Institute programs.

Explanation: The Institute's intramural research program is comprised of the Clinical Branch, the Laboratory of Vision Research, the Office of the Scientific Director, and the Office of Biometry, Epidemiology and Field Studies.

Accomplishments in 1977: One important advance during 1977 was the demonstration that in experimental diabetes the treatment of the diabetic animal with aldose reductase inhibitor effectively delayed the onset of the cataract. This was the first demonstration that the course of diabetic cataracts in the intact animals could be altered. Studies are underway to improve the delivery of the inhibitors in the form of eye drops.

Other advances in cataract research have been made. It now looks possible to grow human lens cells in artificial medium. Thus it is now feasible to establish cell lines of the lens epithelium. This new development may provide insight into the causes of congenital cataracts.

Objectives, 1978: Investigations planned in the Clinical Branch will aggressively explore the disease conditions that are the major contributors to blindness and debilitation.

The Clinical Branch will continue its programs in glaucoma (emphasizing studies of ocular hypertension and the various pharmacological and surgical treatment modalities for controlling glaucoma) and in retinal degeneration and genetically determined ocular diseases, using new diagnostic tests to help categorize and classify these diseases. A continued effort will be made to identify specific defects in ocular degenerative diseases. The diabetic retinopathy research program will continue efforts to establish the mechanism by which abnormal new blood vessels grow in the retina, an important step for preventing blindness from diabetes. The Laboratory of Vision Research will expand its research efforts in retinitis pigmentosa to determine if the loss of one particular retinal receptor is responsible for or the consequence of the disease. Studies will continue on diabetic cataracts to improve the delivery of aldose reductase inhibitors in the form of eye drops. The Office of Biometry, Epidemiology and Field Studies will continue its epidemiological studies to identify risk factors associated with eye disease to measure the effectiveness of alternative treatment modalities through clinical trials, and to examine biostatistical methodology as applied to vision research.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Direct Operations
(Public Health Service Act, Title IV, Part F)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
36	$1,740,000	Indefinite	36	$1,933,000

Purpose: This activity provides funds for salaries and other expenses connected with personnel engaged in activities relevant to the award of National Eye Institute research grants and contracts.

Explanation: The direct operations activity of the National Eye Institute consists of the Office of the Associate Director for Extramural and Collaborative Programs and his supporting staff.

Accomplishments in 1977: Over 564 grant applications and 55 contract awards were administered by this program. The Office of Scientific Information (located under the ECP) developed a computer based information system for use by Institute staff in capturing data in regards to grant and contract information. During FY 1977 this Office was heavily involved in developing data and program substance for the Institute's program analysis document "Support for Vision Research", and the forthcoming second version of the vision research program plan.

Two workshops were conducted concerning special areas of research where the Institute was interested in fostering support, and four (4) program announcements were developed detailing areas of research where grant applications were being solicited. Additionally, hundreds of grantees and prospective grant applicants were counseled concerning the Institute's programs, priorities, needs and opportunities in vision research, and, where appropriate, how to apply for research support.

Objectives, 1978: The Office of Extramural and Collaborative Programs will continue to provide leadership in devising the most feasible funding guidelines for the Institute's grants programs. Clinical trials, both multi-center, utilizing the contracts mechanism and single-clinic trials utilizing the grants mechanism, will be developed to determine their effectiveness in producing research results. It is expected that over 620 grant applications and 61 contracts will be administered in FY 1978. A large effort will be expended during this time period to explain the new program planning report and insure its acceptance and implementation by the vision research community.

NATIONAL INSTITUTES OF HEALTH

National Eye Institute

Program Purpose and Accomplishments

Activity: Program Management
(Public Health Service Act, Title IV, Part F)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
27	$976,000	Indefinite	26	$957,000

Purpose: This activity is the focal point from which decisions are made regarding the overall scientific and administrative direction of Institute programs.

Explanation: This activity consists of the Office of the Director, National Eye Institute and his immediate staff.

Accomplishments in 1977: During FY 1977, the Office of the Director, aware of the potential gains from fostering increased cooperation among the world's scientists in solving common problems of blindness and visual disability, expanded its international activities. The following agreements, which range from broadly-based and long-term formal cooperative research agreements between the U. S. and other countries to conferences and workshops focused on specific disease problems are: (1) U. S. - U.S.S.R. Collaborations - to conduct research on retinal degenerations (including retinitis pigmentosa), cataract and glaucoma; (2) U. S. - Japan Cooperative Agreement - whereby interested scientists in both the U. S. and Japan can select a research area in which they wish to work and then proceed to make tentative arrangements to collaborate with an investigator of their choice; and (3) Workshop on Vitamin A in the Treatment of Xerophthalmia and Keratomalacia - these diseases affect the cornea and are a leading cause of blindness and visual impairment worldwide. The workshop was mandated to identify important research opportunities in the field.

Objectives, 1978: During FY 1978, this Office will continue its program planning efforts initiated in FY 1975 through its Office of Program Planning and Scientific Reports by following up and widely disseminating the second Vision Research Planning Program Report which is due for release in the Spring of 1977. Additionally this Office will continue its program of public information and scientific reporting on the results of research in vision.

WEDNESDAY, MARCH 9, 1977.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

WITNESSES

DR. RICHARD M. KRAUSE, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JOHN R. SEAL, DEPUTY DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
DR. ALFRED M. WEBB, CHIEF, PROGRAM PLANNING AND PROJECTION, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
CHARLES E. LEASURE, JR., EXECUTIVE OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
ROBERT C. PATRICK, BUDGET OFFICER, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF ASSISTANT SECRETARY, COMPTROLLER

OPENING REMARKS

Mr. FLOOD. We will continue with the National Institutes of Health and we now have the National Institute of Allergy and Infectious Diseases, the presentation to be made by Dr. Richard M. Krause, the Director. We have your biographical sketch, which we will place in the record at this point. Do you have anyone with you that you would like us to meet?

[The sketch follows:]

BIOGRAPHICAL SKETCH OF RICHARD M. KRAUSE

Position: Director, National Institute of Allergy and Infectious Diseases.

Birthplace and date: Marietta, Ohio—January 4, 1925.

Education: A.B., Marietta College, 1947, M.D., Case Western University School of Medicine, 1952.

Experience: Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 1975 to present. Professor, Rockefeller University, and senior physician to the hospital, 1968–75. Associate professor, Rockefeller University, and physician to the hospital, 1966–68. Professor of epidemiology and professor of medicine, Washington University School of Medicine, St. Louis, 1965–66. Professor of epidemiology and associate professor of medicine, Washington University School of Medicine, 1962–65. Associate professor, Rockefeller Institute, and physician to the hospital, 1961–62. Assistant professor, Rockefeller Institute, and associate physician to the hospital, 1957–61. Assistant, Rockefeller Institute, and assistant physician to the hospital, 1954–57. Internship and residency training, internal medicine, Barnes Hospital, 1952–54. Research fellow, Department of Preventive Medicine, Case Western University School of Medicine, 1950–51.

Association memberships: Association of American Physicians; American Society for Clinical Investigation; American Society for Microbiology; The Harvey Society; Central Society for Clinical Research; Simga Xi; American Association for the Advancement of Science; American Venereal Diseases Associ-

ation; Infectious Diseases Society of America; Royal Society of Medicine; Practitioner's Society of New York; American Rheumatism Association; American Thoracic Society; American Epidemiological Society; American Academy of Allergy; and American Association of Immunologists.

Member, Infectious Disease Advisory Committee, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 1970–74.

Board of Directors, Royal Society of Medicine Foundation, Inc., 1971 to present (treasurer 1973–75).

Consultant and member, Coccal Expert Committee, World Health Organization, 1967 to present.

Directors council, New York Heart Association, 1973–75.

Chairman, Allergy and Immunology Study Section, National Institutes of Health, 1966–70.

Commission on Streptococcal and Straphylococcal Diseases, U.S. Armed Forces Epidemiological Board (Deputy Director, 1968–72), 1963–72.

Chairman, Research Study Committee and member, Executive Committee, Council on Rheumatic Fever and Congenital Heart Disease, American Heart Association, 1963–66.

Member, Policy Committee, American Heart Association, 1966–70.

Board of directors, New York Heart Association, 1967–73.

Chairman, Advisory Council on Research, New York Heart Association, 1969–71.

Research Committee, St. Louis Heart Association, 1963–66.

Board of directors, St. Louis Heart Association, 1962–66.

Editorships: Section editor, Journal of Immunology, 1974–75. Editor, Journal of Experimental Medicine, 1973–75. Editorial board, Immunochemistry, 1973 to present. Editorial board, Bacteriological Reviews, 1969–73. Editorial board, Infection and Immunity, 1970 to present. Associate editor, Journal of Immunology, 1963–71. Editorial board, Journal of the American Venereal Disease Association. Editorial board, Clinical Immunology and Immunopathology, 1976 to present. Advisory editor, Journal of Experimental Medicine, 1976 to present.

Publications of more than 100 papers on research in infectious diseases and immunology.

Dr. KRAUSE. We have Dr. John Seal, the Deputy Director; Mr. Leasure, the executive officer; Mr. Patrick, who is the budget officer, and we are delighted, of course, that Ms. Wormser is with us.

OPENING STATEMENT

Mr. FLOOD. We have your statement, which will be placed in the record at this point, Doctor.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
National Institutes of Health
Statement by
Director, National Institute of Allergy and Infectious Diseases

on

"Allergy and Infectious Diseases"

Mr. Chairman and Members of the Committee:

Thirty-five years after the introduction of antibiotics, infectious diseases are still our most common illnesses. In 1974 nearly 25% of all who sought medical care did so because of an infectious disease. This represents nearly 200 million patient-visits to physicians. The direct cost for this medical care and the indirect cost due to loss of work amounts to billions of dollars.

One reason infectious diseases have remained so common is that the majority are caused by viruses over which we have little control. Vaccines have been effective in preventing smallpox, polio, measles, and rubella, but there are no vaccines for most viral infections. Furthermore, there are, as yet, very few effective antiviral drugs similar to the antibiotics used to treat bacterial infections. We must, therefore, redouble our efforts to perfect antiviral substances and to develop new and safe vaccines wherever feasible.

Another reason infectious diseases are still a problem is that bacteria can develop resistance to the antibiotics once thought to guarantee cures. For example, a serious form of penicillin resistance has occurred recently in some bacteria causing gonorrhea and childhood meningitis.

Our primary defense against persistent bombardment of bacteria and viruses is the immune system of the body. Vaccines are a way to direct the resources of this system against invasion by a specific bacterium or virus. Early principles of vaccination were developed in almost total ignorance of how this system functions. Now, however, if we are to have new and better immunization methods in the future, we must unravel the remaining mysteries of the immune system.

Our effort to acquire this knowledge has yet another purpose. This concerns the discovery of the causes and treatment of diseases of the immune system.

I am speaking here of illnesses as common as hayfever, and as serious as asthma, as well as others, such as arthritis and kidney disease.

THE IMMUNE SYSTEM AND ITS DISORDERS

The immune system consists of several specialized organs dispersed throughout the body. But they work in concert and remain in communication by means of a systematic traffic of white blood cells and their products. Remarkable progress has been made in delineating the mechanisms which are involved in diseases of the immune system and in the defense against infection.

The immune process begins with the interaction between foreign invaders and three distinct cell types of the immune system. Each of these cells plays a differing role but their coordination is essential. Dissection of this network of interacting cellular and molecular events forms a major emphasis of our Institute program.

Disorders of the immune system can be inherited or acquired. Acquired disorders include asthma and other allergies. In addition, abnormal immune processes are involved in such diseases as rheumatoid arthritis, systemic lupus erythematosus, myasthenia gravis, autoimmune hemolytic anemia, and glomerulonephritis.

An example of an inherited immune disorder on which we have made important progress is a devastating condition known as SCID, for severe combined immunodeficiency disease. It has been estimated that as much as 10% of mortality in newborns is due to SCID. The victims lack effective immune systems. They die of severe infections, usually before age 2, and there is no treatment except bone marrow transplantation. This is frequently impossible because a suitable bone marrow transplant donor cannot be found. NIAID-supported scientists are finding ways to circumvent this problem. At the NIH Clinical Center and at other institutions they have successfully treated several infants by giving them transplants of thymus epithelial cells grown in the laboratory. These

transplants have not been rejected by the infants and their immune functions have been restored to normal levels. Despite initial success, much remains to be discovered. We are hopeful, however, that this innovative procedure may be useful in treating other inherited immune deficiencies and even some of the more subtle defects in autoimmune disorders and malignancy.

Another example of an inherited immune disease with which we have had success is hereditary angioedema (HAE). This is a serious swelling condition which, when it involves the throat, can lead to strangulation. The death rate is as high as 30 percent. NIAID scientists are now able to prevent attacks of HAE through use of a new drug, Danazol. Most important, this compound also actually corrects the inherited biochemical defect associated with the disease. This work has significance beyond the successful treatment of HAE because this is one of the first examples of correcting an inherited abnormality by drug therapy.

The most common acquired diseases of the immune system are asthma and other allergies. An estimated 35 million Americans have an allergic disease. Asthma, alone, accounts for almost 9 million of these patients and causes over 2,000 deaths every year. This does not take into consideration other deaths that occur in which asthma is an underlying cause -- deaths attributed to pneumonia, bronchitis, and emphysema. In 1975, patients with allergies made at least 43 million visits to doctors' offices. We must improve the quality of life for these people.

Our network of 15 Asthma and Allergic Disease Centers was established to bring the fruits of basic research from the laboratory bench to the patient's bedside, and to the clinic. Work by scientists at these Centers and at other grantee institutions has resulted in a number of important accomplishments.

Chemical studies on allergenic substances such as ragweed and grass pollens have led to new benefits for diagnosis and treatment. I have in mind, for example, our ability to isolate the specific components of pollens that cause allergy. These purified allergenic substances will be used to improve

diagnosis as well as treatment by desensitization or allergy shots.

There is new hope for patients who suffer from asthma. The severe shortness of breath they experience is due to the spasmodic contraction of the bronchial muscles that cuts off the air supply to the lung. Scientists are now unraveling the chain of events which leads to this bronchial constriction. With this knowledge, physicians can tailor treatment for the individual by selecting the proper dosage of the most effective drug available.

VIRAL DISEASES

Viruses not only cause well-known acute illnesses such as hepatitis, influenza, the common cold, and certain types of diarrhea; they can also infect the fetus and produce defects in the newborn that often lead to mental retardation. Rubella virus was a major cause of birth defects before the vaccine was licensed in 1969. Today, cytomegalovirus has taken rubella's place as a threat to the unborn infant. It is the leading known viral cause of birth defects, infecting one percent of all newborns and resulting in an estimated 20,000 mentally defective infants annually. There is no vaccine for this virus infection.

Because of the difficulties surrounding the development of preventive vaccines for many viruses, 7 years ago the NIAID launched a special program to find drugs to treat viral infections. Potential antiviral compounds are tested first in animal experiments and then employed to treat several very severe virus infections in man. For example, encephalitis caused by herpes virus, is an almost uniformly fatal illness. In a recent NIAID-supported clinical trial, the death rate was reduced from 70% to 28% in those patients with herpes encephalitis treated with the chemical -- adenine arabinoside.

In another small clinical trial, the antiviral substance, interferon,

eradicated the hepatitis B virus from the blood of patients with chronic hepatitis. This is especially encouraging not only because chronic hepatitis carriers are potential transmitters of the infection to others, but also because progressive liver disease occurs in a significant number of individuals who continue to carry the hepatitis B virus. We need to follow up this initial success and we intend to do so as soon as supplies of costly and scarce interferon can be obtained.

Despite these advances, the development of additional effective and safe antiviral drugs will be difficult largely because of the nature of virus infections. When viruses infect the cells of the body, they divert the cells' own chemical machinery away from the maintenance of life and to the production of more viruses. This interference with cell function leads to cell death. Within days, organs such as lungs, brain and liver can be severely damaged or destroyed. Unfortunately, most drugs which prevent viral multiplication also injure or destroy body cells. They are, therefore, very toxic for man.

Because of the complexity of the problem, we know that our effort in basic virology must be expanded to provide the knowledge necessary for the development of new drugs. This past year I appointed a Virology Task Force composed of leading virologists from all regions of the country. One of its responsibilities is to identify new strategies for developing safe and effective antiviral compounds.

HEPATITIS

Viral hepatitis is a serious infection, with an estimated half-million cases occurring annually. It is transmitted through contaminated food and water and it is still a complication of blood transfusions. Use of improved blood screening tests for hepatitis B carriers has practically eliminated this cause of post-transfusion hepatitis in the United States. Now we must

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establish methods for detecting the virus or viruses causing what is called "non-A, non-B" post-transfusion hepatitis so carriers of these agents, too, can be detected and banned as blood donors.

Animal studies on a hepatitis B vaccine are virtually complete. The vaccine, prepared from the blood of carriers of the virus, is safe and effective in chimpanzees. We still hope to begin preliminary safety testing of this vaccine in volunteers this spring. This would be a first step toward an eventual hepatitis B vaccine trial in high-risk personnel.

Last year, I mentioned trials of a special preparation for preventing hepatitis B in laboratory personnel following accidental exposure. Recent results prove the effectiveness of this serum called hepatitis B immune globulin.

All hepatitis research is severely hampered because of our inability to grow the causative viruses in the laboratory. This problem is being tackled by NIAID scientists who are trying out liver cell tissue cultures as a growth medium. Also, the NIAID, the Center for Disease Control, and the Bureau of Biologics have established, jointly, breeding colonies of chimpanzees and marmosets to be used in hepatitis A virus studies, including development of diagnostic methods and vaccines.

A review of our efforts in acute respiratory diseases, including influenza and bacterial pneumonia, is discussed in a special report prepared for the record.

SEXUALLY-TRANSMITTED DISEASES

Sexually-transmitted diseases are caused by a variety of microbes, including viruses, parasites, and bacteria, as well as unusual bacteria called chlamydia and mycoplasma. The incidence of these diseases continues to increase. There are approximately 2,600,000 gonorrhea infections annually, 2,500,000 cases of non-gonococcal urethritis, and 3,000,000 cases of trichomoniasis, a parasitic infection most commonly transmitted by direct sexual contact.

In 1976, this Institute established its fourth Venereal Disease Research Center at Cornell University in New York. Other Centers are located at the University of Washington, Seattle, Baylor College of Medicine, Houston, and Harvard University School of Public Health, Boston. These Centers are conducting multi-disciplinary studies on diagnosis, prevention, and treatment of venereal diseases. We have described NIAID-supported research within a special report entitled, "Venereal Disease", prepared jointly with the Center for Disease Control. One serious problem deserves your attention.

In recent years, physicians have had to use higher and higher doses of penicillin to cure gonorrhea. This is because the gonococcal bacteria had become increasingly but only partially resistant to the action of penicillin. In 1976, a new and formidable type of gonorrhea was recognized in which the bacteria are completely resistant to penicillin. These gonococci, introduced into the United States from the Philippines, produce an enzyme which actually destroys penicillin and other related antibiotics. NIAID-supported scientists have shown that the production of this enzyme is due to the presence of previously unrecognized genetic material, called a plasmid, within the gonorrhea organism. The new penicillin-resistant organisms have now been found worldwide.

Recognizing the urgency of this matter, the NIAID held a meeting in December 1976 to review the research implications of this potentially serious problem. At present, penicillin and related antibiotics are the very best treatment for gonorrhea. If the penicillin-resistant gonococci become the most common cause of infection, we will have to develop other strategies for treatment and prevention. New public health measures against gonorrhea will depend on results of basic research on bacterial structure, biochemistry, genetics, and epidemiology.

PARASITIC DISEASES

Most Americans usually overlook the possibility of getting parasitic diseases,

but they do occur in this country, particularly in the poor and the young and in members of minority groups. I have already mentioned trichomoniasis as a sexually-transmitted disease. Hookworm infection is endemic in some rural areas of the South; and toxoplasma can cause a serious eye disease as well as congenital birth defects. Americans stationed or traveling abroad are frequently exposed to more serious parasitic infections, particularly since malaria is resurgent in many areas where it had been temporarily controlled.

Outside the United States, the "Big Two" parasitic diseases are malaria and schistosomiasis. Malaria is common throughout Asia, Africa, and Central and South America, causing 1 million deaths annually in African children alone. Schistosomiasis is endemic in Puerto Rico and a number of other countries with at least 200 million infected people. This disease also occurs in New York, Miami, and other cities where significant recent immigration has occurred.

Because of the importance of malaria and schistosomiasis, we have concentrated much of our parasitic disease research on these two infections. Scientists are beginning to decipher the complicated immune mechanisms involved in both malaria and schistosomiasis where not only the causative organism and the patient must be studied but an intermediate "vector", as well. In schistosomiasis this transmitter of disease is the snail; in malaria, it is the mosquito.

Internationally recognized NIAID studies have, in the past, resulted in determination of the genetic basis for susceptibility of the snail to infection with the schistosome parasite. By manipulating the multiple genetic factors involved, we have developed a resistant strain of the snail which is the vector for schistosomiasis in the Western hemisphere. It is possible that introduction of genetically resistant snails into areas where the parasite is endemic might reduce transmission of the disease.

In 1976, a major advance took place in the study of malaria. A NIAID-supported investigator for the first time, cultivated in the laboratory, the

malaria parasite, Plasmodium falciparum. This achievement had eluded researchers for over 25 years. These parasites, grown and harvested in the laboratory will facilitate the development of new drugs, the examination of immune mechanisms, and the development of a malaria vaccine.

GENETIC MANIPULATION

Recombinant DNA research is a matter of much concern to the scientific community, the public and the Congress. It is also a research area of much hope. NIAID-supported scientists and others are anxious to exploit for the benefit of mankind this new technology which enables a scientist to insert genetic material from one cell into another cell and to cross species barriers.

Current recombinant DNA research has its early roots in NIAID-supported studies in bacterial genetics. For example, NIAID has been concerned with genetic factors which control such phenomena as toxin production and antibiotic resistance among bacteria. These phenomena are transferable from one organism to another, and do occur naturally. It was out of such studies, along with a better understanding of the genetic code, cellular structure and function, and the development of highly sophisticated techniques for working with the isolated DNA, that the present recombinant DNA technology emerged.

Last year, the NIAID undertook the development of safer bacteria, known as "hosts," and of other materials, known as "vectors," to be used by scientists working with this new technology. The host bacteria are being so altered that they will not survive outside of very special laboratory conditions. The vectors -- bacterial viruses and plasmids -- are altered so that they transmit genetic material only to the special host bacteria and not to naturally occurring organisms.

This Institute has also undertaken the renovation and development of facilities at the Frederick Cancer Research Center. Here a national site will

be provided where scientists requiring the highest level of physical containment for DNA research can perform their experiments. The facilities initially being funded by the NIAID, National Cancer Institute, and National Institute of General Medical Sciences, will become a major responsibility of the NIAID in 1979 when fully operational.

CONCLUSION

In closing, Mr. Chairman, I firmly believe that success in research on the allergic, immunologic, and infectious diseases will be an important factor in improving the health of a majority of Americans who suffer from these common and frequently debilitating diseases and in reducing the economic costs for the Nation's health care system. The NIAID budget request for 1978 is $153,442,000.

I shall be pleased to answer your questions and supply additional information for the record.

BUDGET PROPOSAL

Mr. FLOOD. Once again your budget proposes an increase. This year the increase is over $12 million. Why is there a need for an increase and how do you intend to spend it?

Dr. KRAUSE. Let me try to summarize that very briefly.

The need for the increase stems first of all, from the medical importance of the two general classes of diseases with which our Institute is concerned.

In the first place, we are concerned with infectious diseases. The infectious diseases account for 25 percent of all patient visits to doctor's offices. That is a lot of sick folks. Infectious diseases is the first problem.

Second, we have the responsibility for the allergic diseases. There are approximately 40 to 45 million patient visits to doctors every year for treatment of their allergic diseases. Ten to fifteen percent of everyone in the country has allergies. This is the background of the problem.

Now, what will we do specifically about these two major problems? For the infectious diseases we must look to the causes of these infections. Viruses are the most common cause of infections. Viruses cause the bulk of infections of the liver, hepatitis, infections of the brain, and many, many more serious ones, as well as the more common ones like the common cold.

We have currently very few effective drugs to treat viruses, and therefore we must enlarge our attack on the development of antiviral substances. One of the things I propose is to increase the research on antiviral substances.

REDUCED TRAINING PROGRAM

Mr. FLOOD. In view of the increase and in view of what you have just said and in the light of the important work assigned to your Institute, why are you reducing the training program? How do you put that together?

Dr. KRAUSE. The training program has been reduced because of an administration decision that we would not have institutional training grants. Our training program has been reduced from about $8 million to $6 million, but that decrease is mainly due to the elimination of the institutional training grants.

Mr. FLOOD. Why? You have just stated a question. What is the answer?

Dr. KRAUSE. This was an administration decision which was made by the Office of Management and Budget.

Mr. FLOOD. You are the Administrator, I guess, are you not?

Dr. KRAUSE. I am the Administrator of this Institute, yes, sir.

MANPOWER DATA

Mr. FLOOD. Do you have any data which shows the amount of manpower now that is currently available in the whole of scientific disciplines that is of interest to your institute and the current future and demands for that kind of manpower?

Dr. KRAUSE. Several years ago, before I arrived at the Institute as Director, the problem was analyzed and there was the estimate that

the pool of individuals who were doing research and work pertaining to our area is between 8,000 and 10,000 individuals. We estimate the need for adding to that pool about 400 individuals every year because about 400 individuals retire from that pool every year through attrition and retirement. Therefore, ideally, to replenish that pool we should train each year about 400 individuals to maintain a steady state.

Mr. FLOOD. What you have, will that do it?

Dr. KRAUSE. We are now turning out between 150 and 200 a year.

Mr. FLOOD. Will your budget do what you want to do?

Dr. KRAUSE. This current training program would not supply that level.

INTERNATIONAL CENTERS

Mr. FLOOD. Also in your budget you show that you support four International Centers for Medical Research?

Dr. KRAUSE. Yes, sir.

Mr. FLOOD. What kind of research do you do at those centers and where are they located?

Dr. KRAUSE. Those centers for international research are located in Pakistan, in Bangladesh, in South America, and in Malaysia. They are associated with universities in this country, including the University of Maryland, Johns Hopkins, Tulane, and the University of California. These centers were set up over 10 years ago and are designed to work on important international health problems, including malaria, schistosomiasis, and also the effects of malnutrition on the occurrence of these international diseases.

SWINE FLU IMMUNIZATION PROGRAM

Mr. FLOOD. Now, the appropriation for the swine flu immunization program, did that include money for your Institute?

Dr. KRAUSE. That is right.

Mr. FLOOD. That was for the purpose of studying vaccine development?

Dr. KRAUSE. That is right.

Mr. FLOOD. How did you use the money?

Dr. KRAUSE. This money has been used for the vaccine testing. We established a large vaccine test program. The vaccine was tested in over 7,000 volunteers. We needed to test the vaccines produced by the four manufacturers in all age groups. It was a large study which involved testing laboratories and clinics in over a dozen hospitals and universities throughout the country. The program was designed to test the vaccines for their effectiveness and for the determination of their reactivity.

We have learned a good deal from that testing program. We have learned, for example, that split-product flu vaccine is a preferable flu vaccine to give to children. Many children, particularly those with cystic fibrosis, for example, need the flu vaccine to be protected against influenza.

We will also continue to use that money to follow these 7,000 people who have been immunized in the test program during this coming

year, and the year thereafter, to determine any long-term effects. Most important to determine in the next year and the following year the amount of protection derived from the vaccination this season.

GUILLAIN BARRÉ SYNDRONE

Mr. FLOOD. Is your Institute involved in the study of the relationship between the swine flu and Guillain Barré syndrome?

Dr. KRAUSE. The demonstration of the relationship was done by the surveillance program at the Center for Disease Control. We have some research going on to examine the possible mechanisms whereby immunization of any kind might lead to the Guillain Barré syndrome.

Mr. FLOOD. Has that been linked previously with vaccine therapy generally?

Dr. KRAUSE. There have been scattered reports of a Guillain Barré syndrome following several different kinds of immunizations. But none of those reports had statistical significance because there were not enough cases involved to prove the relationship without question.

Mr. FLOOD. Was any research conducted on the possible vaccine link now to Guillain Barré prior to that recent swine flu development?

Dr. KRAUSE. What we can say is that in none of the 7,000 or so volunteers who received the vaccine was there any evidence of Guillain Barré syndrome following the vaccine. These studies were done late last spring and summer. We had no indication from the large field trial of this association.

Furthermore, I might say the Army has been giving influenza vaccine since 1944, to all incoming recruits. As a result, influenza is essentially absent from the U.S. Army. They have never seen a particular association between the influenza vaccine and Guillain Barré syndrome in the military.

Mr. FLOOD. There was specific research conducted prior to the recent swine flu development of any link, of any vaccine link and the Guillain Barré?

Dr. KRAUSE. No, sir. What I am saying is that in the influenza vaccine that had been given up until last fall we had not seen an association.

JOINT INFLUENZA WORKSHOP

Mr. FLOOD. It is my understanding that your Institute, the Center for Disease Control and the Bureau of Biologics, that you all participated in this joint influenza workshop, is that right?

Dr. KRAUSE. We have participated in many different workshops.

Mr. FLOOD. With the Center for Disease Control and the Bureau of Biologics people?

Dr. KRAUSE. Yes.

Mr. FLOOD. How often does this group meet?

Dr. KRAUSE. We could supply for the record all the many different meetings they have had, but during the past year the group has met at least eight times on influenza problems.

Mr. FLOOD. What role did this group play in the development of the swine flu program?

Dr. KRAUSE. The group, the BOB, and the Center for Disease Control, and the NIAID——

Mr. FLOOD. What developments came about?

Dr. KRAUSE. First of all, they took the position on the basis of the evidence that there was a threat of swine flu in the next year. Having surveyed the evidence, they recommended that there be a program for the immunization of the American people.

Mr. FLOOD. What were some of the issues considered by this group prior to and during the swine flu program?

Dr. KRAUSE. The issues that were considered were, first of all, the development of the vaccine, the way in which it would be tested for efficacy and safety. Those protocols were written and carried out by our Institute.

Furthermore, the group considered who should receive the vaccine; what the dose and composition should be, and how the vaccine should be made. The group considered the method of the distribution of the vaccine, although the issues pertaining to distribution are really the concern of the Center for Disease Control.

LIVE VERSUS KILLED VACCINE

Mr. FLOOD. What are the advantages, and disadvantages of course, of developing effective live virus vaccines against influenza now rather than the killed vaccine? We know the swine flu vaccine was a killed virus vaccine.

Dr. KRAUSE. There are advantages and disadvantages. I should say we do have a program for development of live vaccine which is going on at the NIH now.

First of all, the advantages of the inactivated vaccine. It is a known product we have used for 30 years and we have a lot of experience with it.

Second, it is a product which has relative ease of administration because it can be injected. The disadvantages of it are, however, that the protection from the vaccine lasts a year to 18 months.

Now, going to the live vaccine, at this juncture it is still an experimental vaccine. Presumably, if it were developed, an advantage would be that protection would last much longer than it does with the inactivated vaccine.

On the other hand, one of the disadvantages we must keep in mind is that the live vaccine would have to be given by dropping or spraying drops into the nose. This is a form of administration that might be difficult, particularly in children.

There are advantages and disadvantages to both, but at this juncture we must bear clearly in mind that the inactivated vaccine has known efficacy; the efficacy of the live vaccine at this stage is unknown.

ASTHMA AND ALLERGIC DISEASE CENTERS

Mr. FLOOD. In the material that you submitted to the committee, you state there are 16 existing asthma and allergic disease centers that require expansion in order to approach the multiplicity of problems of all of these diseases.

Will this budget permit the necessary expansion of these centers of which you speak?

Dr. KRAUSE. This budget will permit a modest expansion of these centers. I have proposed in this budget that we spend $1.4 million on the expansion of work specifically on asthma and allergy, including the centers.

We will be able to increase to some extent our work on the allergic patient. What I am interested in seeing done is that we really improve our diagnostic procedures in these centers; that we improve our methods of treatment.

Mr. FLOOD. What are the more important accomplishments of the centers?

Dr. KRAUSE. Recently one of the most exciting things is the successful treatment of a serious allergic condition, angioedema, which can result in severe swelling. When it occurs in the throat, strangulation and death can result. This is an inherited allergic disease. Just this last year a scientist out at our NIH campus discovered for the first time a specific treatment for that severe allergic disease.

As you know, there are the common allergy shots. One of the things which is very important to improve is the efficacy of those desensitization shots. We have made real progress in this. What goes into those shots is a much better antigen than it has been.

IMPROVED DIAGNOSTIC METHODS FOR ALLERGIES

Mr. FLOOD. What progress are you making in developing improved diagnostic methods to determine which pollen these allergy patients are very, very sensitive to and by so doing thus allow better treatment?

Dr. KRAUSE. We are working on this. We need more purified reagents. One must take the pollen material, purify it and use that purified material in the test procedure.

We are working hard on this. This is going on in several centers. It is important because skin testing must be done with the properly purified material. This indicates the substance to use for desensitization.

CENTERS

Mr. O'BRIEN. Following on the lead the chairman has given, there are 16, I believe, asthma and allergic disease centers in the country, are there not?

Dr. KRAUSE. Yes, sir.

Mr. O'BRIEN. In remote areas diagnostic capacity obviously is limited. Quite candidly, I have the impression if a physician doesn't know someone at one of those centers it may not be possible for him to get his patient in.

As I recall your testimony, you allow $1.4 million, which you suggested was I presume, for the expansion of those diagnostic centers. That sounds like an awful small amount. Should we not give you more money for that?

Dr. KRAUSE. It is a modest amount but you must realize for the increase of $12 million there are a series of other problems that must be addressed as well. I just spoke to the chairman about the problems of

the infectious diseases and we also have the diseases in international health.

Within the framework of the budget, that is as much increase as I am able to give it.

Mr. O'BRIEN. When you say "I," is that a Dr. Krause decision solely?

Dr. KRAUSE. That is the decision——

Mr. O'BRIEN. Is someone editing your recommendation?

Dr. KRAUSE. The recommendation of what we will do with the increase comes from discussions with my staff and also discussions with the Advisory Council of the Institute.

GENETIC MANIPULATION

Mr. O'BRIEN. In your statement you talk about the genetic manipulation, which is a rather exotic term to me.

Dr. KRAUSE. We have about $4 million on recombinant DNA research. We have the responsibility for devising bacteria which are safe bacteria to use in these experiments. We have a responsibility to be sure that these kinds of experiments can be performed safely.

The mission of our Institute is infectious diseases, and the public concern here is, will these experiments create new bacteria which are infectious to man? It is our responsibility to do the research which will lead to safe experiments, and to create for the scientists those bacteria which can be used in this experimentation so that they are not infectious to man.

In addition, we have the responsibility to develop, renovate, and operate the laboratory at Fort Detrick, where these experiments can be done safely.

FUNDING PRIORITIES

Mr. O'BRIEN. Obviously as a professional you are in a better position to evaluate what you are doing in your field than I am. You have $4 million for that and $1.7 million for these centers.

It is not much comfort for an asthmatic who can't get access.

Dr. KRAUSE. The figures you mentioned are program totals. Our increase this coming year in recombinant DNA research is about $0.5 million. The increase for asthma and allergy centers is about $200,000. Our total research in asthma and allergic diseases and clinical immunology is approximately $14 million.

GAO STUDY OF RESEARCH GRANTS

Mr. O'BRIEN. In a study completed in 1976 by General Accounting Office, better controls are needed. It raises questions over the evaluation of grants. It makes the statement that "144 competing grants were not funded though they had equal or better priority scores than 20 noncompeting grants that were funded."

Do you feel an evaluation of noncompeting grants is desirable and necessary?

Dr. KRAUSE. I am familiar with that report. The NIH answered that particular comment in the GAO report, and that answer can be made available to you.

[The information follows:]

Response to GAO Report on Research Grants

DHEW commented in extenso on the GAO Report "Better Controls Needed Over Biomedical Research Supported by the NIH" (Document- HRD-76-58). These comments may be found on pages 36 to 40 of that Report. Subsequently, a Statement of Department Action was filed by John D. Young, Assistant Secretary, Comptroller, and accepted by GAO. The sense of both these comments is captured in an NIH reply to a recommendation of the Report "Investigation of the NIH" by staff of the House Subcommittee on Health and Environment. The text of the NIH reply follows:

> The Committee report identifies several areas of concern with respect to grants management. One of the most fundamental issues raised relates to the funding preference given by NIH to ongoing research projects for the duration of their award period (usually three years), inasmuch as this may preclude support of higher priority applications submitted at a later time. It has been suggested by the GAO in a recent report that the NIH might consider terminating support of research in progress under these circumstances in order to initiate support of new and higher priority awards. However, if this was done, the investment previously made in the terminated project often would be lost. It should be noted that research does not progress at a constant rate with valuable results accumulating in a linear fashion beginning with the first day of the award. In a 1974 study of the NIH peer review system, the RAND Corporation developed information indicating that there are no objective, reliable methods for determining the productivity of research projects after only a year or two of performance. During the earliest phases of a research project and often up until the period when data analysis is fairly well advanced, there may be no more to judge in a "progress review" than the basic considerations that were available to the initial review group when the application was first submitted. Therefore, adequate time must be provided to allow a project to progress to the point when its relative merit and success can be evaluated. If adequate time is not provided, resources devoted to the entire project would be wasted, because research advances may well occur in the later years of a grant as a result of the "investment" during apparently nonproductive years.
>
> In sum, considering the unknowns involved in all research ventures, the subjective nature of priority scores, and the loss of resources devoted to approved ongoing projects if they are prematurely terminated, there appears to be no justification for terminating such projects to provide funds for new projects with better priority scores. In addition, to fail to honor previous commitments by terminating projects without allowing sufficient time for fruition would destroy the faith of scientists and their institutions in the stability of Federal biomedical research programs. For these reasons, this suggestion is considered neither realistic or desirable.

Let me just say this, Mr. O'Brien. Ninety-five percent of the grants funded by our institute are in what we call the first and second decile. That means the top 20 percent of all approved grants. That means everything we fund is either in the excellent category or the very good category.

It is very difficult to discontinue a very good grant after a year or two—and the investigator hasn't really yet had time to show what he can do—and substitute an excellent grant in its place. I think that would be inefficient management.

Remember, in our case, our institute is perhaps unique in that over 90 percent of the grants we fund are in the excellent and in the very good category.

TRANSFER OF RESEARCH KNOWLEDGE TO PHYSICIAN

Mr. O'BRIEN. The number of board-certified immunologists has about doubled in the past few years from what I hear at home. That may have created a problem in getting information transferred from laboratories to the practicing physicians. Do we need a stronger mechanism for that transfer?

Dr. KRAUSE. We do need to do more in the transfer of knowledge and in speaking with the physician and communicating with the physician.

I might say the first thing we have done is to reorganize. In fact, we began the reorganization at our institute a year ago. That was before it has become a more popular occupation in Washington.

I think that reorganization is going to facilitate this transfer of information to the physician. We have in the position of director of our Allergy and Immunology program, Dr. Sheldon Cohen, who is seated behind me. He is an eminent allergist and practitioner at Wilkes-Barre and he is directing that program. He knows the allergists around the country and works with such people as Dr. Robert J. Becker at Joliet, who are familiar with the problems of the practitioners of allergy. We are thinking of ways that we can use our centers to be of assistance to the practitioner, to get to the practitioner. But more than that, what I want to do is to find out from the allergist themselves the ways in which we can be of assistance to them.

There are various ways that this can be done. One can envision, as an example, a telephone system for consultation. One can envision using the centers for postgraduate training or refresher courses in allergy. There are a variety of techniques I think we can use effectively and we will try to do so.

Mr. O'BRIEN. I hope we can assist these people.

Thank you, Mr. Chairman.

HOSPITAL ASSOCIATED INFECTIONS

Mr. EARLY. I sense a tremendous alarm on the part of most people going into the hospital because of picking up infectious diseases. I have read articles that more people die from what they pick up in the hospital than what they went in with. Are you doing any study on that?

Dr. KRAUSE. We have had a program, a modest program, for hospital associated infections. It is a complicated problem. It is made complicated by the fact that many of these infections are in individuals who are undergoing specialized treatment for cancer or arthritis or other serious diseases and their treatment lowers their resistance to infection.

As a result, many of these hospital infections are due to bacteria which are different from the bacteria that were causing common hospital infections many years ago.

We have a modest program in the area. I am sure we should be doing more. It is a problem, and it is one that needs to be sorted out.

First of all, we need more epidemiology in the hospital to find out who is getting sick with these infections and what are the bacteria that are causing it and from where do they get the bacteria. Who is bringing those infectious bacteria to them? Are the patients infecting each other, or are they getting infected from the nurse or the aide on the ward?

Also, once we know what are the bacteria, we must learn more about the way they cause the infection and what we might be able to do to prevent it with new antibiotic or other treatment.

Mr. EARLY. What do you call a moderate program? You say we should be doing more. What should we be doing?

Dr. KRAUSE. I would have to supply for the record what is our actual dollar value in this program.

Mr. EARLY. Will you supply for the record what you think we should be doing and where you think this budget is inadequate in facing that particular problem?

As you know, it is a tremendous problem and psychologically if the people have a fear of going into the hospital, you know it is going to really create another problem.

Dr. KRAUSE. Yes, sir.

Hospital Associated Infections

The problem of patients who acquire infections while hospitalized for another cause is an important and complex issue. Estimates developed by the Center for Disease Control (CDC) from studies in a number of hospitals throughout the country suggest that as many as 5 percent of all hospitalized patients acquire such infections.

Some infections are relatively minor, such as those around the stitches of an operative wound. These usually clear with simple treatment, and add little to the length of stay of the patient in the hospital or to costs. Others, such as the infection around the site of an indwelling catheter or of the knee joint after repair of an athletic injury, may lead to chronic illness or even permanent disability, resulting in loss of professional income and costs of care can be very expensive. Fatalities are not infrequent. There are numerous causes for such infections; many could be prevented by consistently high standards of nursing care, others result from overdependence on antibiotics to prevent infections secondary to surgery.

Many serious hospital associated infections cannot be attributed to poor sterile technics, and do present difficult research problems. Hospital patient populations have increasingly become those who are old, who are receiving major drug therapy for cancer and arthritis, who are subjected to complex surgical procedures, or who have other serious, chronic illnesses including malnutrition. Increasingly, potent drugs suppress normal immunologic protection mechanisms, and allow organisms that normally would be held in check by these mechanisms to become invasive. Also, the lives of patients with various immunodeficiency states or nutritional deficiencies are being prolonged, and these cases contribute to the increased prevalence of infection in hospitalized patients. Finally, the misuse of antibiotics, especially in patients with chronic bacterial diseases, create a situation in which antibiotic resistant organisms become common, and the chances of spread of such organisms increased.

Spread of infection is a particular problem in newborn nurseries, burn treatment centers, and renal dialysis units. Control of infection in these subsections of hospitals is a factor in increased hospital costs.

More than half of hospital infections are caused by gram negative organisms which are common inhabitants of the human gut. Among these are some of the more serious infections of the urinary tract, skin, or other organs which end in septicemia (blood poisoning) and death. Antibiotic resistance is common among the gram negative bacteria.

National Institute of Allergy and Infectious Diseases (NIAID) efforts have several goals. One is to gain increased knowledge of the mechanisms by which bacteria common to the human environment acquire antibiotic resistance. Since there is evidence of transfer of resistance factors between harmless organisms and those with disease potential, such knowledge may provide a more rational basis for antibiotic usage and for prevention of development of resistance. A second goal is a better understanding of the antigenic composition and virulence factors of gram negative organisms in order to explore the feasibility of vaccines. New diagnostic and epidemiologic study technics are also dependent on such knowledge. A third is to counteract the effects of immunosuppressive drug therapy by blocking the effects of the drug on the immune system or by providing stimulants to the immune response. A fourth goal is to counteract the adverse effects of aging and/or nutritional deficiency on defense against infection by exploring the specific ways in which nutrition acts to increase natural resistance. The NIAID is unable to fund more than a token effort in this new thrust.

Spread of virus infections is also common in the hospital environment, but virus infections are a different problem and have not yet been included in reports of NIAID research on hospital associated infections. Fungal infections, however, are a special hazard in hospitals. The problem of fungal or mycotic infections is compounded by the relatively few trained mycologists in diagnostic laboratories and the paucity of physicians skilled in the diagnosis and management of fungal infections in the nation's hospitals, including a high percentage of university hospitals.

The NIAID in 1976 committed a total of $4.6 million to research related to hospital associated infections, including the problems of antibiotic resistance. About $1.6 million of this sum was for research directly related to the problem. These amounts do not include the basic research in immunology; which, although very important, cannot be directly related to solutions of the problem at present. In 1977, we expect to continue this level of support with a cost of living increase of about 6 percent. The FY 1978 budget request envisions only a further cost of living increase.

The deficiency of trained personnel is perhaps the most severe limitation in our present capability to control such infections. Most hospitals have found it necessary for medicolegal reasons to create "infection committees" and to employ physicians and/or nurses trained in infectious disease and epidemiologic investigative technics. The virtual absence of training programs for post-graduate training of physicians and nurses in the investigative epidemiology of infections has created this scarcity. A limited training potential exists at the CDC, in some NIAID and NCI laboratories, and in clinical research activities at a few grantee institutions. These potentials are presently not exploited to any significant degree. The NIAID is developing plans for a more comprehensive role in attacking the more serious problems of hospital associated infections. These plans will better define the immunological, virological, microbiological, mycological, and epidemiological components including training needs.

In summary, the Institute sees unexploited opportunities to do research on epidemiology, research and development on conventional and unconventional (broad spectrum or common antigen) vaccines, novel methods of increasing resistance to infection (e.g.; colonization with antagonistic organisms or scientifically monitored nutrition), provision of new and improved reagents for serotyping and diagnosis and expanded training of investigative epidemiologists, fungal microbiologists and biochemists.

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CYTOMEGALOVIRUS INFECTION

Mr. EARLY. In your statement you suggest this substitute for rubella is a threat to the unborn infant. We have no drugs to treat that.

Dr. KRAUSE. That is right.

Mr. EARLY. Are we working toward that?

Dr. KRAUSE. I spoke earlier in response to one of the Chairman's questions——

Mr. EARLY. If you have already gone into it——

Dr. KRAUSE. No; not that. Let me follow through on it if I may. I didn't speak specifically to your question.

Cytomegalovirus is one of the leading causes since rubella of perinatal infection which can result in mental retardation and birth defects. We have no drugs for most virus infections similar to penicillin for strep-sore throat.

In my view we must have a real thrust for the development of antiviral compounds, for the treatment of virus infections. For cytomegalovirus we should be exploring the possibilities of a vaccine because of this unfortunate outcome.

I should say cytomegaloviruses can be transmitted as a venereal disease. In two of our venereal disease centers they are working on how this virus is spread venereally.

IMMUNE SYSTEM

Mr. FLOOD. Last year you were excited about your efforts to study the immune system. How do you characterize your work currently and in the immediate future?

Dr. KRAUSE. I would say I am even more excited.

This past year, and in the future, I think we are even further along in knowing how the various cells of the immune system cooperate with each other to mount an antibody response. We also know that these cells have to circulate from one organ of the body to the other in order to affect their activity and we know that there is associated with this immune system, in addition to the cells, special substances similar to the hormones of the endocrine system which are required for the immune system to function.

Mr. FLOOD. Are you currently working in this area?

Dr. KRAUSE. Yes, sir, and we are pushing it as fast as we can.

COORDINATION AMONG INSTITUTES

Mr. FLOOD. In view of all that, it seems that your work on the immune system, the impact on the research efforts of all these other Institutes—do you have any kind of a formal mechanism for communicating results and for dividing up the work to be done in this entire immune system?

Dr. KRAUSE. We are spending a good deal of our resources on the fundamental way in which the immune system works. There are many aspects of the work in immunology that pertain to arthritis, that pertain to cancer and pertain to other areas. Immunology is a science like biochemistry, for example, and many of the Institutes will be using that science.

Mr. FLOOD. Do you have any kind of mechanism set up to communicate between each other on this?

Dr. KRAUSE. Our mechanism of working with each other is through many different committees and conferences.

Mr. FLOOD. Do you divide up the work?

Dr. KRAUSE. We share the work, yes, sir. We share it in the sense that we will be working on the immune system but will also try to give a good deal of our attention to those aspects that will eventually pertain to the allergic diseases and the immunological diseases. For example, my testimony mentions the treatment of patients with immunological diseases by giving them transplants of bone marrow cells. The Cancer Institute will more likely work on aspects of the immune system that pertain to cancer. The Arthritis Institute will work on those aspects that will pertain to arthritis. But when it comes to an overlap area, such as arthritis, we have an Arthritis Coordinating Committee with whom we work very closely.

I was on the Arthritis Commission, and I am a member of the NIH Arthritis Coordinating Committee where we coordinate our work on immunology and arthritis.

SEXUALLY TRANSMITTED DISEASE CENTERS

Mr. FLOOD. How many research centers do you support which study sexually transmitted diseases?

Dr. KRAUSE. We have four centers; in New York, Texas, Boston and Seattle.

VD SCREENING TEST

Mr. FLOOD. Last year we talked about a VD screening test that was field tested by the Center for Disease Control. Do you recall that?

Dr. KRAUSE. Yes, sir.

Mr. FLOOD. What are the results of the VD field trials? Can this testing be done on a wide scale?

Dr. KRAUSE. No, sir, not yet.

Mr. FLOOD. Is this for gonorrhea, syphilis, or both?

Dr. KRAUSE. That test is for gonorrhea and at this juncture it is still not one which can be widely applicable. It is not one which can yet be developed commercially though there is a lot of work on it. It is just for gonorrhea.

Mr. FLOOD. Can this test be used on a broad scale?

Dr. KRAUSE. There are still technical difficulties which have kept its introduction from wide scale use.

PENICILLIN RESISTANT STRAIN

Mr. FLOOD. I am sure you know there have been a number of newspaper articles recently, about the new penicillin resistant strain of gonorrhea. How serious is this and what kind of research are you conducting on that specific problem?

Dr. KRAUSE. This is a problem which appeared to arise in the Philippines last year. Those penicillin resistant strains occurred in the United States last fall and there have been some 100 or so reported cases now.

It is a potentially serious problem because in the Philippines it is now causing a sizable percentage of the total amount of gonorrhea.

We had a workshop of all the specialists in this field at the NIH at Christmastime which I called in order to address this problem, to assess the hazards and to determine what we and the Public Health Service should be doing. We are in close communication with the CDC and state health departments to assess how fast it is spreading.

What we need to do now is to monitor very carefully and determine how fast it will spread. The CDC and our venereal disease centers are following it very closely.

We must also work very hard on the mechanism whereby bacteria can acquire this strange capacity to develop extensive resistance to penicillin.

INTEREST IN VENEREAL DISEASE RESEARCH

Mr. FLOOD. Can't we do more research in this area? Is the scientific community interested in pursuing research in these sexual diseases?

Dr. KRAUSE. Yes, sir.

Mr. FLOOD. Are you receiving a lot of grant applications?

Dr. KRAUSE. We have increased our grant applications from almost nothing in 1970. I am happy to say my laboratory at Rockefeller, before I came here, began to do research in this area.

We have received enough good applications to give a total program of about $5 million a year in sexually transmitted diseases. Some of the investigators that are working on the way in which the bacteria acquire penicillin resistance characteristic are the same scientists that are concerned with DNA recombinant research and are now at the National Academy of Sciences discussing that issue. We have recruited some of our best scientists into working on this problem.

Mr. FLOOD. How much more money would you need to conduct additional research on VD?

Dr. KRAUSE. My professional judgment?

Mr. FLOOD. Sure.

Dr. KRAUSE. I would say we are going to allot next year $1 million of what has been given to us. We could expand that program perhaps twice as fast as we are now expanding it so that next year, if the funds were available, instead of $1 million, I would put $2 or $3 million more into the program.

PNEUMONIA VACCINE

Mr. FLOOD. What was the result of that clinical trial on the pneumonia vaccine?

Dr. KRAUSE. That went through one additional year so that there would be additional cases to determine the efficacy of the vaccine. The work is all in and is being analyzed now by the computer.

In other words, there has been some slippage in the output of the information and I expect to have the data available for publication by mid-summer. I can say that in some of the smaller studies that were done in gold miners and at the Dorothea Dix Nursing Home that the vaccine shows remarkable efficacy.

In cooperation with the Heart and Lung Institute, we are getting the vaccine into high risk populations such as patients with sickle cell anemia who are very prone to pneumococcal infections.

Mr. FLOOD. Will the vaccine be available to the general public in the near future?

Dr. KRAUSE. The Bureau of Biologics and the CDC's Advisory Committee on Immunization Practices are going to consider whether it will be licensed later this spring.

MENINGITIS VACCINE

Mr. FLOOD. Another vaccine we have dismissed in the past is the meningitis vaccine for use in children. Do you have any results from the trials conducted in Finland? Do you think this vaccine will be approved by FDA?

Dr. KRAUSE. The A vaccine is now approved by the FDA for adults. The C vaccine is effective for children over the age of two.

Mr. FLOOD. What about the results of the Finnish trials?

Dr. KRAUSE. The Finnish trial showed effectiveness of the vaccine and that will be part of the data which the FDA needs to use in their consideration of final approval.

Mr. FLOOD. But you see FDA approving it as of now?

Dr. KRAUSE. I would hope so; yes.

HEPATITIS B VACCINE

Mr. FLOOD. On the hepatitis B vaccine, has that been tested in humans yet?

Dr. KRAUSE. No. We are completing the trials in chimpanzees and we are now preparing this spring to start cautiously in volunteers, which will be Trappist Monks.

FUNDING OF VACCINE DEVELOPMENT

Mr. FLOOD. How much have you spent overall now for vaccine development in 1977 and 1978?

Dr. KRAUSE. All vaccines?

Mr. FLOOD. Yes.

Dr. KRAUSE. May I submit that for the record?

Mr. FLOOD. All vaccines—pneumonia, influenze, hepatitis, meningitis, et cetera.

[The information follows:]

Funding of vaccine development

Vaccine Development Program:	*Millions*
1976	$9,095,000
1977	11,000,000
1978	11,000,000

NOTE.—Includes bacterial vaccines for cholera, gonorrhea, meningitis, pneumococcal pneumonia and otitis media, streptococcal infection, syphilis, tuberculosis and pertussis, and includes viral vaccines for adeno, hepatitis, influenza, gastroenteritis, parainfluenza, rabies and respiratory syncytial viruses.

FUNDING OF GENETIC ENGINEERING

Mr. FLOOD. Last year we appropriated funds to your institute for the development of facilities and equipment and methods to study and enable the enforcement of the NIH safety guidelines on genetic engineering. How did you use that money?

Dr. KRAUSE. This money has been used in order to let contracts for the development of safer bacteria to do these experiments. We are currently using this money to upgrade the bacteriological laboratories around the country where this sort of work is done.

Mr. FLOOD. You say "we." This is your institute's role in the whole area of genetic engineering?

Dr. KRAUSE. That is right. We will also be using it for the alteration, purchase and installation of equipment for facilities in Bethesda and at Frederick.

BIOHAZARDS

Mr. FLOOD. How do you go about assessing the biohazards associated with recombinants? Will you briefly describe your process?

Dr. KRAUSE. What we are actually doing is determining whether the experiment going on is in compliance with the NIH guidelines.

Mr. FLOOD. I would hope so. That is what you are doing?

Dr. KRAUSE. Perhaps I don't get your question.

Mr. FLOOD. I want to know about the intention of the whole program. We have touched on this in several areas and now we come to you.

Dr. KRAUSE. One of the important things is to determine whether or not the bacteria which are being used, the new bacteria——

Mr. FLOOD. The biohazards——

Dr. KRAUSE. I am coming to that. Are they hazardous. It must be determined if they are hazardous by doing special experiments. We are doing these at NIH in specially devised laboratories.

Mr. FLOOD. You see what is developing now, this Frankenstein monster business.

Dr. KRAUSE. I have your question now. We are carefully trying to determine whether these new bacteria are hazardous. They are being put into various kinds of experimental animals to determine if they develop any untoward reactions.

PROGRAM REVIEW AND EVALUATION

Mr. FLOOD. In the material you submitted to the committee, Doctor, let me quote from this:

> Increased emphasis will be placed on identifying those projects that have either reached the end of their productive life, or no longer enjoy the same priority they once did.

That is what you said. Does that mean that you will be reviewing your noncompeting research grants annually every year for productivity or are you referring to your competing grants only?

Dr. KRAUSE. What does happen is that our total programs are reviewed and some projects are dropped out. For example, we dropped out one international research center. There were several allergy centers which we thought did not have the productivity they should have, and they were not renewed.

We have cut down certain areas of intramural laboratory investigations which had been supported in the past, and which we have cut back on. So we do in fact identify areas which in our judgment are less productive and expand others in their place.

Mr. FLOOD. Are you talking about competing grants, or the noncompeting research grants?

Dr. KRAUSE. We would be talking about competing grants.

BIOMETRY AND EPIDEMIOLOGY

Mr. FLOOD. Also in your budget justification you propose a new program in biometry and epidemiology. Why do you need to initiate those?

Dr. KRAUSE. As I mentioned earlier, infectious diseases and allergies are some of the most common disorders. The National Center for Health Statistics reports on the number of infections that occur in the United States. We know, however, from other surveys that those reports do not reflect the total amount of diseases. It is probable, for example, that only 1 out of 10 cases of hepatitis actually gets reported. So, we need better data on the number of infections occurring and what infections are occurring. From such data we can set priorities and determine what are the most important infections and allergies to work on.

One of the reasons for having an epidemiology and biometry program is to identify the problems and the issues.

Mr. FLOOD. How much will you spend in 1977 and 1978 for biometry and epidemiology?

Dr. KRAUSE. I will have to supply that for the record, but it will start with two professionals and two support personnel. It is a beginning program which will be closely associated with my office to give me guidance on these issues.

Funding of biometry and epidemiology

Salaries and expenses (1977):	
1 professional	$47,000
1 clerical	5,000
Other expenses	3,000
Total	55,000
Salaries and expenses (1978):	
2 professional	99,000
2 technical support	26,000
2 clerical support	19,000
Other expenses	8,500
Total	152,500

Mr. FLOOD. Thank you very much, Doctor.

FUNDING FOR SEXUALLY TRANSMITTED DISEASES

Mr. EARLY. Doctor, you replied to the chairman that you were spending $1 million on gonorrhea study and you suggested you could probably spend $2 million or $3 million. Would $2 million develop

twice as much information twice as fast? What ratio of production would the 100-percent increase bring, in your opinion?

Dr. KRAUSE. At the moment, our funding level is relatively low. The number of grants we can fund is just slightly under 20 percent of the approved grants. This means there is not much inducement, if you will, for scientists to move into this area. Therefore it would certainly help us a great deal if we could increase the actual number of highly competent investigators working in this area.

I would be hard put to tell you whether it would double our pace but I think there is still need for the recruitment to this field of highly gifted and competent scientists and physicians who are interested in it.

EARMARKING OF INCREASES

Mr. O'BRIEN. With reference to your comment about funding being somewhat low, in the extraordinary case of the Appropriations Committee giving you more than you asked for, could that be earmarked or would you be compelled to spread that over the whole area of your responsibility?

Dr. KRAUSE. I think a director of an institute is like the president of a university. They prefer unrestricted funds, but, on the other hand, like any president of a university, we would be glad to take whatever we could get.

Mr. O'BRIEN. Thank you, Doctor.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

VACCINE FOR VIRAL INFECTIONS

Mr. CONTE. Would you explain the particular difficulties involved in finding a vaccine against viral infections? What is it about viruses that makes the development of a vaccine so problematic?

ANSWER. Several highly successful vaccines have been developed for viral infections with the following characteristics: (1) Caused by a single virus type or a few types; (2) causative virus is stable antigenically; (3) natural disease followed by long lasting immunity; (4) virus can be grown in quantity; and (5) in case of live virus vaccine, virus can be reliably attenuated. Examples are poliomyelitis, measles, mumps, and rubella. When infections lack these characteristics, lifelong prevention through immunization is difficult, if not impossible. Examples are influenza—unstable antigen; the common cold—over 100 rhinovirus types; bronchiolitis—respiratory syncytial virus difficult to attenuate; and hepatitis—cannot yet grow virus. Other illnesses are caused by viruses which persist after the initial infection, only to recur later. The use of live vaccines in these instances might lead to such recurrence. Examples are chickenpox—herpes zoster; and fever blisters—herpes simplex. In the case of the herpes viruses, the virus seems to spread directly from cell to cell and to not be exposed to antibody. If antibody cannot combine with the virus, there is little chance for a successful vaccine.

RESISTANCE TO ANTIBIOTICS

Mr. CONTE. Can you explain the process in which bacteria develops resistance to the antibiotics once thought to guarantee cures?

ANSWER. Study of microbial genetics shows that bacterial acquire resistance to antimicrobial agents in two ways. One is chromosomal, where the original susceptible bacterium mutates to a new form which is no longer susceptible to the antibiotic. This mechanism is called transformation. The other is extrachromosomal, where the original antibiotic sensitive bacterium acquires, through

transfer from an antibiotic resistant bacterium, the bit of genetic information (plasmid) which makes the recipient bacterium resistant to the antiobiotic. This mechanism is called conjugation. Both mechanisms are the subject of recombinant DNA technology.

The second mechanism is the more common. Plasmids are loop structures of deoxyribonucleic acids (DNA's) which are free in the cell body and which are commonly exchanged between bacteria. Certain plasmids are known to carry antibiotic resistance (R) factors and can impart resistance to a bacteria that was formerly sensitive. It is probable that the gonococcus, which has previously always been sensitive to penicillin, recently acquired an R factor plasmid from a common intestinal organism and has now become highly penicillin-resistant. Bacterial geneticists predict the same thing will happen to the meningococcus before too long.

DISORDERS OF THE IMMUNE SYSTEM

Mr. CONTE. Can you explain how disorders of the immune system can be acquired? What is the mechanism involved in that process?

ANSWER. Any pathologic process that impairs the functional integrity of cellular components of the immune system, or that results in destruction or loss of the immune-producing products of these cells, can result in immunologic disorders. The body is especially vulnerable when the tissues containing lymphocyte cells are attacked by destructive or biologically altering processes such as toxic chemicals, certain bacterial or viral diseases, leukemia, neoplasms, as well as the cytotoxic drugs and X-radiation used in the treatment of cancer. In these conditions, there can be loss of cellular-immune functions or an actual depletion of cells that either effect immunity or regulate immune processes. In the aging process, there is a natural phyisologic decline in immune function. Also, immune defense may be impaired by protein deficiencies such as in malnutrition, defective protein metabolism as in liver disease, or loss of proteins through a diseased intestinal tract.

BONE MARROW TRANSPLANTATION

Mr. CONTE. I am pleased to see your progress on treatment of severe combined immunodeficiency disease (SCID). Is any work being done on improving bone marrow transplantation techniques?

ANSWER. Yes; current research is attempting to increase the sensitivity of histocompatibility matching tests to enhance the predictability of successful bone marrow transplants. Even more immediate is the need to improve techniques for suppressing the immune system by drugs, total body irradiation, and antithymocyte serum in order to prevent attack by the transplanted cells upon recipient tissue.

Mr. CONTE. How about the development of a wider bone marrow transplant donor system?

ANSWER. Attempting to effect a wider donor system at this time could be considered somewhat premature. It would be necessary first to overcome the problem of the conditions just mentioned—graft versus host disease. Use of unrelated donors would not be practical until we can develop improved typing to identify incompatibilities other than those which are now detectable by HLA matching.

Mr. CONTE. Can bone morrow be "banked" the way certain organs and blood are?

ANSWER. Freezing procedures seem to be feasible for preserving functionally competent bone morrow cells. Presently, this is done when bone morrow is to be held for possible later readministration to the same individual from which it was withdrawn. It is believed that when bone marrow matching problems can be overcome the technique for "banking" will be at hand.

THYMUS CELL TRANSPLANTS

Mr. CONTE. Why aren't the thymus cell transplants used to treat SCID victims rejected by the infants' bodies?

ANSWER. The affected infant does not have sufficient immune function to recognize the transplanted thymus as nonself. Because of this the real problem in thymus transplants is an attack on the defenseless infant by the donor's lymphocytes that are inadvertently transplanted with thymic tissue. The newly de-

veloped technique of using cultured thymic cells is promising because the lymphocytes responsible for rejection have been eliminated in the culture process.

Mr. CONTE. Once immune function has been restored to normal levels, would subsequent thymus transplants be rejected?

ANSWER. Yes, this could be expected.

Mr. CONTE. Would there be a need for later transplants?

ANSWER. No, once imune function is restored by reconstituion we believe that immune competence will last indefinitely.

ASTHMA AND ALLERGIC DISEASE CENTERS

Mr. CONTE. Where are your asthma and allergic disease centers located, and what specific accomplishments have been made at the centers?

ANSWER. The 15 centers are located in Boston at Harvard; in Durham, North Carolina at Duke; in Denver at the University of Colorado and National Jewish Hospital; in San Francisco at the University of California; in Rochester, Minnesota at Mayo Clinic; in Bethesda at NIH/NIAID; in Ann Arbor at the University of Michigan; in Baltimore at Johns Hopkins; in St. Louis at the Washington University; in Chicago at Northwestern; in Madison at the University of Wisconsin; in New Orleans at Tulane; in Omaha at Creighton; and in La Jolla, Calif. at Scripps Clinic.

Among the important accomplishments have been: (1) Development of a new drug to correct the definiency factor in potentially fatal heredity angioedema, (2) successful preventive treatment of potentially fatal bee sting reactions, (3) improvement of practical diagnostic methods for identifying patients at risk of severe allergic reactions, (4) defining specific types of viral infections predisposing children to the development of chronic asthma in later life, (5) elucidation of allergic factors in hypersensitivity pneumonitis and their application to prevent bagassosis as an occupational disease among sugarcane workers, and (6) development of pharmacologic agents that can be administered by inhalation. These control symptoms of asthma and allergic respiratory tract diseases with fewer serious side effects.

POLLEN ALLERGIES

Mr. CONTE. What new advances have there been in the diagnosis and treatment of pollen allergies?

ANSWER. Exact chemical fractions of ragweed and grass pollen grains responsible for allergic respiratory tract disorders have been identified, isolated and purified. This enables diagnostic pinpointing of specific causative agents and in turn their utilization in treatment. Modified pollen materials have markedly improved the efficacy of treatment for pollen-induced hay fever and asthma, resulting in the need for fewer injection treatments and minimizing the risk of unfavorable side reactions.

Mr. CONTE. Why is that desensitization or allergy shots don't always work?

ANSWER. The patient is sometimes so exquisitely sensitive that he cannot tolerate the dosages required to build up blocking antibodies. In other instances the difficulty is the material in the allergy shot. Often the exact pollen factors have not been isolated and identified.

Mr. CONTE. Do you have any figures on the success rate for such treatment?

ANSWER. Approximately 75 percent of patients taking injection treatments achieve varying degrees of improvement and control of symptoms. Use of the newer chemically defined and modified pollen extracts appears to have improved the efficacy of treatment by at least 10 percent, but more time is needed for evaluation.

OVER-THE-COUNTER DRUGS

Mr. CONTE. How effective are over-the-counter drugs in the treatment of asthma?

ANSWER. Some drugs available for over-the-counter purchase are standard preparations whose beneficial properties have been known for many years. These only relieve symptoms and do not have any proven effect on the disease process itself. Since asthma is a disorder that can arise from several different basic causes, there is no one drug that can help all asthmatic patients. Some patients may find varying degrees of relief from such drugs, but the great majority are

not benefited. There is also the unfortunate problem of undesirable side effects produced by these pharmaceuticals when the patient does not have the benefit of supervised medical management.

Mr. CONTE. Is asthma an inherited disease?

ANSWER. A long-standing observation is that asthma tends to appear in families whose histories are characterized by allergic disorders. With the availability of sophisticated tissue typing laboratory techniques, similar to blood typing, it is becoming increasingly evident that there are genetic associations of asthma and allergic disorders.

RECOMBINANT DNA RESEARCH

Mr. CONTE. Is your Institute doing any recombinant DNA research in conjunction with efforts to find new antiviral substances?

ANSWER. One of our grantees is considering taking the genes which code for interferon production and introducing them into a plasmid in *Escherichia coli*, a bacterium, in order to study them independently of the host animal which produces the interferon. Because of inadequate containment facilities at his institution, he has, as yet, not been given permission to do this experiment. This type of experiment would be ideal for containment facilities such as those proposed at the Frederick Cancer Center. If successful this work could lead to a much simpler and cheaper method of producing interferon.

Others are planning research using recombinant DNA technology or allied new laboratory methods to produce specific antibodies *in vitro*. This may be a way to develop antisera against viruses at some time in the future.

INTERFERON

Mr. CONTE. What is "interferon," and why is it so expensive?

ANSWER. Interferon is a glycoprotein which is part of the natural host defense mechanism against virus infection—everyone produces interferon in their body, and this product helps defense against virus infection. Production of interferon occurs when cells are exposed to viruses or to certain nonviral inducers. Following the production of interferon by a cell it is released from the cell. When other cells come in contact with interferon they produce antiviral proteins which block the replication of virus. Relatively large quantities of interferon given to a patient suppresses the multiplication of viruses.

The antiviral activity of interferon is species specific—that is, in order for interferon to be used as a drug in humans, interferon must be produced from human cells. This can be done with human cells grown in culture. A human dose of interferon may be several million units of interferon, and this dose may cost hundreds of dollars, since maximum yields of interferon at present are about 20,000 units per 1 million tissue culture cells. Recent research on new ways to produce and purify this cell protein more economically is a joint venture between the NIAID and NCI. It is also hoped that increased studies on purification carried out by NIAID and NIAMDD will eventually lead to structural definition which will allow chemical synthesis.

MALARIA PARASITE

Mr. CONTE. Would you outline the process which enabled one of your investigators to cultivate the malaria parasite for the first time last year?

ANSWER. The successful serial cultivation of the parasite, *Plasmodium falciparum*, which causes malaria, was reported by Drs. William Trager and James R. Jensen at the Rockefeller University. These two grantees started with a chloroquine-resistant human strain cultivated in the laboratory in *Aotus* monkeys. The culture medium, while complicated, was composed of known chemicals and supplemented with human serum. A small quantity of monkey red blood cells, already invaded by the parasite, was mixed with normal human red blood cells and the mixture held in a thin undisturbed layer. This cell layer was overlayed with culture medium that was slowly and continuously replaced. Above the culture medium, was an atmosphere of carbon dioxide, oxygen and nitrogen. The whole system was incubated at 38° C.

Every 3 to 4 days some of the layer was mixed with about three parts of fresh human red blood cells to effect a 1 to 4 dilution. Periodic microscopic examina-

tion of the cultured red blood cells showed that there had been growth and release of parasites and infection of the freshly added cells. After some 35 days, the culture was still typically infective for an *Aotus* monkey and the culture has been carried for at least 48 days.

Malaria causes, worldwide, some 96 million cases each year and accounts for 1 million deaths in Africa alone. One stage of the complicated life cycle of the parasite, the merozoite, is thought to be immunogenic and the ability to culture them in the laboratory opens up the study of possible vaccines and of substances which function in invasion of the red blood cells.

CENTRALLY FURNISHED SERVICES

Mr. CONTE. You are requesting a fairly large increase for centrally furnished services. What services does that item cover? And how do you justify the increase?

ANSWER. The increase for centrally furnished services represents the increased services and the increased cost of services provided by the NIH management fund in support of the NIH research program. Some of these services include: the clinical center operation and patient care; building maintenance and utilities; scientific and technical review of research and training grant applications; and standard level user charge, which is the payment to the General Services Administration for rental of space.

HOSPITAL ASSOCIATED INFECTIONS

Mr. CONTE. I was surprised by the statistic that some 5 percent of the patients in hospitals acquire an infection after admission which complicates their treatment. What is being done to reduce the incidence of hospital-acquired infections?

ANSWER. The NIAID has established a special emphasis program on hospital-associated infections. This consists of some 57 projects comprising research grants, fellowships, and training grants at an annual funding level of $2.55 million. In addition to research, training of experts in infectious diseases, with emphasis on hospital-associated infections, is also an important facet of this program. Investigators at many institutions are attempting to understand more about the increased appearance of these organisms in the patient, in the hospital setting, and about methods for reducing the number of cases as well as treating the patient. Potential vaccine materials or experimental immune antisera provide promising leads to therapy or prevention. The program directly relates to another special emphasis program on mechanisms of resistance to antimicrobial agents, funded at about $3 million annually, which is attempting to clarify the reasons for the appearance of the drug-resistant microorganisms. Such organisms cause the most difficult and serious problems among hospital patients.

REORGANIZATION

Mr. CONTE. Would you explain what is involved in your institute's reorganization to a program basis?

ANSWER. Until recently, the Institute consisted of an Office of the Director and three major programs. Simply put, the intramural research program performed basic and clinical research in our own laboratories, the extramural program supported basic and clinical research and training in universities and medical schools through grant awards, and the collaborative research program worked to adapt and apply laboratory findings to the development of specific disease control measures through the use of the contract mechanism.

The major thrust of the reorganization was to shift the primary emphasis in extramural research to diseases rather than mechanisms. Two of the new programs are the microbiology and infectious diseases program and the immunology, allergic and immunologic diseases program, each of which uses all available mechanisms to support basic, clinical and developmental research to solve the disease problems in its area. The extramural activities program manages the Institute's research resources and manpower development programs, the scientific review committees and Advisory Council, and provides grant and contract management support for the Institute. The Office of the Director and the intramural research program remain unchanged. We feel that this change relates the Institute's program structure more directly to its research goals and its budget structure, provides a program-oriented directorate to assist the Director in the planning and management of Institute programs, and aids him in marshaling the resources of the Institute toward the achievement of its program goals.

RESEARCH OPPORTUNITIES

Mr. CONTE. Your justification (p. 241) says that a recent review of the state of the art of current research indicated many new research opportunities which should be addressed. What are some of those areas, and does your budget request adequately provide resources for the expansion of research into those areas?

ANSWER. The reference was in relation to a reorganization of our extra-mural activities to provide stronger leadership and increased flexibility in the pursuit of opportunities.

In the area of allegy and immunologic diseases there has been a rapid growth of knowledge about the chemical nature of the substances secreted by white blood cells which set off allergic reactions. This opens up new avenues of pharmocologic research for specific drugs which can neutralize or block these substances.

Chemical identification of pollen constituents responsible for asthma and hay fever enables studies on procedures for more specific diagnosis and desensitization.

Identification of the association of certain histocompatibility antigen types with diseases such as ankylosing spondylitis opens new pathways for study of the genetic control of susceptibility to many chronic and degenerative diseases. Since there is linkage between histocompatibility antigens and immune response genes, the immunological basis for these diseases can then be pursued.

Other opportunities are reflected in the opening statement and answers to other questions.

In the area of microbiology and infectious diseases, progress in understanding virus controlled functions in the host cell has opened up new possibilities for specific antiviral therapy. One such drug, adenosine arabinoside (ara A), is under study in life threatening herpes virus infections. This drug blocks the nucleic acid replication of herpes viruses. Other promising drugs are emerging and should progress to cooperative clinical trials for efficacy in human virus diseases.

Discovery of new viruses responsible for acute gastroenteritis has opened up new opportunities for vaccine development. The role of these new viruses and of other infections of the gut was recognized by the Commission on Digestive Diseases.

Discovery that high molecular weight bacterial polysaccharides are capable of stimulating better antibody responses than current vaccines against meningitis and pneumonia creates opportunities for improved immunization in these diseases.

Identification of multiple serotypes of gonococci and advance in knowledge about the immune response to gonorrhea is opening up a possibility for vaccine development in addition to providing better epidemiologic tools for tracing spread of the disease.

Identification of the role of viruses in causing chronic diseases, for example the degenerative nervous system diseases recognized by the Nobel Prize Committee, has opened up extensive research into the etiology and pathogenesis of many other chronic diseases including those of the musculoskeletal system, respiratory tract, and kidney.

The task force on virology convened by the NIAID is currently preparing a detailed review and recommendations which should provide the Congress with a catalog of opportunities.

Other opportunities are noted in the opening statement and answers to other questions. Recombinant DNA technology provides a particular opportunity that was spoken to by the Director, NIH in addition to the NIAID testimony.

We will be taking advantage of these opportunities within the limits of the NIAID budget request. The question is more that of rate of progress than ability to seize new opportunities.

SUPPORT OF TRAINING PROGRAM

Mr. CONTE. Why are you reducing the number and support of new training awards?

ANSWER. The reduced number of training awards is attributable in part to the fact that funding has not kept pace to rising costs. For example, we spent $8,283,000 on 941 trainees in fiscal year 1975. We spent $7,809,000 on 569 trainees in fiscal year 1976. We expect to spend $8,081,000 on 553 trainees in fiscal year 1977. The influences of inflation together with the decision to eliminate new

institutional training awards in fiscal year 1978 are reflected in the lower number of trainees and dollar projections in the President's budget request.

Mr. CONTE. What is the situation involving the particular disciplines from which you draw your researchers?

ANSWER. We estimate that about 400 investigators leave the research areas of importance to allergy and infectious diseases each year. At current training levels about 150 new trained investigators are entering these fields. Payback provisions have reduced the number of young physicians entering research training and will create shortages of clinical investigators in time.

Immunology is one of the most rapidly growing disciplines in biomedical research and a discipline for which NIAID is the primary training resource.

Mr. CONTE. Is there presently an adequate supply of people trained in those disciplines?

ANSWER. No, both teaching and community hospitals are seeking physicians and nurses trained in epidemiology and infection control. They are also seeking clinical microbiologists for investigative and diagnostic laboratories. The American Association of Immunologists and the American Society for Microbiology maintain job registries and attest that many positions go unfilled for long periods. The president of the Infectious Diseases Society of America has recently documented the shortage of infectious diseases specialists. A GAO study has also documented the shortage of allergists. Quite independent of these assessments, the NIAID is particularly concerned about shortages in clinical microbiology, virology, mycology and epidemiology.

RECOMBINANT DNA

Mr. MICHEL. How much, in the way of recombinant DNA (genetic) research, are you funding?

ANSWER. As best we can now forsee, the total requirements in fiscal year 1978 will amount to about $5.8 million.

Recombinant DNA technology is an outgrowth of bacterial and cell genetic research which has long been supported by NIAID. Recently, the technology has undergone an almost explosive development which has resulted in NIH guidelines designed to minimize the possible biohazards to the public and environment. The funding level in fiscal year 1977 of approximately $5.0 million reflects not only the support of research, but the cost to upgrade parts of several facilities for immediate use to meet the standard set forth in the NIH guidelines and to upgrade the equipment and facilities at a number of grantee institutions.

In fiscal year 1978 we expect to fund basic research, including the study of bacterial plasmids and bacteriophages, for a total of about $1.7 million. Two years ago, the NIAID was delegated responsibility for research and development of safer hosts and vectors for recombinant DNA research and to provide them to scientists to ensure an effective biological method for control of possible biological hazards. The hosts are bacteria so altered that they cannot exist outside the laboratory and the vectors are bacterial viruses or plasmids which are specific for these altered bacteria and cannot infect bacteria normally occurring in nature. This research and development is supported through a contract program funded at about $1 million.

The risks of recombinant DNA research are speculative and are mainly concerned with creation of new microorganisms by insertion of foreign DNA. Intramural scientists have undertaken to assess such risks using specially renovated physical containment facilities and equipment. These experiments, for which preliminary work is nearing completion, will begin this summer or fall and will be funded for about $1 million. There will also be an increased cost of supplemental awards to grants for renovations and equipment needed for compliance with NIH guidelines. Review processes of grants and contracts involving recombinant DNA research have been made more stringent and will frequently require site visits to obtain engineering details on facilities and plans for experiments. This will result in greater administrative costs. The Institute received special funding from Congress to meet such additional costs in fiscal year 1977 and these will continue in fiscal year 1978. All these activities have placed increased demands on the staff and required diversion of effort to meet responsibilities for planning, monitoring and review.

Mr. MICHEL. What is your basic philosophy toward such research? Are you concerned about the ultimate potential here, or do you take the position that it is a new research horizon and therefore must be pursued as far as possible?

ANSWER. It should be understood that the genetic principles of this research are not new and that mutations and recombination of genes are occurring at a steady and rather rapid rate in nature. An example is the recent acquisition of penicillin resistance by the gonococcus. There is scientific evidence that this occurred when a plasmid (DNA molecule) from a bacterial inhabitant of the human gut was transferred to the gonococcus by a combinational event. What is new is the technical capacity to bring about such events in the laboratory by the *in vitro* splicing of portions of two or more DNA molecules. This enables a more rapid and definitive study of which genes control the manufacture of particular substances in the cell. The long range view is that useful proteins, such as insulin and hormones, can be produced cheaply and in quantity by bacteria into which the genes coding for these protein have been introduced.

We believe this technological advance should be utilized to the fullest degree in the pursuit of knowledge about the controlling events in cells, bacteria and viruses. Understanding of these events is necessary if we are to combat problems such as antibiotic resistance. This new knowledge may assist in the understanding of virus-cell interaction and in turn the development of antiviral drugs. In immunology, there are also potential significant benefits in learning how genes control the immune response, how acquired or inborn immune deficiencies may be corrected, and how antibodies or other useful immunological substances could be produced outside the body.

The research is worldwide in developed countries and will go on whether we do it in this country or not. We believe it is wise to pursue this research actively. We must be alert to possible hazards, assess them accurately and keep them at levels where men or the environment will not be threatened in any way.

Mr. MICHEL. Is this genetic research laboratory being built at the Frederick Cancer Center intended to be a model for other research laboratories in the field?

ANSWER. The principles and technology for high degrees of physical containment were worked out and proven in connection with research and diagnostic work with dangerous microorganisms and viruses. Buildings which once housed such research at Frederick are being renovated so that they can be used once again as high containment facilities for certain types of recombinant DNA and other genetic recombinant research. After 8 years of disuse, utility supply and waste lines, ventilation, filter systems and safety cabinets must be replaced, repaired or renovated, tested and made operational.

The renovated buildings will be a model. More important, the operation will provide a training site for safety personnel, engineering technicians, and laboratory workers who are involved in the development and operation of high physical containment facilities elsewhere.

Mr. MICHEL. What is your attitude toward the position of many people that such research poses a danger and must be restricted?

ANSWER. We are in agreement that there can be biohazards to certain types of genetic recombinant research and that there should be means of ensuring that laboratory workers, the public, and the environment are adequately safeguarded. To do this means that the work should be done by scientists that are adequately trained in and have proven themselves to be responsible for biohazard safety procedures. All potential biohazards of any experiments should be assessed in the planning stage and both biological and physical containment appropriate to the potentials utilized. The work should be done under the supervision of institutional biohazard safety committees and an independent safety officer.

We are also in agreement with the desirability of federal regulation of the research through the inspection and licensing of facilities, requirements for approval of all experiments by institutional biohazard safety committees, establishment of training standards for workers, and national registration of all projects.

We do not agree with those who speculate about the uses of the research in "genetic engineering" of human beings. Much of this stems from confusion of recombinant DNA technology with other research in reproductive biology. Even the possibility of being able to insert into the cells of the whole human, genes which may correct a gene defect is too remote to be given any practical consideration at this time. Should this arise some years hence, there are well understood and utilized safeguards on human experimentation. The development of Institutional human research committees made up of ethicists, lawyers, and other public representatives has provided protection to the public in what might be considered more risky research.

DRUGS FOR VIRAL INFECTIONS

Mr. MICHEL. Are your pleased or disappointed with the progress, or lack of such, that is being made in developing drugs to combat viral infections?

ANSWER. The "antiviral era" began in 1957 when interferon was recognized to be a broad spectrum antiviral drug. The development of interferon as an antiviral drug was slowed by the fact that methods to produce and purify high titers of this material had to be developed. We know how to produce interferon in tissue culture and preliminary clinical trials in man have shown that this antiviral may be an effective treatment for hepatitis B and herpes zoster infections. This is very exciting research, and represents progress in the field of antiviral therapy which the practicing physician can hope to use.

Other exciting antiviral therapy includes use of amantadine for treatment of influenza infections and use of adenine arabinoside (ara-A) for treatment of herpes encephalitis and other herpes infections. The clinical efficacy of both interferon and ara-A have been demonstrated in the past year. We are satisfied that the current progress is as rapid as resources allows. To continue to develop new antivirals will require the initiation of new laboratory and clinical studies. The costs of clinical studies are escalating rapidly.

INTERFERON

Mr. MICHEL. You have developed an antiviral substance called interferon to treat hepatitis B, but your statement indicates that this is costly and in short supply. Why is that? Where does it come from?

ANSWER. Chronic hepatitis B patients have carried this disease for many years. The virus multiples in the cells of the liver. Interferon treatment administered for long periods of time, for several months, reduces the symptoms and signs of hepatitis in the patient. Interferon must be given daily at fairly high doses. Interferon is costly to produce because it is a protein that must be produced by human cells, for example, in cultures of human leucocyte cells or human fibroblast cells, and there are now only a few laboratories in the world which can produce it in sufficient quantities for clinical studies.

Many cells are needed to produce enough interferon to treat one patient and after a cell has produced and excreted interferon into the medium, the interferon must be concentrated and purified. As it proves to be clinically effective other laboratories and drug companies can be expected to become involved in the production of interferon, the drug should become more plentiful and the cost can be expected to go down. It is also possible that through additional chemical analysis the structure of interferon will be identified and chemical synthesis feasible. There is need for intensified studies of this sort which are at present very limited because of the highly sophisticated and expensive technology involved.

VIROLOGY TASK FORCE

Mr. MICHEL. You have appointed a virology task force to among other things identify new strategies for developing safe and effective anti-viral compounds. How long is this effort expected to take?

ANSWER. We are now investigating new antivirals including interferon, amantadine, rimantadine, adenine arabinoside (ara-A) and adenine arabinoside monophosphate (ara-AMP). Other antivirals are undergoing tests in animal model systems. Development of antivirals is a new area of research, and it is likely that new drugs with antiviral potential will be recognized over the next several years, much the same way as new antibiotics were recognized. Many years are required to bring an antiviral compound from the stage of initial discovery to use in man. Unlike antibiotics, in order for antivirals to be effective, they must penetrate the tissue cells and attack the virus replication sites without affecting normal activities of the cells. Once a compound is found to be effective in *in vitro* systems it must then be tested in animals, toxicity data acquired, and carefully controlled and monitored clinical trials in man initiated. This process takes time and money. We anticipate the need for intensified effort over the next decade if new antiviral drugs are to be available for life threatening virus infections. Even longer effort may be needed for the development and testing of drugs for the more common virus diseases. Much will depend on progress in basic research.

HEPATITIS

Mr. MICHEL. You mention that hepatitis research is being hampered by an inability to grow causative viruses in the laboratory. Why can't it be done in the lab?

ANSWER. Despite considerable success at growing human tissue cells in the laboratory and getting many viruses to grow freely in such tissue cultures, we really cannot account for our lack of success with hepatitis virus type B or type A.

Liver cells have been grown in tissue culture, but it may be that they are not fully functional. In any event, they are not the true diploid type which would be acceptable for use in providing vaccine. Or it may be that the virus inoculum is too impure, a mixture perhaps of complete and interfering or defective virus particles or some other inhibitor which prevents the virus inoculum from gaining entrance to the cell and growing. We have some limited effort aimed at these problems. Lastly, it should be recalled that only recently have we had specific tests enabling us to identify type A and B hepatitis viruses. By elimination we now know there must be at least one other type of hepatitis virus for which we have no test, let alone system for cultivation.

VACCINE FOR HEPATITIS B

Mr. MICHEL. How long would you estimate it will be before a vaccine for hepatitis B is ready for public use? You are apparently beginning preliminary testing in volunteers this spring.

ANSWER. Trials to be started this spring are designed to evaluate the safety of the vaccine in humans. Studies conducted thus far in approximately 100 chimpanzees have shown the vaccine (inactivated with formalin) to be noninfectious, antigenic, and free from detectable adverse reactions. The initial studies in adult volunteers will take approximately 1 year. We should be able to start field trials for efficacy evaluation in 1978 or 1979. Once efficacy is demonstrated, the NIAID will have accomplished its goal of establishing hepatitis B vaccine feasibility. Hopefully, industry will develop the vaccine and perform trials that will support licensure application. It is estimated that vaccine for public use is at least 5 years in the future. One pharmaceutical company is known to be interested and our scientists have cooperated with their scientists in developing industrial technology. We have also been consulted by other companies but so far these do not seem to be actively working on the problem.

GONORRHEA

Mr. MICHEL. How serious is this new strain of gonorrhea which is apparently resistant to penicillin?

ANSWER. The Center for Disease Control monitors the appearance of cases caused by this new penicillin-resistant strain of the gonococcus. At least 115 cases in 18 different States and Guam have now been confirmed by CDC laboratory experts. This strain appears to be slowly spreading through the United States. Spread could become more rapid as the resistant strains are seeded into promiscuous population groups.

In addition, this strain, which apparently originated in the Far East, is also being seen in a number of countries in Europe and Latin America. In certain parts of the Philippines nearly 50 percent of the strains circulating in the population are now resistant to penicillin. Clinically the disease produced is much the same as that produced by the other sensitive strains; but the problem is serious because it introduces a new diagnostic requirement, requires treatment by substantially more expensive antibiotics and increases the chance of resistance spreading via plasmid transfer to other species of bacteria infecting humans.

Mr. MICHEL. Is there any way to treat it?

ANSWER. Experts at a conference called by the NIAID on December 17, 1976, to discuss this problem agreed that the most effective method for treating this disease was by administration of the antibiotic spectinomycin. Spectinomycin has been formally recommended by the CDC as the drug of choice for treating all cases of laboratory proven penicillin-resistant gonorrhea. Unfortunately, the cost of the antibiotic alone will be approximately $4 to $5 per patient for spectinomycin versus about $.50 to $.75 per patient treated with penicillin. Also it has been shown

that resistance to spectinomycin can be induced and that with wide scale usage possibly may not continue to be effective. Other promising antibiotics are being studied.

FUNDING OF GRANTS APPLICATION

Mr. MICHEL. In the fields covered by your Institute, how many of the grant applications received this year are being funded, and second, how many of those approved by the study groups are being funded?

ANSWER. In fiscal year 1977, it is anticapted that 1,104 regular research grant applications will be received pertaining to the activities of the National Institute of Allergy and Infectious Diseases. Although there is still one advisory council session remaining this year, it can be estimated that 925 applications will be approved for funding. As shown in the budget justification, the Institute expects to fund 272 new and competing applications in 1977. This represents 24.6 percent of total applications received and 29.4 percent of total applications approved. However, more recent data as to the average cost of a grant, particularly in the allergy and immunology program area, indicates that 228 new and competing applications will be funded. This would reduce the funding rate of approvals to 24.6 percent.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Amounts Available for Obligation 1/

	1977	1978
Appropriation	$141,000,000	$153,442,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $695,000; 1978 - $777,000.

National Institute of Allergy and Infectious Diseases

Budget Mechanism

	1977 Appropriation			1978 Estimate		
	No.	FTE[1]	Amount	No.	FTE[1]	Amount
Grants						
Regular						
Noncompeting	751	---	$57,630,000	756	---	$60,789,000
Competing	159	---	11,419,000	199	---	15,979,000
New	113	---	7,680,000	159	---	11,153,000
Supplemental	(4)	---	100,000	(4)	---	100,000
Subtotal	1,023	---	76,829,000	1,114	---	88,021,000
Special						
International centers for medical research	4	---	2,400,000	4	---	2,400,000
Research career program	95	---	2,624,000	95	---	2,624,000
Subtotal	99	---	5,024,000	99	---	5,024,000
Total grants	1,122	---	81,853,000	1,213	---	93,045,000
Training programs						
Individual awards						
Noncompeting	112	112	1,511,000	129	129	1,621,000
New	73	73	845,000	56	56	650,000
Institutional awards						
Noncompeting	47	208	3,550,000	65	307	4,210,000
New	40	171	2,175,000	---	---	---
Total training programs	272	564	8,081,000	250	492	6,481,000
Research and development contracts	150	---	14,961,000	154	---	15,279,000
Intramural research	---	---	28,398,000	---	---	30,440,000
Direct operations	---	---	6,622,000	---	---	7,111,000
Program management	---	---	1,085,000	---	---	1,086,000
Total			141,000,000			153,442,000

[1]/Full time equivalent.

DHEW - National Institutes of Health

CROSSWALK - 1977 Column of 1978 Justification

INSTITUTE: National Institute of Allergy and Infectious Diseases

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM									
	Research Grants			Training Program		Res. & Develop. Contracts	Intramural Research	Direct Opers.	Program Mgmt.	Total
	Regular Programs									
	Noncompeting	Competing	Specials	Indiv.	Inst.					
Immunology, allergic and immunologic diseases. . .	$22,296	$7,510	$1,493	899	$2,199	$2,900	---	---	---	$37,297
Microbiology and infectious diseases . . .	35,334	11,689	3,531	1,457	3,526	12,061	---	---	---	67,598
Intramural research. . . .	---	---	---	---	---	---	$28,398	---	---	28,398
Direct operations.	---	---	---	---	---	---	---	$6,622	---	6,622
Program management	---	---	---	---	---	---	---	---	$1,085	1,085
Total	57,630	19,199	5,024	2,356	5,725	14,961	28,398	6,622	1,085	141,000

DHEW - National Institutes of Health

CROSSWALK - 1978 Column of 1978 Justification

INSTITUTE: National Institute of Allergy and Infectious Diseases

(Dollars in thousands)

PROGRAM ACTIVITY	MECHANISM									
	Research Grants					Res. & Develop. Contracts	Intramural Research	Direct Opers.	Program Mgmt.	Total
	Regular Programs			Training Program						
	Noncompeting	Competing	Specials	Indiv.	Inst.					
Immunology, allergic and immunologic diseases. . .	$23,153	$11,021	$1,493	$881	$1,711	$3,000	---	---	---	$41,259
Microbiology and infectious diseases . . .	37,636	16,211	3,531	1,390	2,499	12,279	---	---	---	73,546
Intramural research. . . .	---	---	---	---	---	---	$30,440	---	---	30,440
Direct operations.	---	---	---	---	---	---	---	$7,111	---	7,111
Program management	---	---	---	---	---	---	---	---	$1,086	1,086
Total. . . .	60,789	27,232	5,024	2,271	4,210	15,279	30,440	7,111	1,086	153,442

Summary of Changes

1977 Estimated obligations	$141,000,000
1978 Estimated obligations	153,442,000
Net change	+12,442,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within grade increases	---	$109,000	---	+$115,000
2. Wageboard pay increases	---	704,000	---	+80,000
3. FTS rate increase	---	101,000	---	+8,000
4. Increased cost of Federal Employees Compensation Fund	---	14,000	---	+26,000
5. Increased cost of service and supply	---	3,058,000	---	+95,000
6. Payment for centrally furnished services	---	10,531,000	---	+927,000
Standard Level User Charges	---	(402,000)	---	(+38,000)
Subtotal				+1,251,000
B. Program:				
1. Research Grants				
a. Support of 111 new and 156 competing renewal awards in 1977 converted to noncompeting in 1978	---	57,630,000	---	+21,503,000
b. Support of 159 new and 199 competing renewal awards in 1978	---	19,199,000	---	+27,232,000
2. Training programs				
a. Support of 40 (171 trainees) new institutional awards in 1977 converted to noncompeting in 1978	---	3,550,000	---	+2,262,000
b. Support of 73 new individual awards in 1977 converted to noncompeting in 1978	---	1,511,000	---	+896,000
c. Support of 56 new individual awards in 1978	---	845,000	---	+650,000
3. Research and development contracts				
a. Support of 34 new contracts in 1977 converted to continuations in 1978	---	11,361,000	---	+3,960,000
b. Support of 21 new contracts in 1978	---	3,600,000	---	+2,000,000

4. Intramural research				
a. Expansion or initiation of research in the areas of immunology, virology and nucleic acid recombinants	---	28,398,000	---	+1,058,000
5. Direct operations				
a. Expanded support of grant and contract activity, interferon procurement. .	---	6,622,000	---	+339,000
Subtotal				+59,900,000
Total, increases . . .				+61,151,000
Decreases:				
A. Built-in:				
1. One day less pay in 1978. . .	---	14,094,000	---	-58,000
B. Program:				
1. Research grants				
a. 262 noncompeting awards in 1977 terminated or converted to competing in 1978.	---	57,630,000	---	-18,344,000
b. 113 new and 159 competing renewal awards in 1977. .	---	19,199,000	---	-19,199,000
2. Training programs				
a. 22 (72 trainees) noncompeting institutional awards in 1977 terminated in 1978. . . .	---	3,550,000	---	-1,602,000
b. 40 (171 trainees) new institutional awards in 1977 deleted in 1978	---	2,175,000	---	-2,175,000
c. 56 noncompeting individual awards in 1977 terminated in 1978	---	1,511,000	---	-786,000
d. 73 new individual awards in 1977 deleted in 1978 .	---	845,000	---	-845,000
3. Research and development contracts				
a. 17 continuation contracts in 1977 terminated in 1978.	---	11,361,000	---	-2,042,000
b. 34 new contracts in 1977.	---	3,600,000	---	-3,600,000
4. Direct Operations				
a. Decrease of 3 positions from 1977	93	6,622,000	-3	-58,000
Subtotal			-3	-48,651,000
Total, decreases.			-3	-48,709,000
Total, net change			-3	+12,442,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase Or Decrease Pos.	Increase Or Decrease Amount
233	Immunology, Allergic and Immunologic Diseases	---	$37,297,000	---	$41,259,000	---	$+3,962,000
236	Microbiology and Infectious Diseases	---	67,598,000	---	73,546,000	---	+5,948,000
239	Intramural Research	480	28,398,000	480	30,440,000	---	+2,042,000
	Standard Level User Charge		(325,000)		(343,000)		(+18,000)
240	Direct Operations .	93	6,622,000	90	7,111,000	-3	+489,000
	Standard Level User Charge		(77,000)		(97,000)		(+20,000)
241	Program Management.	48	1,085,000	48	1,086,000	---	+1,000
	Total Obligations	621	141,000,000	618	153,442,000	-3	+12,442,000
	Standard Level User Charge		(402,000)		(440,000)		(+38,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	621	618	-3
Full-time equivalent of all other positions	62	62	---
Average number of all employees	678	675	-3
Personnel compensation:			
Permanent positions	$11,091,000	$11,306,000	+$215,000
Positions other than permanent	437,000	448,000	+11,000
Other personnel compensation	522,000	534,000	+12,000
Subtotal, personnel compensation	12,050,000	12,288,000	+238,000
Personnel benefits	2,044,000	2,091,000	+47,000
Travel and transportation of persons	426,000	518,000	+92,000
Transportation of things	105,000	112,000	+7,000
Rent, communications and utilities	580,000	640,000	+60,000
Printing and reproduction	235,000	255,000	+20,000
Payment for centrally furnished services	10,531,000	11,458,000	+927,000
Project contracts	14,961,000	15,279,000	+318,000
Other services	6,682,000	7,373,000	+691,000
Supplies and materials	2,900,000	3,225,000	+325,000
Equipment	550,000	675,000	+125,000
Grants, subsidies and contributions	89,934,000	99,526,000	+9,592,000
Insurance claims and indemnities	2,000	2,000	---
Total obligations by object	141,000,000	153,442,000	+12,442,000

Significant Items in House and Senate
Appropriations Committee Report

Item	Action taken or to be taken
1977 Senate Report	
1. The Committee urges Director, NIH to give urgent consideration to the steps that should be taken to remedy this situation either by planning a suitably-designed new building on the NIH campus or by adapting containment facility available at Fort Detrick to the needs of NIAID research in infectious diseases. (page 56 of Senate Report)	1. A committee has been established to look into this situation and prepare a pre-design report establishing basic design criteria for a research laboratory facility suitable for experiments involving recombinant DNA molecules and the role they play in infectious diseases. This report should be completed early in 1977.

Authorizing Legislation

	1978 Authorization	1978 Appropriation Requested
PUBLIC HEALTH SERVICE ACT		
Title III, Part A, Section 301 -- Research and Investigation, in General	Indefinite	
Title IV, Part D, Section 431 -- National Institute of Allergy and Infectious Diseases.	Indefinite	$148,061,000 2/
Title IV, Part I, Section 472 -- National Research Service Award Act of 1974	1/	$ 5,381,000 3/

1/ Authorization expires September 30, 1977; Extension legislation is pending.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $1,100,000 for old training program.

National Institute of Allergy and Infectious Diseases
(Comparable)

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
1968	$89,014,000	$89,014,000	$92,107,000	$88,998,000
1969	93,190,000	89,747,000	93,747,000	91,468,500
1970	96,417,000	96,417,000	98,908,000	97,722,500
1971	94,739,000	96,412,000	96,912,000	96,412,000
1972	94,765,000	101,430,000	107,150,000	103,517,500
1973	95,614,000	107,647,000	129,233,000	107,647,000 1/
1974	98,667,000	112,718,000	113,974,000	111,063,000 2/
1975	110,321,000	105,760,000 3/	121,917,000	119,369,000
1976	109,022,000	119,229,000 4/	119,229,000 4/	127,163,000 5/
1977	135,615,000	139,615,000	143,615,000	141,000,000
1978	153,442,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P. L. 93-192.

3/ Excludes R&D contracts not considered by House due to lacking authorization.

4/ Excludes fellowships and training grants--not considered due to pending legislation ($7,934,000).

5/ Includes $7,934,000 training programs authorized under Continuing Resolution.

NOTE: The figures presented in this table have been adjusted to reflect the transfer of major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amount originally contained in this account in previous years for this particular program has been removed for comparability purposes.

National Institute of Allergy and Infectious Diseases
(Actual)

Year	Budget Estimate To Congress	House Allowance	Senate Allowance	Appropriation
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	102,389,000	105,000,000	97,342,000
1971	99,219,000	102,249,000	102,749,000	102,368,000
1972	99,342,000	106,662,000	112,979,000	109,117,500
1973	112,649,000	113,414,000	135,000,000	113,414,000 1/
1974	98,693,000	112,744,000	114,000,000	111,089,000 2/
1975	110,404,000	105,843,000 3/	122,000,000	119,452,000
1976	108,711,000	118,918,000 4/	118,918,000 4/	126,852,000 5/
1977	135,615,000	139,615,000	143,615,000	141,000,000
1978	153,442,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P. L. 93-192.

3/ Excludes R&D contracts not considered by House due to lacking authorization.

4/ Excludes fellowships and training grants--not considered due to pending legislation ($7,934,000).

5/ Includes $7,934,000 training programs authorized under Continuing Resolution.

Justification

National Institute of Allergy and Infectious Diseases

	1977 Appropriation		1978 Estimate		Increase Or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Immunology, Allergic and Immunologic Diseases	---	$37,297,000	---	$41,259,000	---	+$3,962,000
Microbiology and Infectious Diseases .	---	67,598,000	---	73,546,000	---	+ 5,948,000
Intramural Research .	480	28,398,000	480	30,440,000	---	+ 2,042,000
Direct Operations . .	93	6,622,000	90	7,111,000	-3	+ 489,000
Program Management .	48	1,085,000	48	1,086,000	---	+ 1,000
Total	621	141,000,000	618	153,442,000	-3	+12,442,000

General Statement

The mission of the National Institute of Allergy and Infectious Diseases is research on all infectious diseases and diseases of the immune system, including asthma and other allergies. The Institute funds basic studies in immunology, bacteriology, virology, parasitology, and mycology. Because these disciplines cross-cut missions of other components of NIH, NIAID-supported research often provides new knowledge fundamental to targeted efforts of Institutes oriented toward the other organ systems or specific disease entities.

In its attack on infectious and immunologic diseases, the NIAID strives to recognize and define a set of important national public health problems in these areas, whose solution would be helped by an increased research effort; to decide upon the nature and extent of federal intervention in the research process judged most likely to expedite the funding of a solution; and to support, in the long term national interest, a large body of free-ranging, problem oriented, investigator-inspired research and the appropriate research training.

Prevention of disease is a central and pervasive objective of the Institute's activities. The evidence of recent years linking infection to chronic and degenerative diseases, often mediated through induced disorders of the immune system, has reinforced the need for research to find new ways to prevent or treat virus infection. The full understanding of the immune system which forms the body's primary defense mechanism and how it can be regulated is essential if new ways are to be found to treat and prevent diseases.

Immunology, Allergic and Immunologic Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Biology of the immune system . .		$20,140,000		$22,280,000		+$2,140,000
Asthma, allergic and immunologic diseases.		13,054,000		14,441,000		+ 1,387,000
Immunogenetics and transplantation .		4,103,000		4,538,000		+ 435,000
Total. . . .		37,297,000		41,259,000		+ 3,962,000
Budget Mechanism.						
Research grants						
Regular						
Noncompeting	291	22,296,000	293	23,153,000	+2	+ 857,000
Competing. .	106	7,510,000	144	11,021,000	+38	+ 3,511,000
Special						
International Centers for Medical Research . .	---	---	---	---	---	---
Research career program . . .	54	1,493,000	54	1,493,000	---	---
Subtotal .	451	31,299,000	491	35,667,000	+40	+ 4,268,000
Training programs .	105	3,098,000	96	2,592,000	-9	- 506,000
Individual .	69	899,000	68	881,000	-1	- 18,000
Institutional	36	2,199,000	28	1,711,000	-8	- 488,000
Research and development	29	2,900,000	31	3,000,000	+2	+ 100,000
Total . . .	585	37,297,000	618	41,259,000	+33	+ 3,962,000

Program Purpose

This program conducts and supports research and research training on a wide variety of diseases attributable to deficiencies or disorders in the responses of the body's complicated immune mechanisms, including allergies. In the past few years advances in research have defined the immune system as an organ system made up of the white blood cells, bone marrow, thymus, lymph nodes, spleen, and elements of the liver. This organ system is under genetic control and is the primary host defense mechanism against microbes, viruses, and other antigenic materials derived from the environment.

The major subprograms include:

1. Biology of the immune system - research concerned with the physiology, cellular composition and molecular biology of the immune system.
2. Asthma, allergic and immunologic diseases - research on mechanisms and treatment of asthma and other allergies and on disorders of the immune system as they relate to processes involved in the pathogenesis of at least some chronic respiratory, gastrointestinal, endocrine, skin, neurologic, arthritic, immunoplastic diseases.
3. Immunogenetics and transplantation - research on immunogenetic factors and processes which result in the improvement in donor-recipient matches for organ transplantation and on the genetic determinants of certain diseases linked to histocompatibility antigens.

Items of special concern included in these major subprograms are asthma and allergic disease centers, the immune system and its disorders, clinical immunology, and the serum bank which makes possible most research on tissue transplantation and genetic linkages.

Statistics show that asthma affects from 1% to 4% of the population. It is the most common chronic disease of childhood and a leading cause of school absenteeism. Estimates for direct medical care costs in 1972 were $850 million with a total socioeconomic cost of $1.3 billion. Mortality ranges from 3 to 5 thousand per year. About 17% of the population suffers from allergies. Hay fever is the most common and accounted for over 12 million physician's visits in 1974. It ranked 9th among the top 60 most common disease classifications and accounted for nearly 2% of all visits to office based physicians. Eczema and dermatitis ranked 14th and asthma 23rd.

Program Plans for 1978

The 1978 budget estimate for immunology, allergic and immunologic diseases of $41,259,000 represents an increase of $3,962,000 compared with the 1977 figure of $37,297,000. The program plans are described briefly below:

Biology of the immune system - immunology is at the threshold of understanding the function of the immune system in cellular and biochemical terms. The recognition of distinct classes of different antibodies, each with different biological roles, has opened up a new avenue to explore the immune mechanisms. There are numerous opportunities for studying the developmental history and differentiation of T ("thymus") and B ("bone marrow") cells, the chemical nature of membrane receptors, the mechanisms of suppressors and tolerance, and the biochemical nature as well as the function of the lymphokines (complex biochemical substances, produced by lymphocytes, which act to regulate various functions of the immune system components). New diagnostic tests and methods of treatment have already been derived from this better understanding and more can be expected.

Asthma, allergic and immunologic diseases - much can be done to improve diagnostic procedures in allergy. For example, further development is needed on the radioallergoabsorbent technique (RAST TEST) to measure specific antibodies of the IgE class. Opportunities for research on treatment of autoimmune diseases may stem from studies on the mechanisms that normally prevent autoimmune responses, including those collectively referred to as immunologic tolerance. In order to approach these multidiscipline problems from the basic and clinical point of views, the 16 existing asthma and allergic disease centers require expansion. A program will be undertaken to study the natural history and pathogenesis of allergy and infection in the pathogenesis of chronic respiratory tract diseases. In clinical immunology, emphasis will be placed upon immunogenetic

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influences on disease susceptibility and genetic control over the immune pathogenesis. The thrust will be the application of modern immunology to clinical medicine.

Immunogenetics and transplantation - it is not recognized that a principle genetic chromosomal region exists in all vertebrae species and this regulates a variety of important immunological functions and interactions. This major histocompatibility complex (MHC) was first identified in organ and tissue allografts because it influenced immunological rejection. Highest priorities will be given to detailed studies on the genetic organization of the MHC, the chemical nature of MHC gene products, and the mechanisms by which these products regulate the functions of MHC.

Immunological research is the most rapidly advancing field and NIAID is the major supporter of basic research in this area. It is also the sole source of Federal support for clinical research in allergy. The National Heart, Lung and Blood Institute has a role in asthma to the extent it results in chronic obstructive pulmonary disease but is not involved in the fundamental solutions to asthma as an allergic disease nor in the means for prevention or treatment of the allergic state.

Microbiology and Infectious Diseases

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Microbial biology. . . .		$39,883,000		$43,392,000		+$3,509,000
Infectious diseases. . .		12,168,000		13,238,000		+1,070,000
Disease prevention . . .		11,491,000		12,503,000		+1,012,000
Recombinant DNA technology.		4,056,000		4,413,000		+357,000
Total.		67,598,000		73,546,000		+5,948,000
Budget Mechanism:						
Research grants						
Regular						
Noncompeting	460	35,334,000	463	37,636,000	+3	+2,302,000
Competing.	166	11,689,000	214	16,211,000	+48	+4,522,000
Special						
International Center for Medical Research	4	2,400,000	4	2,400,000	---	---
Research career program	41	1,131,000	41	1,131,000	---	---
Subtotal	671	50,554,000	722	57,378,000	+51	+6,824,000
Training programs. . . .	167	4,983,000	148	3,889,000	-19	-1,094,000
Individual	112	1,457,000	109	1,390,000	-3	-67,000
Institutional.	55	3,526,000	39	2,499,000	-16	-1,027,000
Research and development contracts	121	12,061,000	123	12,279,000	+2	+218,000
Total.	959	67,598,000	993	73,546,000	+34	+5,948,000

Program Purpose

This program conducts and supports research and research training on the causes, characteristics, prevention, control and treatment of a wide variety of diseases believed to be attributable to infectious agents, including bacteria, mycoplasma, fungi, viruses, rickettsia and parasites, such as protozoa, worms and arthropods. The investigations will increase knowledge on etiology, pathogenesis, mechanisms of injury and repair, mechanism of action of drugs or biological products including those generated in the immune response to microbial agents and the host-microbial agent interaction. Such studies are fundamental to the development of new technology for diagnosis, therapy, and prevention of infectious diseases.

The major subprograms include:

1. Microbial biology - research is oriented to in vitro and in vivo investigations on microbial agents and host defense systems related to these agents.

2. Infectious diseases - includes all research in humans related to infection by microbial agents except that specifically related to prevention. Included is all clinical, epidemiological, diagnostic, and therapeutic research on the many different diseases caused by infections.
3. Disease prevention - research based on the principle that most infection should be preventable, with emphasis on vaccines, methods of chemoprophylaxis, other manipulations of the immune system, and environmental control.
4. Recombinant deoxynucleic acid (DNA) - research involving bacteriophages, bacterial plasmids, mechanisms of antibiotic resistance, recombination and integration, bacterial restriction enzymes and cell biology.

Items of special concern included in these major subprograms are hepatitis, influenza and other respiratory infections, sexually transmitted diseases, hospital associated infections, nucleic acid recombinants, tropical diseases and meningitis.

Statistics show that influenza and pneumonia rank fourth among all diseases causing death. Some 500 thousand cases of hepatitis are estimated to occur annually. Some feeling for the socioeconomic impact of infectious disease is conveyed by estimates for a few diseases such as: 14 million cases of genital herpes per year with attendant problems of neonatal infections and increased risk of cancer of the cervix; 200 thousand cases of herpes zoster annually; 1.8 million cases of gastroenteritis annually; 5% of the patients in hospitals acquire an infection after admission which complicates their treatment. There are 2.7 million gonococcal infections per year, and the appearance of penicillin resistant gonococci strains threatens to complicate and increase the cost of treatment.

Program Plans for 1978

The 1978 budget estimate for microbiology and infectious diseases of $73,546,000 represents an increase of $5,948,000 compared with the 1977 figure of $67,598,000. The program plans are described briefly below:

Microbial biology - efforts will be enhanced towards cultivation of hepatitis and other viruses not now grown in vitro as the first step towards immunization and new diagnostic technologies; for the study of the factors of viral integration and persistence as they may apply to live virus vaccines now in use or proposed; and to more rapidly pursue the knowledge required for antiviral development. Research towards a base for immunization for the gonococcus and chlamydia responsible for non-gonococcic urethritis will be accelerated. Broader support will be given to the efforts related to the diseases identified by the World Health Organization's special program on parasitic diseases.

Infectious diseases - expansion of clinical virology research for diagnostic and therapeutic research in a wide variety of viral diseases. Initiation of studies of the socioeconomic impact of infectious diseases in population subunits and development of data which can provide guidance as to the relative importance of specific entities will receive major emphasis. Controlled clinical trials on the use of interferon in treatment of chronic hepatitis will be started.

Disease prevention - expand and intensify efforts to develop and bring to field trials those viral and bacterial vaccines now known to be of importance; begin work towards improvement of the pertussis antigen for a decrease in reactionogenicity over that now available in DPT vaccines; expand efforts to explore the use of subunit vaccines; and bring into being still new vaccines for special purposes. Explore the use of chemoprophylaxis on a broader basis to prevent infections. Develop better understanding of adverse affects of vaccines and how these can be avoided.

Recombinant DNA technology - the NIAID has been assigned NIH responsibility for operation of facilities for safe work on genetic recombinants and will further

develop such facilities. It will also continue to support grants in this exciting new area of research towards realization of the benefits that are foreseen from applications of this technology. A major requirement is that of assessment of the biohazards associated with recombinants and the responsibility for this assessment is primarily within NIAID with collaboration from NCI and NIGMS for the support. NIAID is also providing safer vectors and hosts to scientists involved in this area of research.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Intramural Research.	480	$28,398,000	480	$30,440,000	---	+$2,042,000

Program Purpose

Intramural research relates directly to both of the Institute's major program areas. Scientists in laboratories and clinics in Bethesda and at the Rocky Mountain Laboratories in Hamilton, Montana perform research studies on the prevention, diagnosis and treatment of infectious and immunologic diseases. The research is multi-disciplinary and ranges from laboratory studies in basic virology and immunology to the clinical evaluation of new treatment therapies. Intramural scientists work closely with extramural staff in the development of vaccines and their testing and also provide guidance and review for other contract activities.

Program Plans for 1978

The 1978 budget estimate for Intramural Research of $30,440,000 represents an increase of $2,042,000 compared with the 1977 figure of $28,398,000. The program plans, including expected accomplishments are described below.

Research on the development of a vaccine against hepatitis will continue to be a high priority item. There are an estimated 500 thousand cases of viral hepatitis each year and prevention by vaccination would produce both economic and health benefits far in excess of the $650 million the disease is costing annually. Interferon, a naturally occurring substance in man, appears to be involved in the recovery from viral infections in animals. It has exhibited both therapeutic and prophylactic activity in animal and human studies, especially in hepatitis and some forms of herpes conjunctivitis. Studies to determine the structure of human interferon and to synthesize it are being conducted in collaboration with NIAMDD.

Other Institute scientists are working on better methods of viral diagnosis, and the development of an effective antiviral substance. Increased activity in the prevention and treatment of gastroenteritis, of which there are 1.8 million cases annually, will be pursued. Researchers will continue to explore the antigenic and immunologic determinants of resistance and recovery from parasitic diseases and also will attempt to gain a greater understanding of the structure and virulence of fungi in an effort to understand drug resistance.

Another area of concern to Intramural scientists is the field of recombinant DNA technology. Institute staff will be defining the hazards associated with this emerging field and also initiating new studies bearing on understanding the drug resistance of certain bacteria.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations . .	93	$6,622,000	90	$7,111,000	-3	+$489,000

Program Purpose

Scientific and administrative staff, working closely with advisory groups, develop and administer Institute extramural programs in grants and contracts. The Institute has organized its activities into two major program areas, Microbiology and Infectious Diseases and Immunology, Allergic and Immunologic diseases, to reflect the two major thrusts. Also included are the contracts and grants management personnel as well as those individuals concerned with the analysis and evaluation of programs.

Program Plans for 1978

The 1978 budget estimate for Direct Operations of $7,111,000 represents an increase of $489,000 compared with the 1977 figure of $6,622,000. Three administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service. The program plans are described below.

There are currently in effect approximately 150 contracts and over 1,100 grants. NIAID staff will continue to demand rigorous review of each contract and grant award through a process of dual review utilizing non-government reviewers. The recent reorganization has more clearly established the separation of program staff from the review process and introduced additional evaluative activities. Increased emphasis will be placed on identifying those projects that have either reached the end of their productive life or no longer enjoy the same priority they once did, so that the funds and efforts involved can be redirected toward new opportunities. Another area that will be reviewed is the Dollar Allocation to Program Areas (DAPA). This process allows additional funding to be made available to certain selected areas of special emphasis at the expense of other worthy but perhaps not as highly relevant grant activities. A subcommittee of the National Advisory Allergy and Infectious Disease Council is reviewing the program and, along with the Institute staff, will be making a recommendation to the Director on its continuance.

New programs in Biometry and Epidemiology and in Clinical Studies are planned for initiation in 1978. Additional demographic and other statistical information will be necessary if the Institute is to fully implement a more comprehensive program of evaluation of priorities and relevance.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.	48	$1,085,000	48	$1,086,000	--	+$1,000

Program Purpose

This program is responsible for the over-all coordination and direction of the Institute's activities. It includes policy formulation, program planning, administrative, financial and personnel management, and is responsible for conducting the affairs of the Institute in the most efficient manner. This activity provides funds for salaries and expenses for the varied functions and offices under this program.

A recent review of the state of the art of current research indicated many new research opportunities which should be addressed. Alert to these new responsibilities, the NIAID has recently undergone a reorganization to coordinate the decision-making process. This will enable the Institute to make more effective use of its present research resources and will greatly enhance the transfer of new technology from the research laboratory to patient care.

Program Plans for 1978

The 1978 budget estimate for Program Management of $1,086,000 represents an increase of $1,000 compared with the 1977 figure of $1,085,000. The program plans are described below.

The reorganization of the Institute to a program basis implemented in 1977 will be closely monitored to insure continued efficiency. New and innovative methods will be initiated to achieve even greater efficiency. The administrative management activity will be studied and improved to effect greater efficiency in operation. Information dissemination will be stressed in an effort to relay the results of recent research to physicians, scientists, and the general public. Program planning and evaluation activities will continue assessment of the state of ongoing research in allergic and infectious diseases, and in conjunction with Institute scientists, formulate plans and future directions for Institute supported research.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Immunology, Allergic and Immunologic Diseases (PHS Act, Title IV, Parts D and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$37,297,000	Indefinite	---	$41,259,000

Purpose: This program conducts and supports research and research training on a wide variety of diseases attributable to deficiencies or disorders in the responses of the body's complicated immune mechanisms, including allergies.

Explanation: The program accomplishes its objectives through a carefully considered mix of activities supported by selected research project and center grants, training awards, and, where the state of the art permits, Federally initiated subprograms, principally of coordinated contract activities.

Accomplishments in 1977: The NIAID Asthma and Allergic Diseases Program has encouraged application of basic data to important aspects of diagnosis and treatment including: (a) development and standardization of broncho-provocation inhalation tests for monitoring allergic asthma, (b) improved methods for isolation and purification of specific allergenic components in respiratory tract disorders and severe insect sting reactions, (c) sensitive laboratory diagnostic techniques utilizing small blood samples, (d) development of chemically modified allergens for immunotherapy, and (e) evaluation of pharmacologic preparations bypassing side effects of conventional cortisone derivatives.

Among contributions of the Clinical Immunology and Immunopathology programs have been: (a) demonstrations of interactions of viruses and chemicals with components of host cell membranes clarifying autoimmune phenomena, (b) definition of functional units of the immune system making possible genetic counseling, antepartum diagnosis and immunologic reconstitution by bone marrow and thymus transplants, and (c) information on the biology and chemistry of the complement system applicable to diminishing the inflammatory components of glomerulonephritis, vasculitis, and rheumatoid arthritis.

Research support under this activity included 451 research grants at an average cost of $70,000; 105 training awards for $3,098,000; and 29 contracts at an average cost of $100,000.

Objectives for 1978: Grant support will be given to studies in the broad field of fundamental immunology and, through centers, for the transfer of this knowledge to clinical research. Specific objectives will be reached by targeted contract activities related to transplantation biology, immunology and reagent materials. Every effort will be made to continue funding the highest quality fundamental and developmental studies of the immune response system. These studies are not only relevant to understanding the ways in which the body is protected; but also the mechanisms by which many diseases, such as cancer, heart and kidney disease, are produced.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Microbiology and Infectious Diseases (PHS Act, Title IV, Parts D and I)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$67,598,000	Indefinite	---	$73,546,000

Purpose: This program is intended to permit the conduct and support of research and appropriate research training on the causes, characteristics, prevention, control and treatment of a wide variety of diseases believed to be attributable to infectious agents (including bacteria, mycoplasma, fungi, viruses, rickettsia and parasites, such as protozoa, worms and arthropods).

Explanation: The program accomplishes its objectives through a carefully considered mix of activities supported by research project and center grants, training awards, and, where the state of the art permits, Federally initiated subprograms, principally of coordinated contract activities.

Accomplishments in 1977: Microbial biology research was significantly increased in 1977. Research efforts were concentrated in the areas of virology, mycotic diseases, parasitic diseases and sexually transmitted diseases. Intensive study of the structure, antigenic composition and determinants of virulence of the gonococcus has led to recognition of differing serotypes with differing human virulence.

Major emphasis was given to the virus diseases, including the respiratory viruses, viral hepatitis, gastroenteritis and herpes. Extensive studies on interferon, a naturally occurring antiviral in man, have been carried out. The NIAID focused on vaccine development and improvement as one of its major thrusts in the area of disease prevention.

The NIAID was assigned responsibility to develop a safer vector and host system for research involving E. coli host systems. Renovations of a facility for biohazard containment in which to perform DNA recombinant research was begun.

Research support under this activity included 671 research grants at an average cost of $75,000; 167 training awards for $4,983,000; and 121 contracts at an average cost of $100,000.

Objectives for 1978: In venereal diseases there will be continuing emphasis on the sero typing, antigenic structure and mechanisms of venereal disease production. Work on the nongonorrheal - nontreponemal forms of disease will be expanded.

Agreement on the potential hazards of recombinant DNA research and the limited availability of safer hosts and vectors for genetic material should permit acceleration of this field of research which has large ultimate potential for practical benefits in medicine and agriculture.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Intramural Research (PHS Act, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
480	$28,398,000	Indefinite	480	$30,440,000

Purpose: This program activity supports the work of scientists and physicians engaged in research on the prevention, diagnosis and treatment of immunologic and infectious diseases.

Explanation: Funds provided for this activity finance salaries, equipment, supplies and operating costs for Institute personnel and also provide a proportionate share of centrally furnished services.

Accomplishments in 1977: Information on the potential hazards of recombinant DNA molecules was gained. A vaccine for hepatitis B is ready for clinical trial and one for infantile diarrhea is being developed. Other significant developments have occurred in malarial research and the identification of different serotypes of some fungi which may help explain differences in virulence and drug resistance.

Objectives for 1978: Studies will concentrate on gastroenteritis, respiratory illnesses, and basic virologic and parasitic disorders. Research on the immune system and on recombinant DNA molecules will also be emphasized.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Direct Operations (PHS Act, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
93	$6,622,000	Indefinite	90	$7,111,000

Purpose: Personnel funded under this program administer the extramural research programs of the Institute. This includes the handling of 150 active contracts and over 2,000 grant applications.

Explanation: Applications are received by the Division of Research Grants and referred to program officials for review and processing. Awards are made on the basis of Study Section priority scores and program relevance.

Accomplishments in 1977: Scientific and administrative support was given to approximately 1,122 research grants, 564 trainees, and 150 research and development contracts in the various fields of research related to the Institute's mission.

Objectives for 1978: Scientific and administrative staff will continue to develop, administer, and advise on extramural programs of grants and contracts including an estimated 358 new or competing grants, 56 new individual training awards, and 21 new contracts.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Program Management (PHS Act, Title IV, Part D)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
48	$1,085,000	Indefinite	48	$1,086,000

Purpose: This program provides direction and coordination of all Institute activities. The Director, Deputy Director and Associate Directors, as well as their immediate staffs and central management positions are included.

Explanation: Funds provided under this program are used for salaries and associated expenses.

Accomplishments in 1977: The Institute reorganized its management structure and improved its priority setting apparatus. Information activities were increased both to the general public and the practicing physician.

Objectives for 1978: During 1978 Program Management staff will concentrate on refining the review and evaluation procedures established in 1977. Individuals and groups outside of the Institute will be drawn into the advisory process in a more significant way. The process by which on going projects are re-evaluated will be reviewed and improved.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

Program Purpose and Accomplishments

Activity: Direct Operations (PHS Act, Title IV, Part D)

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WEDNESDAY, MARCH 9, 1977.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

WITNESSES

DR. NORMAN KRETCHMER, DIRECTOR
DR. DONALD FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JAMES B. SIDBURY, DIRECTOR, INTRAMURAL RESEARCH PROGRAMS, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
JOEL R. HEDETNIEMI, EXECUTIVE OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
ARTHUR D. FRIED, BUDGET OFFICER, NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
NORMAN MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN F. WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now we will hear from the National Institute of Child Health and Human Development.

This presentation will be made by Dr. Norman Kretchmer, who is the Director.

We have your biographical sketch, Doctor, which we will place in the record at this point.

[The sketch follows:]

NORMAN KRETCHMER, M.D., PH. D.

Date and Place of Birth: January 20, 1923, New York City.
Residence: 8 North Drive, Bethesda, Md. 20014.
Married, 3 children, Social Security Number: 090–14–1489.

EDUCATION

1940–44, Cornell University, B.S., animal physiology; 1944–47, University of Minnesota, M.S. (1945), physiological chemistry; Ph. D. (1947), physiological chemistry; 1948–52, State University of New York, College of Medicine, New York City, M.D.

FELLOWSHIPS AND HONORS

1952–53, Commonwealth Fund Fellow, Montefiore Hospital.
1955–56, Henry L. Moses Alumni Prize in Basic Research, Montefiore Hospital.
1957, Commonwealth Fund Traveling Fellowship, St. Mary's Hospital, London and University of Paris.
1958, E. Mead Johnson Award for Research in Pediatrics, American Academy of Pediatrics.
1965, Alpha Omega Alpha (Faculty).
1965, Honorary Member, Faculty of Medicine, University of Chile.
1965–66, Commonwealth Fund Fellow, Atomic Energy Laboratory, Saclay, Paris.
1969, Alumni Medallion for Distinguished Service to American Medicine, College of Medicine, Downstate Medical Center, New York.
1969, Borden Award, American Academy of Pediatrics.
1971–76, Harold K. Faber, Professor of Pediatrics, Stanford University.
1973–74, Guggenheim Fellowship in Human Development.
1975, Honorary Degree, Doctor of Science, Medical College of Ohio at Toledo.

POSITIONS

1944–47, Teaching Assistant and Junior Scientist, University of Minnesota.
1947–48, Assistant Professor of Pathology and Biochemistry, University of Vermont.
1948–52, Fellow and Research Associate of Pathology, Long Island College of Medicine.
1950–55, Lecturer of Biology, Brooklyn College.
1953–56, Assistant Professor of Biochemistry in Pediatrics, Cornell University.
1956–58, Assistant Professor of Pediatrics, Cornell University.
1958–59, Associate Professor of Pediatrics, Cornell University.
1959–69, Professor and Executive Head, Pediatrics, Stanford University.
1969–72, Chief, Division of Developmental Biology, Stanford University.
1969–72, Chairman, Program in Human Biology, Stanford University.
1969–74, Professor of Pediatrics, Stanford University.
1970, Visiting Professor, University of Lagos, Lagos, Nigeria.
1972, Chief, Section of Developmental Medicine, Stanford University.
1974, Clinical Professor of Pediatrics, Howard University.
1974, Consultant/Lecturer, National Naval Medical Center, Bethesda, Md.
1974–75, Acting Director, National Institute on Aging, Bethesda, Md.
1974, Director, National Institute of Child Health and Human Development, Bethesda, Md.

CLINICAL TRAINING AND APPOINTMENTS

1952–53, Intern, Montefiore Hospital, New York City.
1953–55, Assistant Resident, Pediatrics (6 months/year), New York Hospital.
1953–54, Assistant Pediatrician to Outpatients, New York Hospital.
1954–55, Pediatrician to Outpatients, New York Hospital.
1955–59, Assistant Attending Pediatrician to Outpatients, New York Hospital.
1959–69, Physician-in-Chief, Pediatrics, Stanford University Hospital.
1969–76, Pediatrician, Stanford University Hospital.
Military service: 1942–43, air student, U.S. Air Force; 1968–71, pilot, Civil Air Patrol.

MEMBERSHIPS AND APPOINTMENTS

1960–63, Ross Laboratory Research Award Committee, Western Society for Pediatric Research.
1960–64, Special Consultant, National Institute of Arthritis and Metabolic Diseases, Hematology Training Committee, U.S.P.H.S.
1960–64, Member, Scientific Advisory Board, National Cystic Fibrosis Research Foundation.
1961–67, Member, Advisory Committee, Maternal and Child Health Bureau, State of California.
1962–65, Consultant, U.S. Naval Hospital, Oakland, Calif.
1962–66, Member, Medical Advisory Board, Foundation for International Child Health.
1963, Member, Medical Advisory Board, San Francisco Chapter, National Foundation.
1964–68, Member, Medical Advisory Council, Food and Drug Administration.
1964–67, Member, Committee on Medical Education, American Academy of Pediatrics Chairmen, District X.
1964–68, Member, Study Section on Human Embryology and Development, U.S.P.H.S.
1965, Chairman, Delegation on Developmental Physiology, U.S.S.R., for the Department of Health, Education and Welfare.
1965–66, Medecin Attache, U.S. Embassy, Paris, Office of International Research—NIH.
1966–71, Chairman, Medical Advisory Board, Foundation for International Child Health.
1967–68, Member, Panel 15, Committee on Research in the Life Sciences, National Academy of Sciences.
1967–69, Special Consultant, World Health Organization.
1967–68, Member, Joint Council of National Pediatric Societies.
1969–71, Board of Scientific Counselors, NICHD, National Institutes of Health.
1970–73, Committee on Undergraduate Studies, Stanford University.

1971–74, Perinatal Biology and Infant Mortality Research and Training Committee, NICHD, NIH.
1971–74, Chairman, Scientific Advisory Board, Fels Institute for Human Development, Yellow Springs, Ohio.
1974, Member, Executive Committee, International Pediatric Association.
1974, Member, Scientific Council, Institut de la Vie, Paris.
1974, Consultant, Office of the Director, NIH.
1974, Temporary Advisor, Maternal and Child Health, World Health Organization, Geneva.
1974, Member of the Board, U.S.A.-Israel Science Foundation.

EDITORIAL BOARD MEMBERSHIPS

1958–64, Pediatrics; 1959–63, Annales Pediatrici—Editor; 1961, Biologia Neonatorum, Excerpta Medica, Human Development Biology, 21st Edition, Stanford Medical Bulletin, Advisory Board; 1967–75, Advances in Pediatrics; 1971, Archives de Pediatrie; 1971, Monographs in Pediatrics, Basel, Switzerland; and 1973, Editor, Series in Clinical Pediatrics, John Wiley & Sons.

SOCIETY MEMBERSHIPS

American Academy of Pediatrics (Fellow).
American Association for the Advancement of Science (Fellow–1963).
American Association of University Professors.
American Board of Pediatrics (Licentiate–1957).
American Chemical Society.
American Institute of Biological Sciences.
American Pediatric Society.
American Society for Biological Chemists.
American Society for Clinical Investigation (Member of Council 1964–67).
American Society for Clinical Nutrition.
American Society for Human Genetics.
Association of American Medical Colleges.
Harvey Society.
Histochemical Society.
International Organization for the Study of Human Development (President 1970–76).
International Pediatric Association (Member, Executive Committee 1974–77).
Perinatal Research Society.
Salt and Water Club.
Sigma Xi.
Society of Growth and Development.
Society for Pediatric Research (President 1967–68).
Western Society for Clinical Research.
Western Society for Pediatric Research (President 1966–67).

HONORARY MEMBERSHIPS IN SOCIETIES

Chilean Society of Biology, Chilean Society of Endocrinology, Chilean Pediatric Society, Czechoslovakian Society of Pediatrics, Finnish Pediatric Association, Italian Pediatric Society, Nigerian Pediatric Society, Societe Francaise de Pediatrie de Paris, Argentine Pediatric Society, and Dominican Pediatric Society.

Mr. FLOOD. Also we will place in the record your statement which we have.

[The statement follows:]

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

National Institutes of Health

National Institute of Child Health and Human Development

Statement of the Director

Mr. Chairman and members of the Committee:

The National Institute of Child Health and Human Development is dedicated to the principle that the early phase of the human life cycle offers exceptional opportunities for the prevention of diseases, disorders and social and psychologic handicaps that may affect the individual at any time during the life span. The mission of the NICHD is to seek early opportunities for prevention of disease and disability.

The NICHD fosters a steady expansion of useful knowledge about child and maternal health and disease, human development, fertility regulation and the many health-related factors of a diverse and dynamic population. In addition, the NICHD serves as the scientific focal point for federal agencies concerned with improved health for mothers and children and with family planning.

Progress Report

The NICHD has considerable progress to report since last year:

The Institute is proceeding with its plan to establish a series of Major Research Programs, each concerned with a critical problem or disorder of pregnancy, infancy or early childhood. This concept has been received with enthusiasm by the scientific community. Over 250 inquiries have been received from teams of investigators all over the country. We anticipate that current funds will allow us to establish at least one Major Research Program on the prevention of

prematurity and two more dealing with diabetes in pregnancy.

The promised major initiative on adolescent pregnancy is now under way. The NICHD has been appointed lead agency on adolescent pregnancy for the Public Health Service and has planned conferences, devised a plan for interagency and inter-Institute coordination and encouraged the submission of grant and contract proposals. NICHD-supported investigations will concentrate on social and behavioral influences on teenage sexual activity and contraceptive use, on factors affecting the pregnant teenagers' decisions on abortion and childrearing, and on the impact of early childbearing on the parents and the extended family.

I would like to describe a few representative examples of NICHD research advances which contribute to the health of persons of all ages.

High-Risk Pregnancy and Infant Death

NICHD-supported studies on the premature infant and initiation of labor in the mother may lead to the prevention of low birth weight. One NICHD-supported investigator has succeeded in identifying a specific population of women who have a 40% risk of recurrent premature delivery.

Investigators using animal models of human pregnancy have shown that many drugs currently used in hospitals to prevent premature birth may also endanger the fetus by interfering with its supply of oxygen and other vital substances. A search is now under way for drugs which will stop uterine contractions in the mother with minimal dangerous side effects on the fetus.

Nutritional, behavioral and biochemical studies supported by the NICHD have improved life prospects for premature infants and other infants at risk. Recent work has shown that the amino acid nutrients taurine and cystine are essential for premature infants, and should be included in the formulae used in intravenous feeding. Another study has shown that premature infants and infants of diabetic mothers are better able to regulate their blood sugar levels and take in adequate calories when their formula contains the normal breast milk sugar galactose in addition to glucose.

Studies have shown that premature infants have fewer lapses of breathing when placed on a gently oscillating water bed shortly after birth. It is thought that the motion of the water bed mimics the motion of the fluid environment in the mother's womb, and thus eases the infant's transition into life outside the womb.

Biochemical studies have laid the groundwork for further advances in the prevention of respiratory distress syndrome (or hyaline membrane disease), a disorder which has always been the major killer of premature infants. As a result of NICHD-supported research, the mechanisms which control the production of surfactant, a substance necessary for normal lung function, have now been described in detail. Hormones of the adrenal gland have been shown to stimulate production of this surfactant when administered to animal fetuses in utero, thus hastening maturation of the lung and preventing respiratory distress after birth. This preventive approach is now being tested, by others, on human subjects.

The NICHD funds more than 100 studies on sudden infant death syndrome (SIDS). They have shown that no single mechanism is responsible for SIDS and that victims of the syndrome suffer from subtle problems of the nervous system that contribute to failure of the heart and lung under stress. The stress which eventually brings about death may be as mild as a common cold.

Studies of so-called "near miss" babies who have survived one or more prolonged lapses of breathing indicate that these infants exhibit abnormalities in their brain waves during sleep and that they continue to have many brief lapses of breathing detectable by means of a breathing monitor. Other preliminary studies have revealed several cases of infants who exhibited abnormal cry patterns in their first few weeks of life and later died of SIDS. These findings, if supported by further research, might provide several simple means for early identification of infants at risk for SIDS.

Infants born to diabetic mothers are another group at high risk of death and disability. These infants have a high rate of newborn mortality and congenital anomalies; they often exhibit excessive growth in the womb followed in many cases by birth injuries and dangerously low blood sugar in the first weeks of life.

Investigators in the Intramural Program of the NICHD are acutely conscious of the ethical problems involved in using pregnant women as subjects for the study of diabetic pregnancy. Therefore, they have chosen to concentrate on the development of suitable animal models. One model is a pregnant Rhesus monkey which has been pretreated with

drugs to give it a high blood sugar level comparable to that of the diabetic human. Studies of these animals have shown that high blood sugar in the mother inappropriately triggers certain hormones in the fetus--hormones which wouldn't ordinarily appear until after birth. Information from these studies can be applied directly to the human diabetic pregnancy and will result in advances in diagnosis and therapy.

Congenital Malformations and Genetic Disorders

Some of the most important research advances under NICHD sponsorship in the past year are in the area of birth defects. One investigator has shown that cytomegalovirus (CMV), an infectious agent known to occur with fairly high frequency in newborn infants, can be transmitted to the fetus from the birth canal of the mother during the birth process. Cytomegalovirus infections acquired from an infected mother before or during birth may be a far greater hazard to the infant than has been previously realized. It is now believed that from 3.5 to 7 percent of newborn infants may be at high risk of suffering losses in eyesight or hearing due to this infection. Recognition of the serious nature of the problem may lead to early diagnosis and treatment as well as prevention of educational and behavioral problems later in life.

Other studies supported by the NICHD have begun to illuminate the nebulous area of genetic susceptibility to birth defects. For years it has been known that environmental agents and genetic background somehow work together to determine an individual's chances of being born with a birth defect. The mechanisms responsible for this interaction of gene and environment are only now becoming known. Basic research in molecular biology has shown that there are certain protein molecules

called receptors within the mammalian cell. They combine with hormones, drugs, and other substances which enter the cell from outside. Once these foreign substances are bound by receptors they can trigger the action of certain genes which then determine whether the cell will undergo normal or abnormal development. Thus, we may soon be able to determine the exact molecular basis for certain congenital malformations. Another NICHD scientist has shown that in certain laboratory animals and also in man, susceptibility to poisonous agents in the environment is determined by a single genetic locus which codes for an enzyme involved in metabolizing poisonous compounds. This enzyme, acting in concert with recently identified receptors, determines whether poisonous substances entering the cell will be able to trigger the activity of the gene. It appears likely that this receptor system may determine which individuals are most susceptible to environmental toxins, birth defects, degenerative diseases such as cancer, and drug overdose. It may be possible in the future to identify children at high risk for these disorders.

Another NICHD breakthrough has been the transfer of the genes for the manufacture, production, and synthesis of hemoglobin and other proteins from the mouse to the bacterium E. coli by means of DNA recombinant techniques. Such research may eventually permit mass production in bacterial culture of vital biologic products such as human insulin and human growth hormone.

A significant advance relevant to genetic counseling and the prenatal diagnosis of genetic disorders occurred when NICHD-supported

investigators discovered a means of detecting cystic fibrosis using cells grown in tissue culture. Cystic fibrosis is one of the most common genetic diseases of Caucasian populations and is invariably fatal. A reliable screening procedure would be a step to prevention and early treatment of this disorder.

Fertility, Infertility and Family Planning

In addition to all of its studies directed at the health of pregnant women, fetuses, infants and children, the NICHD conducts a massive and vigorous program in reproductive biology and population studies.

NICHD-supported investigators have recently achieved a major advancement with the discovery of a long-sought hormonal substance called "inhibin," which appears capable of indirectly suppressing sperm production. Inhibin is expected to provide the key to the alleviation of certain types of male infertility and to the development of new contraceptives for the male.

Animal studies currently in progress have identified new compounds which may prove useful as ovulation inhibitors. Additional studies on natural steroids show the promise of formulating a safer oral contraceptive. The need for continued evaluation of contraceptive safety and development of alternatives is indicated by studies which have shown an association between the use of current oral contraceptives and cancer of the skin, cancer of the cervix and non-cancerous tumors of the liver. Further studies are under way to

determine the risk of heart disease among women on oral contraceptives, the factors underlying oral-contraceptive-induced high blood pressure and vascular disease, the risk of complications of intrauterine devices, and the long-term physiological and psychological effects of vasectomy and tubal ligation.

Investigations into the mechanisms of reproduction and fertility regulation are supplemented by behavioral and demographic studies aimed at understanding the factors that influence childbearing decisions and the effects these decisions have on children, their families and the population as a whole. Recent behavioral studies have shown that birth order plays a large role in determining the amount of attention an infant receives. First-born children enjoy a considerable advantage over other siblings and last-born children experience a disadvantage. These differences in parental attention are reflected in differences in learning ability which can be detected as early as three months of age.

In studies aimed at determining the causes and effects of changes in the overall fertility rate of the population, NICHD-supported investigators are seeking to devise theoretical models to explain how couples' decisions regarding family size are influenced by income and working wives.

Developmental Disabilities

The mental retardation program of the NICHD has achieved significant results in both postnatal and prenatal prevention of mental retardation. NICHD-supported investigators have shown that disadvantaged mothers,

whose children are at high risk for mental subnormality, can be taught to provide adequate stimulation for their children, thus substantially reducing the risk of retardation. The preventive implications of this study are enormous, for it is estimated that there are more than 3 million retarded persons in the United States whose handicap derives from behavioral deprivation in early childhood.

Other studies have shown that intermittent or daily alcohol abuse by a pregnant woman can cause brain malformation and subsequent mental retardation in her infant. This problem, called the fetal alcohol syndrome, can serve as a very specific model for detailed study of the role of environmental agents in the causation of mental retardation.

Learning disorders are another group of problems of early childhood of interest to the Institute.

The term developmental dyslexia is commonly used to refer to a reading disability that cannot be clearly attributed to a deficiency in intelligence, motivation, eyesight or any other factor known to be required for reading achievement. Useful as the term "dyslexia" has proven to be, there is growing concern among parents and educators that mere labeling of problem readers eclipses work in diagnosis and therapy. The NICHD is responding to this concern through a two-pronged research effort aimed at (1) developing accurate, standardized criteria for the diagnosis of dyslexia, and (2) determining the exact sequence of steps involved in the acquisition of reading skills. Research of this sort, combined with more refined methods of diagnosis, may enable us

to identify specific subgroups of dyslexic children blocked at specific stages of the reading process and to devise specific therapies applicable to each subgroup.

Prevention of Adult Disease

The NICHD supports many nutritional studies aimed at determining the long-term effects of undernutrition and overnutrition in infancy and early childhood. A major advance in understanding the link between childhood and adult obesity occurred recently when investigators discovered that nutritional intake determines the total number of fat cells in the body at a period early in development. This finding suggests that early dietary management can decrease the severity and prevalence of adult obesity. Other studies are planned to determine the effect of dietary factors in childhood on individuals who are genetically susceptible to such disorders as diabetes, hypertension and atherosclerosis.

Conclusion

Because the early phase of the life cycle, from conception through adolescence, is the period which offers maximum opportunity for the prevention of disease and disability, the NICHD has made a systematic effort to identify problem areas in which increased scientific investment is certain to lead to advances in preventive medicine.

This statement has dealt with research accomplishments in those areas which will be the foci of our endeavors in 1978. The health problems selected are ones which have an intense impact on the population, including children and adults. It would be impossible to estimate their

net cost to the nation, but incomplete figures currently available suggest that the benefits derived from early treatment, prevention or alleviation could be enormous. The NICHD believes that research on these problems must be pursued with maximum vigor until clinical solutions can be transmitted to other federal agencies and to the medical community for incorporation into our health care system.

Mr. Chairman, the NICHD requests $155,761,000 for 1978. I would be pleased to answer any questions and to furnish any additional information for the record that the Committee desires.

Mr. FLOOD. Do you have some people with you that you would like me to meet?

Dr. KRETCHMER. To my right is Dr. James Sidbury, who is the Director of the Intramural Research Programs of the Institute. To my immediate left, Mr. Joel Hedetniemi, the Executive Officer, and to my far left Mr. Arthur Fried, the Budget Officer.

INCREASES FOR ALTERNATIVES TO ABORTION

Mr. FLOOD. Doctor, your budget proposes an overall increase of $10 million over the 1977 level. I understand $5 million of that increase is for the Department's alternatives to abortion strategy.

How do you plan to spend that particular $5 million? What particular kind of research activities? Population research? Research on mothers and children or what?

Dr. KRETCHMER. Both, as a matter of fact. The definition of alternatives to abortions was stated in Mr. Califano's remarks at the press briefing on President Carter's budget amendments. Alternatives to abortion would include not only family planning, but also studies of reproductive processes, as well as problems of prenatal development.

This approach could lead to the development of a new field called fetal medicine. Thus, we are distributing the $5 million over those program areas defined broadly as reproductive biology and research related to pregnancy and antenatal problems.

1978 BUDGET INCREASE

Mr. FLOOD. Now, you have told us how you intend to spend that $5 million. Would you now tell us how you intend to spend the second $5 million? That total increase is $10 million in 1978.

Dr. KRETCHMER. Yes, sir.

The $10 million is distributed as you might expect over the Institute's two major programs. Research for mothers and children would receive about 60 percent and population research about 40 percent of the $10 million. These amounts include a small increase going into the intramural program. With regard to special problems of mothers and children, the bulk of the money would go to high risk pregnancy, congenital malformations, and nutrition.

The bulk of the money going into population research would go in the area of research on reproductive processes for both male and female.

ADOLESCENT PREGNANCY

Mr. FLOOD. What is the extent of the current research now going on aimed at reducing the incidence of teenage pregnancy?

Dr. KRETCHMER. The problem of adolescent pregnancy, as you know——

Mr. FLOOD. What kind of projects do you have? How many dollars?

Dr. KRETCHMER. The amount of money is currently very small. It is about $500,000 which we intend to expand in 1978.

The principal approach to adolescent pregnancy is really two-pronged. One is the study of the physiology of the pregnant adolescent, and the other is in studies of social and behavioral science.

The National Institute of Child Health and Human Development has responsibility for a variety of behavioral science research. We believe that we will learn most about teenage pregnancy from the behavior of the teenager and particularly the early teenager. This group is of critical concern.

Mr. FLOOD. Maybe I should ask you this: Is this problem of teenage pregnancy now—is this actually a research problem or should we take that $5 million you have in the budget for this and increase the budget for the Health Services Administration for their programs in order to provide the teenager with family planning services, medical care?

Dr. KRETCHMER. Mr. Chairman, I don't think you can disassociate the one from the other.

On the one hand, there is a good deal of research activity needed. The research activity would be into aspects of the high risk of this kind of pregnancy and in what we would call motivational research. This research would then interface with the activities of the Health Services Administration and particularly the Bureau of Community Health Services in regard to how they would then deliver the results of this research to the public; in this case, to the teenager.

I am using the wrong word; it is not the teenager, but rather the early adolescent. The women below the age of 17 are our major concern for high risk pregnancy.

Ms. WORMSER. I would like to add to the answer to your question, Mr. Chairman.

There are other programs aimed at the health services objectives—$10 million in the family planning program; $14 million which has been proposed to be added to the community health center program; and $4 million to the Center for Disease Control and its health education program. The service and the education aspects would be carried out through those programs and the research through this one.

Mr. FLOOD. You have been doing your homework.

EFFECTS OF CONTRACEPTIVE DRUGS ON ADOLESCENT GIRLS

Is sufficient information available to the medical community about the effects of the contraceptive drugs on the adolescent girls?

Dr. KRETCHMER. Yes; there is information available and the mechanisms for that information——

Mr. FLOOD. Are these girls exposed to special risks now in using these contraceptives?

Dr. KRETCHMER. Insofar as we know, they are not exposed to any greater risks than any other woman using a contraceptive drug. These are the kinds of studies we support.

Mr. FLOOD. Is the information available to the medical community?

Dr. KRETCHMER. Absolutely. It is also widely available to the public through a variety of mechanisms. For example, it is available through newspapers, through open meetings, and through pamphlets from this Institute and other agencies of the Public Health Service.

If I may add one thing: The Deputy Assistant Secretary for Population Affairs has brought together an interagency group concerned with research in this particular area. The NICHD is the lead agency for the group, which also includes the National Science Foundation, Agency for International Development, and the Bureau of the Census.

CONTRACEPTIVE EVALUATION AND SAFETY

Mr. FLOOD. How much are you going to spend in 1977 and 1978 to evaluate the safety of all these contraceptive drugs and the devices too?

Dr. KRETCHMER. Approximately $5.2 million in 1977 and $5.4 million in 1978.

Mr. FLOOD. Do you think that is adequate in the light of all this great concern now that many people have about the possible relationship between the oral contraceptives and possible cancer and heart attacks and other things?

Dr. KRETCHMER. We are utilizing this money to examine as carefully as we can the problems related to oral contraceptives, as well as contraceptive devices and this money is being used to support the most superior research.

We certainly have produced data with the amount of money spent previously.

Mr. FLOOD. Do you think what you have is adequate?

Dr. KRETCHMER. To answer your question, I would have to say we have other studies we could find if there were more money available.

Mr. FLOOD. Your budget calls for $50 million for population research. Why are you only investing $5 million for contraceptive evaluation?

Dr. KRETCHMER. We invest $5 million for contraceptive evaluation and another approximately $10 million for contraceptive development and behavioral studies.

Most of the money, about $35 million, is being spent for population research, for what we call basic studies in reproductive biology. The answer to the development of new contraceptive agents or new approaches to the ability to regulate female as well as male fertility will be derived from these basic studies.

The other money, for contraceptive development, safety, and behavioral sciences, is money invested for more immediate results.

Mr. FLOOD. Briefly outline your plan and for the record develop it as you like for fiscal 1977, for fiscal 1978, for contraceptive evaluation. That is quite a question. You may want to do that for the record.

Dr. KRETCHMER. I will be glad to supply it.

Mr. FLOOD. Fiscal 1977 and 1978 now.

Dr. KRETCHMER. I had better supply it for the record.

CONTRACEPTIVE EVALUATION PLAN FOR 1977 and 1978

The program in contraceptive evaluation will continue in FY 1977 and 1978 to direct its efforts to the evaluation of the safety of fertility regulating methods which are currently in use particularly with respect to long-term safety. The emphasis is on the enumeration of hazards associated with contraceptive use and the identification of risk factors, which should provide a rational basis for counseling individuals at special risk to use methods of contraception which are less hazardous to them. In FY 1977 funding for contraceptive evaluation is estimated at $5,195,000. In FY 1978, $5,385,000 is requested which represents an increase of $190,000.

The ultimate goal of this research effort is the prevention of health hazards associated with various methods of contraception. This is to be achieved through improvements in the safety of methods of contraception and fertility regulation. Specifically, the program's aims are: a) to define precisely the risks associated with the use of methods of contraception and fertility regulation currently in use as well as those under development; b) to identify subpopulations of users who are especially vulnerable to the hazards of particular methods; and c) to develop new knowledge leading to the understanding of the mechanisms by which adverse medical effects come about.

Specific research projects will be continued or newly developed in FY 1977 and 1978. Examples of these are described below:

Contraceptive Steroids

1. Research on the risk of myocardial infarction among women on contraceptive steroids in relation to dose, duration of use and other risk factors like obesity, hypertension, diabetes, age, smoking, abnormalties in lipid metabolism and stress will be continued.

2. Factors associated with oral-contraceptive-induced hypertension, its natural history, reversibility and response to therapy will continue to be studied.

3. Ongoing research concerned with the risks of liver adenoma, cancer, and cardiovascular effects among oral contraceptive users will proceed.

4. Cancer of the breast and of the reproductive organs, or of other organ sites, is the most important unresolved hazard among women on contraceptive steroids. Most previous studies have revealed no risk. It is known, however, that cancer does not occur until a decade or more after exposure to a hazardous compound. With the widespread use of oral contraceptive steroids commencing in this country around 1965 it is timely now to research extensively the relationship between oral contraceptives and cancer.

5. Contraceptive steroids result in abnormal carbohydrate metabolism. It is not known whether contraceptive steroids increase the risk of diabetes. A case-contol study is projected to answer this question.

6. Some women who discontinue contraceptive steroids experience prolonged secondary amenorrhea. There is suspicion that the recent increase in pituitary adenoma may be related to contraceptive steroids. The relationship between contraceptive steroids and pituitary adenoma in women with secondary amenorrhea will be studied.

7. The pill affects risk factors of vascular disease. A delayed effect of pill exposure may be premature atherosclerosis. Two research strategies are proposed. One will make use of an ongoing longitudinal

follow-up study of women on contraceptive steroids. Another will make use of the case-control design. Furthermore, the postulated relationship between exposure to contraceptive steroids and malignant pulmonary hypertension will be studied.

8. The risk of thromboembolism is increased when a higher estrogen dose is used, which was common before 1970. Low dose estrogen preparations are now available. The relative risk of thromboembolism and of other complications for these will be assessed.

9. Little progress has been made in understanding the mechanisms of certain adverse effects among pill users. Certain metabolites of contraceptive steroids accumulate during the pill cycle and may do so at a different rate in some women. Currently women are given the same dose with no consideration to factors which could affect their ability to metabolize the contraceptive steroids. Research will be initiated to determine whether these and other aspects are related to the risk of certain complications among pill users. Leads to understand the possible mechanism of thromboembolism will also be thoroughly explored.

10. Research on the adverse effect of contraceptive steroids on other systems and organs will be initiated.

11. Studies will be developed of the specific effects of estrogens and certain progestins on target tissues in certain organs, including binding to hormone receptors which are not involved in the contraceptive effect.

Intrauterine Devices

1. Research will continue on the risk of complications related to intrauterine devices (IUD's) which are currently in use in the United States.

2. Studies will be developed to identify possible hazards of new IUD's.

3. Pelvic inflammatory disease among IUD users is in part caused by a fungus infection possibly unique for intrauterine devices. Techniques for the early diagnosis and management of this infection will be studied.

Abortion

To monitor risk to subsequent pregnancies after induced pregnancy termination, a continuing surveillance is necessary to assess the safety of new methods. For example, it is important to define to what extent trauma to the cervix is related to subsequent risk of premature labor.

Sterilization

1. Research will be continued on the delayed long-term effects on the health of men who have been vasectomized several years ago.

2. Studies of autoimmune disease in different animal species after vasectomy will be supported. Vasectomized males with tendency towards immunological problems will be studied extensively. Selected clinical studies of vasectomized males will be continued. It appears crucial to investigate fully the extent to which reversible vasectomy is possible.

3. Several new techniques have been introduced for tubal ligation. Their immediate complications are incompletely understood. Furthermore, an increase in menorrhagia among women with tubal ligations has been suggested. A research project to clarify these questions will be developed.

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Ms. WORMSER. I think we also should consider in this context the kind of research going on in FDA where there is considerable effort on the evaluative side of both the drugs and devices, whereas here again it is more basic research.

If I may expand upon this point.

FDA's involvement concerns the safety and effectiveness of drugs and devices, as opposed to policies regarding use, delivery, impacts, et cetera of population planning. FDA participation in population research lies primarily in sponsoring or monitoring the progress of research necessary to carry out its regulatory responsibilities relating to oral contraceptive safety. In addition the FDA maintains a reporting system which serves as a clearinghouse for information concerning adverse reactions associated with contraceptives.

Mr. OBEY. Could I suggest one thing? I apologize but I came over here in hopes that a quorum call would be later because I have to be on the floor to manage this next bill, but I do have a number of questions I would like to ask the Doctor concerning the same question asked by the chairman because I am concerned, as I think the thrust of his question was, on the adequacy of the amounts devoted to research on various birth control devices. I would appreciate it if you could answer them as specifically as possible.

Mr. FLOOD. It will be inserted at this point in the record and you will reply for the record then.

[The following questions have been submitted by Mr. Obey to be answered for the record:]

APPROPRIATIONS FOR POPULATION RESEARCH

Mr. OBEY. Your request for the Center for Population Research for fiscal year 1978 is $52,751,000. Will you please provide the appropriation for the Center each year in constant dollars since 1972.

ANSWER. Below is a table that compares CPR actual appropriations with constant dollar appropriations.

CPR APPROPRIATIONS FISCAL YEAR 1972-78

[In thousands of dollars]

	Actual	Constant [1]
Fiscal year:		
1972	$36,098	$36,098
1973	41,944	40,011
1974	39,388	35,322
1975	45,414	36,823
1976	47,823	36,246
1977 (estimate)	49,707	35,206
1978 (estimate)	52,751	35,081

[1] Constant dollars were derived by means of a biomedical Research and Development deflator.

Mr. OBEY. Does the decrease in constant dollars imply that you have the population problem under control and that there isn't that much more to be done?

ANSWER. No; a great deal more needs to be done to help resolve many population-related problems in the United States. Some of the more serious problems include the health hazards associated with various methods of fertility control; unsatisfactory control of fertility reported by millions of couples, which indicates the need to develop a variety of safe and effective methods of contraception; the continuing rise in the number of children borne by unmarried girls under age 20; and the impact of changing demographic patterns on the social and economic life of our Nation.

CONTRACEPTIVE SAFETY

Mr. OBEY. Questions have been raised recently about the safety of many of the most widely used contraceptive techniques. Will you please provide us with the data available on the number of women who cannot use the pill or the IUD or have opted to not use them because of their concern about its possible long-term effects.

ANSWER. It has been estimated that 6.7 million married women in the United States were using oral contraceptives in 1973. Survey data indicate that in 1973, 42 percent of the women who had ever used the pill had discontinued its use and that 78 percent of those discontinuing did so because they had experienced severe side effects or feared possible adverse effects. Applying these rates to the 6.7 million women using oral contraceptives in 1973, it can be estimated that at least 2.2 million women have discontinued because of side effects or anxiety about possible effects. The effect of recent questions about pill safety can only have been to increase this number by an unknown amount. If this increase is only 10 percent, an additional 670,000 women would have discontinued, and if recent concerns affected 25 percent, the additional number would be 1.7 million.

Survey data indicate that IUD's were used by about 1.8 million women in the United States in 1973. Concerns about long-term safety of these devices relate primarily to septic abortion. Publicity about this concern has abated since the Dalkon Shield was removed from the market in 1975. In 1974–75 many women had Dalkon Shields removed but we do not know how many were replaced with other types of IUD's or how many of these women may have changed to other forms of contraception. Presumably the 25 percent rate of discontinuance of IUD use generally observed 3 years after insertion was increased by patient and/or physician concern for long-term safety. An increase from 25 percent to 35 percent in the discontinuance rate would affect 180,000 women in the United States.

Mr. OBEY. Is it true that many physicians are now refraining from prescribing the pill because they do not believe that it is safe?

ANSWER. It appears from conversations with a number of physicians that they are being cautious now about prescribing the pill to women who may have risk factors for demonstrated adverse effects such as thromboembolism. These physicians do not recommend oral contraceptives, or recommend low dosage forms, for women with histories suggesting a predisposition to these complications. We have no information to indicate that prescribing the pill is reduced in women with negative histories.

Mr. OBEY. Is it possible that the evaluations of the safety of the pill and IUD's which your institute is presently conducting, might indicate that they are really unsafe for prolonged use and that the pill might have to be removed from the market?

ANSWER. It is conceivable that evaluations of the safety of the oral contraceptives now being conducted or to be initiated in the next year or so might eventually indicate that these agents are unsafe for prolonged use but such studies will require a number of years for definitive answers. The most important unresolved question about safety of contraceptive steroids is whether they may cause cancer. Most studies to date have revealed no risk but it is known that cancer does not usually occur until a decade or more after exposure to a hazardous agent. Since 1965, more than 20 percent of married women in the United States have been using contraceptive steroids, and now is the appropriate time for extensive research to resolve this question.

Other serious adverse effects of the pill may ultimately be resolvable by finding ways to identify the specific individuals at risk and recommending that they use alternative methods. Also, if the mechanisms by which these effects are induced can be discovered, it should be possible to modify formulations to avoid these risks.

Concerning IUD's, it does not seem likely that evidence will indicate these to be unsafe for prolonged use although certain designs may be safer than others for some individuals and certain indications for removal or selection of a different contraceptive method may be identified.

Mr. OBEY. Would it be a good idea in your judgment to avoid these possibilities by making a major effort to develop a wide range of alternative effective contraceptives?

Answer. There is no question that current concerns about the safety of oral contraceptives and IUD's mandate development of alternative safe and effective

methods of fertility regulation. The Institute is currently supporting research in this direction. These efforts involve the development of new drugs, improvement in composition of present oral contraceptives, search for safe and effective contraceptive agents for the male, better methods of drug administration and studies on the efficacy and acceptability of natural family planning methods. Future endeavors will include attempts to improve both vaginal and intrauterine contraception.

NEW BIRTH CONTROL METHODS

Mr. OBEY. A recent Ford Foundation report indicates that we are not adequately exploiting the pure research findings made available by your Institute to develop new and better methods of birth control. Is that true?

ANSWER. The answer is a qualified yes. At the present time, we can only pursue research on the more promising leads. A number of potential leads have not been pursued because funds are limited. On the other hand, even under the best of circumstances, it is not possible or desirable to explore every lead. There are honest differences in opinion as to what constitutes a research finding that is worthy of intensive study.

FUNDING RATE OF APPROVED POPULATION RESEARCH GRANTS

Mr. OBEY. Would you please supply the proportions of your approved grants which you were able to fund for population research for each fiscal year from 1972 through 1978 (expected).

ANSWER. The following table shows the approved grants, funded grants, and what percentage the funded grants represent of the total approved grants.

CPR FUNDED/UNFUNDED TABLE

	Total grants approved	Total grants funded	Percent
Fiscal year:			
1972	287	166	57.8
1973	333	168	50.5
1974	323	131	40.6
1975	359	185	51.5
1976	376	153	40.7
1977 (estimate)	440	118	26.8
1978 (estimate)	470	131	27.9

PEER REVIEW SYSTEM

Mr. OBEY. I understand that your institute evaluates grant proposals on a peer review basis. Could you please explain your rating system and provide information on the range of ratings of proposals which received funding?

ANSWER. First, it should be understood that all Institutes' grant applications at NIH are evaluated under the peer review system. The peer review is conducted by NIH study sections composed of outstanding non-Federal scientists who are experts in their field. The review is based on scientific merit which includes an assessment of the importance of the proposed research problem; the originality of the approach; the training, experience and research competence or promise of the investigator; the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. The final recommendation of the study section, which is made by majority vote of the members, is for one of three options: approval, disapproval or deferral. For the approved applications, each member privately records a numerical score based on his opinion of the overall merit of the application. After the meeting, the arithmetic means of these scores are computed by NIH staff and then merged with the scores from the two previous meetings of the study section. This composite distribution is then normalized to a specific mean and standard deviation that is common to all study sections. This normalized score is used by this Institute in order to iron out potential differences that might occur between the ratings of one study section when compared with another. This is especially significant for the NICHD because the Institute receives applications from practically all of the 50 or so NIH study sections.

Applications are recommended for funding no the basis of these normalized scores. Before the Institute can fund any grant application, it must have been approved by the National Advisory Child Health and Human Development Council. Currently we are projecting a funding rate of approximately 31 percent of approved applications.

INJECTABLE CONTRACEPTIVE FOR WOMEN

Mr. FLOOD. Last year you will recall we talked about the development of new methods of fertility regulation. One method we talked about at some length was to develop an injectable contraceptive for women. What is the status of that work?

Dr. KRETCHMER. There is a great deal of work still to be accomplished in the development of an injectable contraceptive for women. This drug will not be ready to go on the market in the United States for at least 5 years, although in some other countries they are using an injectable for women as a contraceptive.

An issue, Mr. Flood, is that the side effects from synthetic steroids, now used in the oral contraceptives and in the injectable contraceptives, appeared to be much more marked than natural steroids. Thus, there has been a great deal of research in an attempt to get an injectable using a natural steroid, or to develop something new entirely.

CONTRACEPTIVE METHODS FOR WOMEN

Mr. FLOOD. Are there any other contraceptive methods for women that you have currently under study?

Dr. KRETCHMER. Yes; one of the interesting approaches is to use new hormones which are very small chemicals resembling a protein and which can suppress the hypothalamus. These hormones inhibit this gland in the brain which would then prevent hormones from stimulating the ovary. That is a possibility scientists are looking into in great detail.

Another approach to contraception is to attempt to develop a contraceptive which is useful in the male.

CONTRACEPTIVES FOR MEN

Mr. FLOOD. What about contraceptives for men?

Dr. KRETCHMER. Because both men and women have this gland in the brain, this hormone research can be applied to males as well.

Mr. FLOOD. Are you working on injectable contraceptives for men?

Dr. KRETCHMER. Yes; but we really don't have a good contraceptive for men except to use vasectomy or to use really marked doses of sex hormone. There is a hormone, discovered recently, which is secreted by the testes and which inhibits the development of sperm. There is a great deal of work now being accomplished on that hormone in our extramural centers.

NATURAL FAMILY PLANNING METHODS

Mr. FLOOD. Are you still supporting research on natural family planning methods?

Dr. KRETCHMER. Oh, yes. We have a large project going on at the moment in Los Angeles.

Mr. FLOOD. How much are you going to spend in 1978 on that?

Dr. KRETCHMER. I don't remember offhand, but I will supply that for the record.

Mr. FLOOD. Tell us about it for a moment.

Dr. KRETCHMER. The natural approach is really two pronged in the sense one can use body temperature as well as a determination of the consistency of cervical mucous. This combination of body temperature and evaluating the cervical mucous apparently can work effectively as a technique for a natural method for family planning.

The problem is, we don't have enough volunteers in this study in Los Angeles, but these numbers are increasing.

With regard to how much money is concerned, I will have to supply that for the record.

[The information follows:]

NATURAL FAMILY PLANNING PROJECT

Title: "Efficacy of Two Methods of Natural Family Planning (contract No. NO1 HD 6-2826).

Contractor: Cedars-Sinai Medical Center, Los Angeles, Calif.; project director: Maclyn Wade; fiscal year 1978 funding: $500,000 (estimated).

SIDE EFFECTS OF VASECTOMIES

Mr. FLOOD. We have also talked in the past about potential adverse side-effects of the vasectomies. What do you have to report this year about that? Is there still some concern about this operation, or have you found it to be absolutely safe?

Dr. KRETCHMER. The word "absolutely" in medicine does not exist. I don't think we can say that anything is absolutely safe. What we have found is that there are antibodies produced to sperm in vasectomized animals and man. In other words, the body is reacting to itself. In the rabbit these antibodies have produced disease. This has not proved to be the case in humans, but this is something we follow closely.

This is another area where we are using epidemiologic studies in addition to the laboratory work which must be done. I hope to have more to report on this next year. We stay suspicious but so far we have nothing adverse to report.

SUDDEN INFANT DEATH SYNDROME

Mr. FLOOD. How much do you plan to spend in 1977 and 1978 on research on the sudden infant death syndrome?

Dr. KRETCHMER. We estimate we will spend about $7.7 million in the general field of sudden infant death in 1977 and approximately the same level in 1978.

Mr. FLOOD. Again in your opening statement you said no single mechanism is responsible for sudden infant death. What does that mean? Does that mean that you and all your scientists have hit a dead end on this problem?

Dr. KRETCHMER. No, we believe a combination of mechanisms is responsible. One factor is the sleep pattern of the baby. Another involves the breathing pattern. A third involves the previous history of the

baby. A premature infant is more likely to die of sudden infant death. In other words, you can't pinpoint the problem to one enzyme or one molecule. Maybe someday we will be able to do that, but at the moment we have involved the brain, lung, esophagus, and history of the child.

Mr. FLOOD. Is there any possibility at all of developing in the near future some way to detect within the first few hours after birth which children are a risk for sudden infant death?

Dr. KRETCHMER. Not really. We know the premature infant is at more risk. We know that the baby who has continued spells of lack of breathing is probably at more risk. We have accurate data to indicate those babies with an abnormal cry are more at risk. I think eventually we will be able to answer your question, but our research is going, as most research goes, slowly but surely.

Mr. FLOOD. For the record give us a list of other institutes which support research on sudden infant death and the amounts they are going to spend in 1977 and 1978.

Dr. KRETCHMER. I would be delighted to do that for the record. We do have an interagency committee on sudden infant death which involves the Health Services Administration.

In the appropriation for 1977 the Health Services Administration was given funds for SIDS counseling and education.

[The information follows:]

SIDS RESEARCH IN OTHER NIH INSTITUTES

The National Institute of Child Health and Human Development is the only Institute which will support research on the sudden infant death syndrome in 1977 and 1978. Research currently supported by other institutes could contribute to our understanding of SIDS but is not directly related to discovering causes, identifying infants at risk, and exploring preventive approaches.

NUTRITION

Mr. FLOOD. In your budget justification you refer to your institute's work on nutrition. Now, we have several other than NIH Institutes also conducting research on nutrition. Which one has the lead responsibility in this area and how do you coordinate your efforts?

Dr. FREDRICKSON. Would you like me to respond to that?

Dr. KRETCHMER. May we both respond to it?

Dr. FREDRICKSON. Mr. Chairman, the situation with nutrition is somewhat like the situation with physiology in medical school. People can't find the body yet it is very much alive. So is nutrition. For the last two decades much of nutrition research has departed from the older pattern of discovering vitamins and dealing with the minimum requirements for children and adults. Whole new areas of basic and cellular physiology studies have been spawned, teaching us a great deal more about how elements in the diet really work in cells and make the body healthy.

Mr. FLOOD. Which institute has the lead responsibility?

Dr. FREDRICKSON. There is about $72 million in nutrition research in the NIH budget The largest contributor to that is the National Institute for Arthritis and Metabolic and Digestive Diseases. The second largest is the Institute before you here.

Mr. FLOOD. How do you coordinate all of them?

Dr. FREDRICKSON. They are now coordinated by a Coordinating Committee for Nutrition at the NIH level, which has interagency connections. This group recently finished an analysis of what we are doing in nutrition research. Because it is time, I think, to rejuvenate nutrition research in two directions, we are considering whether to change the lead role from the Arthritis, Metabolism and Digestive Diseases Institute to the National Institute of Child Health and Human Development. That is a point I have under consideration at the present time.

Mr. FLOOD. Doctor, suppose you tell us what your institute is doing, and how does that differ from the cancer and the Arthritis Institutes?

Dr. KRETCHMER. The National Institute of Child Health and Human Development is interested in preventive medicine, particularly since we are concerned with the development of man.

What happens in the child will later be seen in the adult as disease or disability. If you mention the National Cancer Institute or the National Institute of Arthritis, Metabolism, and Digestive Diseases, they are primarily interested in nutrition as it relates to a particular disease—nutrition and cancer, nutrition and arthritis, nutrition and gastrointestinal disease, nutrition and kidney disease.

The National Institute of Child Health and Human Development is interested more in whole patterns of development. For example, the problem of obesity. How can we look at the nutrition early in life relative to later obesity?

The antecedents to adult disease such as atherosclerosis and hypertension may have originated early in life because of nutrition problems. That is why we study intrauterine, maternal, and infant nutrition.

We are vitally interested in nutrition as it relates to growth and development of the child and how that child will then be later reflected in the man. It is that kind of nutritional work that we support.

CYSTIC FIBROSIS

Mr. NATCHER. Dr. Kretchmer, in your statement you say that investigators have discovered a means of detecting cystic fibrosis using cells grown in tissue culture. Is this a reliable test, Doctor, for the early detection of this disease?

Dr. KRETCHMER. Mr. Natcher, I would answer your question by saying that we were more optimistic when we wrote those words in the opening statement than I am as we sit before you today. I would have to be very cautious about saying whether that is a reliable test. There is no question that cells derived from people with cystic fibrosis seem to behave differently and look different with special stains under the microscope than cells derived from people without cystic fibrosis. It is not really a very reliable test because we are really not at the core of this very major problem of cystic fibrosis. We do not know the key cause of cystic fibrosis.

I would have to answer your question by hedging and saying, "No, I don't believe we have a reliable new test but we are actively doing research on cells derived from patients with cystic fibrosis."

Mr. NATCHER. How much will you spend on cystic fibrosis research in 1977 and in 1978, Doctor?

Dr. KRETCHMER. Our research in cystic fibrosis is research at a really quite basic level and the research on patients with cystic fibrosis is primarily carried out by two institutes, the National Institute of Arthritis, Metabolism, and Digestive Diseases and the National Heart, Lung, and Blood Institute.

I will submit the figures for our Institute for the record.

[The information follows:]

NICHD OBLIGATIONS FOR CYSTIC FIBROSIS

In fiscal year 1976 the NICHD obligated approximately $70,000 on cystic fibrosis. Of this amount, $50,000 was for the Institute's intramural program, and $20,000 for one grant project. It is expected that similar amounts will be obligated in 1977 and 1978.

Mr. NATCHER. Are there any other institutes supporting research on cystic fibrosis? Can you tell us how much is involved moneywise as far as other institutes are concerned? Do you have any figures?

Dr. FREDRICKSON. We have those and can submit them for the record.

Mr. NATCHER. We will place them in the record at this point.

[The information follows:]

NIH SUPPORT OF CYSTIC FIBROSIS

[In thousands of dollars]

	1977	1978
NIAMDD	2,100	2,100
NHLBI	1,600	1,600
NIAID	1,150	1,250
NICHD	70	70
DRR	113	132
Total	5,033	5,152

CONGENITAL MALFORMATIONS

Mr. NATCHER. Now, again, Doctor, referring to your statement, you say that the mechanism responsible for the interaction of genes and environment are only now becoming known.

What kind of work are you supporting in this area and what will it mean insofar as the future is concerned?

Dr. KRETCHMER. Our interest in this particular subject is primarily on the mechanism for the development of congenital malformations.

All the Institutes contribute to studies of gene action because it is such an immense and important field. We know certain hormones can make a gene act when it wouldn't otherwise act. Through the work of DNA recombination, we are learning a great deal about the gene and how it acts.

The future of this work is hopefully in the prevention of congenital malformations by understanding how they happen.

Mr. NATCHER. How much have you budgeted for this kind of research in 1978?

Dr. KRETCHMER. In the area of congenital malformations, we have about $14 million, and this would cover the whole gamut of congenital malformations.

LEARNING DISORDERS

Mr. NATCHER. An area this committee has always been interested in is your work concerning learning disorders, Doctor, in children. How much do you plant to spend on this group of problems and what progress can you report to the committee at this time?

Dr. KRETCHMER. We are very much concerned about the area of learning disabilities. Certainly, if we talk about learning disorders and include in that reading disabilities, we are dealing with millions of people. The estimate is 2 to 15 million people.

What we did to make this particular area visible was to develop a new Human Learning and Behavior Branch. In that Branch, we put approximately $8 million. This $8 million is used for problems of learning, specifically problems of communication and reading.

The area we are most concerned with, since it is such an important activity in the development of a person, is the problem of dyslexia and the problem of reading.

What we are trying to do is to define the problem. We are doing research in terms of definitions so we can take the pieces of the problems and work them out.

We are also supporting studies on the basic mechanism for learning as an approach to the question of how an individual learns to read.

We study how the brain develops and what interrelationships exist between brain cells during development.

PROFESSIONAL JUDGMENT BUDGET

Mr. NATCHER. Doctor, in your professional judgment, how much more money can you use to support research on mothers and children and, if additional money is approved, in what areas would you invest this additional money?

Dr. KRETCHMER. In my professional judgment, we could use approximately $20–25 million above the President's budget. We would budget this money into areas that you and the chairman have touched on, such as the high risk pregnancy and the premature infant. This is an area where death and disability can be prevented if we understand more about premature labor. We could then presumably prevent the baby from being premature.

We would budget into congenital malformations, and learning and dyslexia. We would put some of this money into the general field of mental retardation, primarily in the area that I would define as human genetics.

We would also budget into the area of antenatal and postnatal nutrition as well as the related fields of reproductive biology, population behavioral sciences, and family planning.

Mr. FLOOD. I was going to ask you especially about the use of additional funds for nutrition.

DIABETES AND PREGNANCY

How much do you plan to spend in 1977 and 1978 to study the special problems of the diabetic mother and her offspring?

Dr. KRETCHMER. We plan to budget approximately $5 million in each of these years.

Mr. NATCHER. Have you any potential breakthrough in this area? Do you have any promising work currently under way?

Dr. KRETCHMER. Yes, we do. Because of previous research we can now dramatically decrease maternal mortality in diabetic women by providing prenatal care. However, we can decrease the rate even further, as well as improve prospects for babies born to diabetic women. For example, the infants of diabetic mothers are usually very big babies—they may weigh 10 or 12 pounds—but are really very immature.

Mr. NATCHER. Do you have a breakthrough on the horizon?

Dr. KRETCHMER. Yes, I think we do.

Using the rat as an animal model, we can now study how these infant animals become very large within the uterus.

We would like to move further into the area of the genetics of diabetes. This is a very complex area, as the mechanism probably involves more than one gene.

We are also involved in studying, along with the National Institute of Arthritis, Metabolism, and Digestive Diseases, a complicated model in the human—the native American in the Southwestern part of the United States. After the age of 35, about 50 percent will have diabetes.

MENTAL RETARDATION AND DEVELOPMENTAL DISABILITIES

Mr. FLOOD. Now in the area of mental retardation and the developmental disabilities, you state that some of the problems of mental retardation can be minimized if the parents provide adequate stimulation for their children. Can you elaborate on that?

Dr. KRETCHMER. Yes. This is a research area of social and educational psychology aimed at factors which might affect mental performance.

Researchers are learning how to increase the potential of the child by using techniques applied within the home. Children who are not stimulated are known to function at a lower level, but research has shown that mothers specifically trained to work with and stimulate children can help the child to realize his or her full potential. This is true not only with mentally retarded children, but with almost all children.

Mr. FLOOD. Are you working with the Maternal and Child Health Care program so that they can begin teaching mothers to provide this adequate stimulation for their children?

Dr. KRETCHMER. Yes.

For the past 3 years we have collaborated with the Maternal and Child Health staff of the Bureau of Community Health Services——

Mr. FLOOD. The preventive complications in this thing are simply enormous.

Dr. KRETCHMER. I agree. We meet with the staff from Maternal and Child Health, and the National Institute of Mental Health. The three of us, have contributed to a program now going on in Prince Georges County.

We are thinking about supporting a similar project at the University of Maryland.

AUTOMATED SYSTEM OF CHROMOSOME ANALYSIS

Mr. FLOOD. Last year again we talked about an automated system that would make possible in some way chromosomal analysis screening for genetic defects.

Dr. KRETCHMER. That system is almost ready to go. Maybe Dr. Sidbury knows whether it is being used or not.

Dr. SIDBURY. The prototype has been constructed and is about to be field tested.

CHILD ABUSE AND NEGLECT

Mr. FLOOD. How much money are you allocating in this budget for research on child abuse and neglect?

Dr. KRETCHMER. Except in terms of our work on behavioral sciences, we do not have any money in research on child abuse and neglect. That effort is in the Office of Child Development, which is under the Assistant Secretary for Human Development.

Mr. FLOOD. What activities do you support that we know about in this problem?

Dr. KRETCHMER. Maternal-infant relationships. We spend $25 million in behavioral and social science related to mother, child and family. We are the institute that has the largest amount of money going into behavioral and social science. We support the development of fundamental knowledge, and then results of this work are handed over to the Office of Child Development or to the community at large.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record:]

Mr. FLOOD. Doctor, the "Authorizing legislation" page of your budget shows an amount of $56,333,000 requested, under title X of the Public Health Service Act, for population research in 1978. Do these funds represent all of your population research activities?

ANSWER. That figure covers research grants, contracts, and intramural programs for population research. If we were to add administrative overhead costs for these activities, the amount would be $60,566,000 for 1978. No research training funds are included, though, since they are authorized separately, under title IV.

ADOLESCENT PREGNANCY

Mr. MICHEL. How much in the way of funds is being allocated to this initiative on adolescent pregnancy?

ANSWER. In fiscal year 1977 approximately $900,000 has been allocated for the adolescent pregnancy initiative. Funding in fiscal year 1978 is estimated at $1 million.

Mr. MICHEL. Have you established any time frame for completion of this initiative, or is it more or less open-ended?

ANSWER. The initiative on adolescent pregnancy is open-ended. Reports from studies on both the consequences and determinants of adolescent pregnancy will begin to appear in the next year or 2, but many of these studies will identify needs for further research. It is anticipated that adolescent pregnancy and its attendant complications—toxemia, intrauterine infection, and prematurity—will require considerable research effort for the foreseeable future. While the incidence of pregnancy among adolescents between 18 and 20 years of age appears to be falling, the incidence of pregnancy among adolescents under 16 years of age appears to be rising. Adolescents under 16 years of age who become pregnant are at highest risk for the complications mentioned above. Research to determine

the sociological, psychological, and cultural contributions to attitudes about sexual activity and the use of contraceptive measures will also be an important part of the Institute's efforts in this area.

SUDDEN INFANT DEATH SYNDROME

Mr. MICHEL. Where do we stand with the research on sudden infant death syndrome? Are we anywhere near determining cause and prevention?

ANSWER. During 1976 the NICHD continued to expand its research efforts in the sudden infant death syndrome. The objectives of the Institute's SIDS research program are to increase understanding of the causes and underlying mechanisms of the syndrome; to identify infants at risk of becoming victims; to explore preventive approaches; to elucidate the impact of a sudden and unexpected infant death on the subsequent behavior of parents, siblings, and the extended family; and to inform the scientific and general communities about SIDS through workshops, conferences, and publications.

As a result of Institute-supported investigations between 1972 and 1976, it is evident that SIDS babies are not the healthy infants before death that they were once believed to be. These infants appear to have subtle physiologic defects of a neurologic, cardiorespiratory and/or metabolic nature, yielding increasing evidence that the syndrome is not caused by a single mechanism as previously believed. Instead, a number of developmental, environmental, and pathological factors are involved, which under a complex set of circumstances interact to produce a sudden and unexpected infant death.

NICHD supported scientists have shown that periodic cessation of breathing (apnea) and associated changes in heart rate in infants during sleep are characteristics in the early months of life. Research has also revealed that frequent apneic periods are more likely to occur in infants considered to be at high risk for SIDS, for example, those who are growth retarded in utero, or prematurely born. Prolonged apneic episodes ultimately affect availability of oxygen to tissues. There is also preliminary evidence that infants at risk for SIDS may be identified by characteristic cry patterns. Other studies using animal models have shown that stimulation by certain liquids (cow's milk, sugar-water) of the nerve controlling the function of the upper airway can cause apnea that may result in death. A higher incidence of brief apneic pauses and more frequent regurgitation of stomach contents have been documented in studies of "near miss" infants than in infants not exhibiting "near miss" episodes. Furthermore, varying patterns of heart rate in relation to specific sleeping stages (deep sleep or REM sleep, rapid eye movement) has been observed in normal infants. Studies are underway to determine if similar or different and unusual patterns exist in "near miss" infants and siblings of victims. These findings are disclosing several possible causes for the appearance of apneic episodes in apparently healthy infants.

Emphasis in 1978 will be directed toward exploiting the above mentioned early leads in addition to defining the neurologic, respiratory, infectious, genetic, and environmental factors which singly or in any combination may contribute to the syndrome. As always, the major stress will be toward early identification of probable victims of SIDS and evaluation of preventive approaches.

USE OF CONTRACEPTIVES

Mr. MICHEL. Last year we talked about your studies in the area of contraception and population control, and you said one of the things you were trying to find out is why people who really need information about contraception don't avail themselves of it. Do you have any findings as yet in this regard?

ANSWER. Our findings to date indicate that effective use of contraception is related, in part, to the age at which young women become sexually active. Those who become sexually active early tend to use contraceptives more irregularly than those who first intercourse does not occur until the late teens. Young black women frequently report they either wanted to become pregnant or did not mind getting pregnant, and those who do not give this reason for not using contraception say that (1) they had intercourse too infrequently, (2) were too young, or (3) did not regard themselves as likely to become pregnant. The main reason

for not using contraception given by white teenagers was that they thought intercourse occurred at times of the month when they could not become pregnant. A study of first-time mothers in New York City showed that most teenagers were not trying to become pregnant but that they suffered from problems of weak motivation to avoid pregnancy, poor knowledge of the risk of pregnancy and problems of access to any methods or to safe and effective methods of contraception.

As an indication of the poor knowledge of risk of pregnancy, only 10 percent of the adolescent mothers accurately reported the time during the menstrual cycle when they were most likely to conceive. Although in one study few blacks or whites claim a lack of access to contraceptives, some investigators feel that embarrassment or other difficulties in obtaining contraceptives are important factors in their nonuse. One study has found that women seeking abortions frequently state their nonuse was influenced by what they perceived as negative attitudes of physicians toward contraceptives while women who use contraceptives perceive physicians' attitudes as helpful. Preliminary findings in another study indicate that many men simply assume that their partners are on the pill, suggesting either irresponsible attitudes or lack of communication.

SOCIAL SCIENCE FUNDING

Mr. MICHEL. What is the amount you are allocating for social science research this year? Last year, it was $8.1 million.

ANSWER. When considering the social sciences narrowly defined to include only socio-demographic studies, we have allocated approximately $8.5 million in fiscal year 1977. However, when considering the broader area of both social and behavioral sciences, the allocation for fiscal year 1977 is approximately $27 million. The bulk of the behavioral science research, as distinguished from the social science research, is in psychology.

MOTHER-CHILD INTERACTION

Mr. MICHEL. Can you report to us any results from the behavioral study of mother-child interaction?

ANSWER. The Institute is currently supporting about $500,000 for research grants concerned with mother-infant and parent-child interaction. These investigations involve both human and animal subjects and cover a range of research topics. For example, three infant responses related to sharing have been identified: (a) showing, (b) giving, and (c) partner play. Sharing is a nearly universal response by age 2. Recent studies have found that showing, for example, pointing with an index finger, begins to be a definitive response at about 13 months of age. Sharing by the infant stimulates both verbal (naming of objects, describing properties of objects, talking about the infant's activities with objects) and nonverbal (demonstration of how objects can be manipulated) responses in mothers that are usually of an instructive nature. Other research has suggested that newborns, while limited in their vocalizations, provide a potent stimulus to parents and other adults to converse with the infant and, as a result, newborns are exposed to the language of their culture practically from the day of their birth. These observations are important in the area of mother-child interaction and may also have relevance for the development of learning capabilities in infants as well.

TEENAGE PREGNANCY RATE

Mr. MICHEL. Is the teenage pregnancy rate still increasing?

ANSWER. Pregnancy rates are somewhat difficult to compute since they require information not only on live births but also on spontaneous and induced abortions, events for which statistics are more difficult to obtain. To make comparisons over time we may assume that the rate of spontaneous abortion is constant and combine data on live births with data on induced abortions. Such calculations imply a slight, but continuing, rise in the pregnancy rate for women aged 14–19.

The birth rate for women under age 16 continues to rise while the birth rate for older adolescents continues to decline. The birth rate for 14-year-olds rose 7.6 percent from 1970 to 1975 and the rate for 15-year-olds rose 1 percent during the same period. Birth rates for older teenagers fell by 6.2 percent for 16-years-olds and by 26.4 percent for 19-years-olds during the period 1970 to 1975.

The birth rate to unwed teenagers continues to rise, going from 22.4 births per

1000 women age 15–19 in 1970 to 24.2 in 1975, an increase of 8 percent. This was during a time when the birth rate to older unmarried women fell by a substantial degree (by 18 percent for women 20–24 and 33 percent for women 30–34).

The number of babies born to unmarried teenagers reached an all-time high of 233,500 in 1975.

FUNDING FOR SIDS RESEARCH

Mr. MICHEL. How much are you allocating for sudden infant death research, and how much are the other Institutes allocating

ANSWER. NICHD funding for SIDS research in fiscal year 1977 is estimated at $7,700,000. We expect it will be funded at approximately the same level in fiscal year 1978. The National Institute of Child Health and Human Development is the only Institute which will support research on SIDS in 1977 and 1978. Research currently supported by other Institutes could contribute to our understanding of SIDS but is not directly related to discovering causes, identifying infants at risk, and exploring preventive approaches.

TRAINING PROGRAM

Mr. MICHEL. I note you have $9.2 million budgeted for training programs. Is there really a shortage of researchers in the fields covered by your Institute so that we need that much for training?

ANSWER. Yes; we believe that more investigators are needed in the fields covered by our Institute. Although specific data are not available, we estimate requirements for 300 additional trainees supported through the individual and institutional NRSA mechanism. A study is being conducted by the National Academy of Sciences from which we hope to get better information concerning specific shortage areas as well as the magnitude of the manpower pool with which we are dealing.

Current indications of the need include the demands for training resources that come to us through grant applicants who have identified a real need for the number of researchers they seek to train. These grant applicants comprise the community of research institutions which, in turn, are the future employers of the trained researchers. Moreover, it has been estimated that 10 percent of grant recipients each year are new researchers. This attrition in the manpower field suggests there is a need to train new investigators in order to replenish the pool of scientists who do the research.

RESEARCH GRANT FUNDING

Mr. MICHEL. In the fields covered by your Institute, what percentage of the grant applications received this year are receiving funding, and then what percentage approved by the study sections are receiving funding?

ANSWER. Approximately 23 percent of the grant applications received are receiving funding, and about 31 percent of those approved are being funded.

BUDGET INCREASE

Mr. CONTE. Dr. Kretchmer, you have been provided with an additional $5 million in the Carter administration's budget for research associated with alternatives to abortion and the problems of adolescent pregnancy. What research will be supported by this additional $5 million? and is $5 million really enough to deal with the enormity of this problem?

ANSWER. The $5 million will be used to fund research grants in those program areas defined broadly as reproductive biology and research related to pregnancy and antenatal problems, including antenatal nutrition and other factors in fetal development. Since we will be funding approximately only 29 percent of those competing grants which have been approved, many worthwhile projects could be supported with additional funds. Of course, the $5 million increase will be used to fund the highest priority grants.

NUTRITION RESEARCH

Mr. CONTE. I know that your Institute is very involved in childhood nutrition and nutrition research. Could you provide some information on the importance

of this research, and how childhood nutrition may affect adults many years later?

ANSWER. Nutrition research has advanced sufficiently so that we can define the essential nutrients of diet. However, the importance of nutrition as an instrument of preventive and curative medicine, and its impact on adult health, is only beginning to be fully appreciated. We know, for example, that malnutrition during pregnancy can significantly affect the development of brain cells in the fetus and that overnutrition can produce an obese infant, predisposed to obesity in adulthood and to the disease states that are associated with obesity. It is known that nutrition can modify the outcome of diseases of genetic origin. There is increasing evidence that components of our diet may lead to degenerative diseases. The application of these and future discoveries can have important significance for adult health and quality of life.

Mr. CONTE. I understand that your Institute recently prepared a staff paper on nutrition research. Can you share some of the conclusions of that report with us? Where should we be headed in nutrition related research?

ANSWER. As the result of discussions among NICHD staff and consultation with non-Federal scientists, we have identified several priority areas for future nutrition research.

Highest priority would be given to studies to define optimum nutrition for pregnant women, particularly for adolescents 15 years of age and younger, in order to enhance structural and functional fetal development and to minimize pregnancy risks such as toxemia and pregnancy associated hypertension.

Emphasis would also be given to research to determine the comparative metabolic competence of normal infants, low birth weight infants and prematurely born infants.

A key effort would involve studies on the impact of substitution or supplementation of dietary components on physical and intellectual growth and development in low birth weight and prematurely born infants.

We would promote research to determine the biological, behavioral, and cultural determinants of taste and food preferences. Important areas of concern include the early identification of tendencies to obesity in infancy and the relationship of obesity in childhood to adult obesity and to chronic diseases associated with obesity.

Mr. CONTE. Given the importance of nutrition research, do you believe that adequate amounts of money are being devoted to it? What particular areas are being neglected because of lack of funds?

ANSWER. In fiscal year 1977 we are supporting research at a level of about $13.5 million in the broad area of nutrition, and we expect that amount to increase by about another $0.5 million in fiscal year 1978. While we are supporting research on some important problems given the current level of support, there are other significant problems that could be addressed if additional funds were made available. Additional funds could be used to support studies to find out the most appropriate way to feed low birth weight infants and sick newborns. Recent technologic advances have made it possible to identify the various components of human milk, in terms of both nutritional and immunologic factors. Identification of these components will make possible the precise determination of their physiologic functions. This information could be applied to the improvement of diet formulas so that mothers could make a choice about how to feed their babies.

BIRTH DEFECTS

Mr. CONTE. I understand that over 10 percent, perhaps as many as 15 percent of all Americans suffer from some form of birth defect. What research is your Institute pursuing in this area? Are there particular parts of birth defect research that are presently underfunded?

ANSWER. Birth defects or congenital anomalies may be either genetically based or occur as a result of some physical, nutritional, infectious, chemical or hormonal influence on the developing embryo. The Institute is supporting ongoing projects that address a variety of topics, including studies of human malformations, experimental developmental biology, embryonic development, morphogenesis, development of the fetus, and the newborn.

In fiscal year 1977 we are supporting research on congenital anomalies at a level of about $13.3 million, and we expect that amount to increase by about $1 million in fiscal year 1978. If additional funds become available, we would increase our research efforts aimed at identifying genetic antecedents of structural

and metabolic impairments. Emphasis would be given to studies on the effects of drugs—both therapeutic and nontherapeutic, but not drugs of abuse—on the pregnant woman and her fetus. We would also encourage research aimed at defining physiological and behavioral modifications in the newborn, child, and adolescent rooted in early maternal exposure to drugs and other pharmacologically active materials.

MENTAL RETARDATION

Mr. CONTE. What about research on childhood mental retardation? Is the Institute involved in that? Does it appear anywhere other than the specific retardation line item?

ANSWER. Research on mental retardation is supported through a variety of activities in the NICHD. For example, it has been shown that mental ability is dependent upon birth order, birth trauma, and a variety of events that take place during pregnancy. These latter would include environmental influences such as poor nutrition, infection, and drugs such as alcohol. Socio-cultural environment, too, is a major contributor to mental disability in children. Environmental factors would include the ability and efficiency of the mother, the home environment, and problems related to cultural deprivation. Consequently, the Institute's major initiatives in the area of mental retardation involve investigations of high risk pregnancy, especially pregnancy in the adolescent; nutritional studies which relate to specific needs of the infant; and investigation of the mechanisms of genetic and congenital problems involved in brain development. As you can see, mental retardation research involves the entire mothers and children research program.

DYSLEXIA

Mr. CONTE. Sometimes particular health problems seem to fall between the jurisdictional cracks between health institutes. One of those seems to be dyslexia. Is any serious research being done on dyslexia? How much money is being put into dyslexia research? In your professional judgment, is that an adequate amount?

ANSWER. Developmental dyslexia is the most prevalent learning disorder among children who are of normal intelligence and have adequate vision and hearing. Our research program in this area is in its early stages, with some $400,000 being allocated in the 1978 budget request. In my professional judgement the NICHD could use an additional $1 million to expand this research, with emphasis on speech and language acquisition and acquisition of reading capability as related to dyslexia. A specific objective is to develop an achievement test which could assess the major components of reading. This will be an important tool to help resolve the problems of definition and diagnosis of dyslexia.

PREMATURE DELIVERY

Mr. CONTE. In your statement you referred to the identification of a specific population of women with a high risk of recurrent premature delivery. What sort of population is that? How can premature delivery be safely prevented?

ANSWER. Women who have a high risk of recurrent premature delivery include adolescents, particularly those of age 15 years or younger; women who are over 35 years of age; and women who have had six or more previous pregnancies that terminated beyond 20 weeks gestation (full term=37 weeks gestation). These risk conditions are exacerbated by lower socioeconomic status, poor nutritional status, and previous premature delivery.

Bed rest for the patient at high risk for premature labor during the last 12 weeks of pregnancy has been used with some success to prevent the premature onset of labor.

The most certain means of preventing prematurity is for the pregnant women to be young, but older than 16 years of age; to be of good socioeconomic status; to be within normal limits of weight for height; and to have a good reproductive history.

SUDDEN INFANT DEATH SYNDROME

Mr. CONTE. Could you tell me more about your research into sudden infant death syndrome (SIDS)? Have there been any major advances? Or is everything still largely supposition?

ANSWER. During 1976 the NICHD continued to expand its research efforts in the sudden infant death syndrome. The objectives of the Institute's SIDS research program are to increase understanding of the causes and underlying mechanisms of the syndrome; to identify infants at risk of becoming victims; to explore preventive approaches; to elucidate the impact of a sudden and unexpected infant death on the subsequent behavior of parents, siblings, and the extended family; and to inform the scientific and general communities about SIDS through workshops, conferences, and publications.

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NICHD supported scientists have shown that periodic cessation of breathing (apnea) and associated changes in heart rate in infants during sleep are characteristics in the early months of life. Research has also revealed that frequent apneic periods are more likely to occur in infants considered to be at high risk for SIDS, for example, those who are growth retarded in utero, or prematurely born. Prolonged apneic episodes ultimately affect availability of oxygen to tissues. There is also preliminary evidence that infants at risk for SIDS may be identified by characteristic cry patterns. Other studies using animal models have shown that stimulation by certain liquids (cow's milk, sugar-water) of the nerve controlling the function of the upper airway can cause apnea that may result in death. A higher incidence of brief apneic pauses and more frequent regurgitation of stomach contents have been documented in studies of "near miss" infants than in infants not exhibiting "near miss" episodes. Furthermore, varying patterns of heart rate in relation to specific sleep stages (deep sleep or REM sleep, rapid eye movement) has been observed in normal infants. Studies are underway to determine if similar or different and unusual patterns exist in "near miss" infants and siblings of victims. These findings are disclosing several possible causes for the appearance of apneic episodes in apparently healthy infants.

Emphasis in 1978 will be directed toward exploiting the above-mentioned early leads in addition to defining the neurologic, respiratory, infectious, genetic, and environmental factors which singly or in any combination may contribute to the syndrome. As always, the major stress will be toward early identification of probable victims of SIDS and evaluation of preventive approaches.

CYSTIC FIBROSIS

Mr. CONTE. What is being done to develop a screening procedure for cystic fibrosis?

ANSWER. We are actively examining cells derived from patients with cystic fibrosis in an effort to develop a means of detecting cystic fibrosis using cells grown in tissue culture. Although it is clear that cells derived from people with cystic fibrosis react differently and appear different under the microscope (using special stains) than do cells from people who do not have cystic fibrosis, we have not developed a reliable test as yet. The key cause of cystic fibrosis remains unknown.

MALE CONTRACEPTIVE

Mr. CONTE. What research is being done to develop an effective male contraceptive? How much effort is being devoted to this project?

ANSWER. Clinical trials currently underway suggest that sperm production can be blocked without concomitant decrease in the male sex drive. However, drugs which are now available have certain limitations involving insufficient effectiveness and short duration of action. Therefore, we are examining several compounds which are much more potent and longer acting than the ones currently used. The most promising of these drugs will then be subjected to toxicological evaluation before we use them in men. We project a time lag of about two years before the first clinical trial.

In fiscal year 1976, we supported 11 projects at a cost of $1,318,000 for research related to male contraceptive development. Also, 13 projects were funded, at a total of $1,075,000, which evaluated existing methods of male contraception (including sterilization). In addition, 61 projects with funding totaling $3,608,000 were supported for research into the basic reproductive processes of the male. This information is needed in order to gain new leads for use in the development of male contraceptives. Fiscal year 1977 funding for research related to the development of male contraceptives is estimated at $1,400,000. Male contraceptive evaluation funding is estimated at $1,130,000 and approximately $3,800,000 will be spent in fiscal year 1977 on research into the basic reproductive processes of the male.

NUTRITION

Mr. CONTE. How are the various Institutes coordinating their research on nutrition? Are there any jointly funded projects in this area? Who has overall responsibiity for nutrition?

ANSWER. We have a coordinating committee for nutrition at the NIH level which has interagency connections. The committee recently completed an analysis of what is being done in nutrition research throughout NIH. It is anticipated that interaction of members of this committee will promote a more effective NIH effort in this area. There are no jointly funded projects in nutrition at this time. The National Institute of Arthritis, Metabolism and Digestive Diseases is currently providing the most funding for nutrition research. However, Dr. Fredrickson is now considering designating the lead role to the NICHD.

JUSTIFICATION OF THE BUDGET ESTIMATES

Appropriation Estimate

National Institute of Child Health and Human Development

For necessary expenses to [To] carry out [except as otherwise provided,] titles IV and X of the Public Health Service Act with respect to child health and human development, [$145,543,000] *$155,761,000.*

(Department of Health, Education, and Welfare Appropriation Act, 1977; additional authorizing legislation to be proposed for $65,535,000.)

Explanation of Language Changes

The proposed language changes are being made to have consistency among the various appropriations of NIH.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Amounts Available for Obligation[1/]

	1977 Appropriation	1978 Estimate
Appropriation	$145,543,000	$155,761,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $5,000; 1978 - $55,000.

National Institute of Child Health and Human Development

Budget Mechanism

	1977 Number	1977 FTE[1]	1977 Amount	1978 Number	1978 FTE[1]	1978 Amount
Grants						
Regular						
Noncompeting	878		$ 60,626,000	893		$ 64,856,000
Competing	94		7,315,000	121		8,712,000
New	214		14,690,000	216		16,425,000
Supplemental	(30)		600,000	(30)		600,000
Subtotal	1,186		83,231,000	1,230		90,593,000
Special						
Mental retardation research centers	12		5,608,000	12		5,608,000
Research career programs	76		1,940,000	77		1,968,000
Subtotal	88		7,548,000	89		7,576,000
Total research grants	1,274		90,779,000	1,319		98,169,000
Training Programs						
Individual awards						
Noncompeting	108	108	1,540,000	215	215	3,323,000
New	152	152	2,328,000	25	25	400,000
Subtotal	260	260	3,868,000	240	240	3,723,000
Institutional awards						
Noncompeting	52	353	4,977,000	56	385	5,479,000
New	10	50	900,000			
Subtotal	62	403	5,877,000	56	385	5,479,000
Total training programs	322	663	9,745,000	296	625	9,202,000
Research and development contracts	199		20,641,000	205		21,290,000
Intramural research						
Laboratory and clinical research	---		14,545,000	---		16,985,000
Epidemiology and biometry	---		679,000	---		682,000
Direct operations	---		7,848,000	---		8,157,000
Program management	---		1,306,000	---		1,276,000
Total	---		145,543,000	---		155,761,000

[1] Full-time equivalents

DHEW - National Institutes of Health

Crosswalk - 1977 Column 1978 Justification

INSTITUTE: National Institute of Child Health and Human Development
(in thousands)

Program \ Mechanism	Research Grants										
	Regular Program		Specials		Training Programs		Research and Development	Intramural	Direct	Program	
	Noncompeting	Competing	Multi-disciplinary Centers	Other	Indiv.	Inst.	Contracts	Research	Operations	Management	Total
1. Research for mothers and children.....	$38,165	$14,302	$5,608	$1,308	$2,490	$4,144	$ 5,441				$71,458
2. Population.....	22,461	8,303		632	1,378	1,733	15,200				49,707
3. Intramural research.....								$15,224			15,224
4. Direct operations.....									$7,848		7,848
5. Program management.....										$1,306	1,306
Total obligations....	60,626	22,605	5,608	1,940	3,868	5,877	20,641	15,224	7,848	1,306	145,543

DHEW - National Institutes of Health

Crosswalk - 1978 Column 1978 Justification

INSTITUTE: National Institute of Child Health and Human Development
(in thousands)

Program \ Mechanism	Research Grants						Research and Development Contracts	Intramural Research	Direct Operations	Program Management	Total
	Regular Program		Specials		Training Programs						
	Noncompeting	Competing	Multi-disciplinary Centers	Other	Indiv.	Inst.					
1. Research for mothers and children.....	$40,967	$16,142	$5,608	$1,336	$2,431	$3,893	$5,533				$75,910
2. Population.....	23,889	9,595		632	1,292	1,586	15,757				52,751
3. Intramural research....								$17,667			17,667
4. Direct operations.....									$8,157		8,157
5. Program management.....										$1,276	1,276
Total obligations..	64,856	25,737	5,608	1,968	3,723	5,479	21,290	17,667	8,157	1,276	155,761

Summary of Changes

1977 Estimated Obligations	$145,543,000
1978 Estimated Obligations	155,761,000
Net change	+ 10,218,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	--	$ 136,000	--	+$ 93,000
2. Wage Board pay increases	--	50,000	--	+ 1,000
3. Federal Employees' Compensation Fund	--	8,000	--	+ 16,000
4. Increased service and supply fund costs	--	790,000	--	+ 95,000
5. Federal Telecommunications System.	--	75,000	--	+ 3,000
6. Payment for centrally furnished services	--	7,015,000	--	+ 1,885,000
(Standard level user charge)..	--	(219,000)	--	(52,000)
Subtotal	--	---	--	+ 2,093,000
B. Program:				
1. Research Grants:				
a. Regular Program				
(1) Noncompeting continuations converted from competing status	--	60,373,000	--	+22,342,000
(2) Competing (new, continuations and supplementals)	--	22,605,000	--	+25,737,000
b. Special Programs				
(1) Research career programs.	--	1,940,000	--	+ 28,000
2. Training Programs:				
a. Individual				
(1) Noncompeting fellowships converted from competing status and associated increased costs	--	1,540,000	--	+ 2,425,000
(2) Competing fellowships	--	2,328,000	--	+ 400,000
b. Institutional				
(1) Noncompeting fellowships converted from competing status and associated increased costs	--	1,180,000	--	+ 909,000

Summary of Changes - Continued

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
3. Research and Development Contracts: (increase in effort in population and research for mothers and children contract programs).	--	$20,641,000	--	+$ 649,000
4. Intramural Research:				
a. Program increase to support Zero Base Analysis employment projections for other-than-permanent full-time positions.	--	16,285,000	--	+ 700,000
Subtotal.....	--	---	--	+53,190,000
Total Increases...	--	---	--	+55,283,000
Decreases:				
A. Built-in:				
1. One less day of pay.....	--	8,352,000	--	- 32,000
Subtotal.....	--	---	--	- 32,000
B. Program:				
1. Research Grants:				
a. Regular Program				
(1) Noncompeting completed or converted to competing status.....	--	60,373,000	--	-18,112,000
(2) Competing completed or converted to non-competing status.....	--	22,605,000	--	-22,605,000
2. Training Programs:				
a. Individual				
(1) Noncompeting completed...	--	1,540,000	--	- 642,000
(2) Competing fellowships completed or converted to noncompeting status.....	--	2,328,000	--	- 2,328,000
b. Institutional				
(1) Competing fellowships completed or converted to noncompeting status.....	--	900,000	--	- 900,000
c. Training Grants				
(1) Noncompeting completed...	--	3,797,000	--	- 407,000
3. Program Management				
a. Decrease of 2 positions.....	49	1,315,000	-2	- 39,000
Subtotal.....	--	---	-2	-45,033,000
Total Decreases...	--	---	-2	-45,065,000
Total Net Change..	--	---	-2	+10,218,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
52	Research for mothers and children.....	---	$71,458,000	---	$75,910,000	---	+$4,452,000
57	Population.....	---	49,707,000	---	52,751,000	---	+ 3,044,000
61	Intramural research.	199	15,224,000	199	17,667,000	---	+ 2,443,000
	Standard level users charge....		(112,000)		(134,000)		(+22,000)
64	Direct operations...	129	7,848,000	129	8,157,000	---	+ 309,000
	Standard level users charge....		(107,000)		(137,000)		(+30,000)
65	Program management..	49	1,306,000	47	1,276,000	-2	- 30,000
	Total obligations.....	377	145,543,000	375	155,761,000	-2	+10,218,000
	Standard level users charge.....		(219,000)		(271,000)		(+52,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	377	375	-2
Full-time equivalent of all other positions	65	84	+19
Average number of all employees	441	456	+15
Personnel compensation:			
Permanent positions	$ 8,558,000	$ 8,698,000	+ 140,000
Positions other than permanent	644,000	1,004,000	+ 360,000
Other personnel compensation	330,000	350,000	+ 20,000
Subtotal, personnel compensation	9,532,000	10,052,000	+ 520,000
Personnel benefits	1,334,000	1,383,000	+ 49,000
Travel and transportation of persons	355,000	360,000	+ 5,000
Transportation of things	55,000	60,000	+ 5,000
Rent, communications, and utilities	450,000	470,000	+ 20,000
Printing and reproduction	250,000	250,000	---
Other services:			
Project contracts	20,641,000	21,290,000	+ 649,000
Payment for centrally furnished services	7,015,000	8,900,000	+ 1,885,000
Other	3,437,000	3,475,000	+ 38,000
Supplies and materials	1,550,000	1,650,000	+ 100,000
Equipment	400,000	500,000	+ 100,000
Grants, subsidies, and contributions	100,524,000	107,371,000	+ 6,847,000
Total obligations by object	145,543,000	155,761,000	+ 10,218,000

Significant Items in House and Senate

Appropriation Committee Reports

Item	Action taken or to be taken
1977 Senate Report	
1. The Committee directed that increased emphasis be focused on finding ways to identify potential SIDS victims and that the Institute should coordinate its program with that of the Health Services Administration (page 58).	1. The Institute supports research contracts which are concerned with identifying risk indices by studying infants who have succumbed to SIDS and infants who are products of problem pregnancies, or whose delivery was complicated by the premature onset of labor. Preliminary work has been completed on the establishment of a SIDS Case Register to both identify and follow-up infants at risk for becoming victims of the syndrome. Coordination of SIDS activities with the Health Services Administration (HSA) is accomplished through the Interagency Panel on the Sudden Infant Death Syndrome which explores applications of new research findings for identifying infants at risk.
2. The Committee expects the Institute will report during the hearings exactly what has been done to initiate and increase support for the mental retardation programs of the Institute (page 59).	2. The Institute's efforts to initiate and increase support for its mental retardation programs give emphasis to the search for causes and means for preventing mental retardation and related developmental disabilities. This support permits investigations into all causes of mental retardation including its leading causes found in disorders of pregnancy and infancy, genetic disorders, and environmental sources. A detailed presentation of what this Institute has done to increase support for mental retardation programs is covered in the special Congressional report on Mental Retardation which has been submitted to the Senate Appropriation Committee.

Authorizing Legislation

Legislation	1978 Authorization	1978 Appropriation Requested
Public Health Service Act, Section 301 - Research and Investigations, in general.....	Indefinite	
Public Health Service Act, Title IV, Part E - National Institute of Child Health and Human Development.....	Indefinite	$93,616,000 2/
Public Health Service Act, Title IV, Part I - National Research Service Awards.....	1/	5,812,000 3/
Public Health Service Act, Title X, Section 1004 - Family Planning and Population Research Act of 1975.....	1/	56,333,000 2/

1/ Authorization expires September 30, 1977; extension legislation is pending.

2/ Funding estimate only.

3/ Funding estimate only. Excludes $3,390,000 for old training programs.

National Institute of Child Health and Human Development

COMPARABLE

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$ 64,105,000	$ 64,105,000	$ 69,175,000	$ 64,092,000
1969	71,191,000	66,656,000	72,156,000	68,923,500
1970	71,649,000	68,895,000	76,597,000	71,836,000
1971	89,723,000	89,856,000	89,856,000	90,180,000
1972	99,636,000	105,567,000	121,532,000	112,326,000
1973	110,031,000	125,881,000	155,452,000	125,881,000 1/
1974	106,611,000	125,186,000	135,186,000	125,387,000 2/
1975	110,092,000	105,133,000 3/	128,271,000	126,067,000
1976	106,231,000	127,058,000 4/	127,058,000 4/	136,573,000 5/
1977	129,883,000	140,343,000	150,343,000	145,543,000
1978	155,761,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction authorized by P.L. 93-192.

3/ Excludes funds for research and development contracts which were not considered by the House due to expiration of authorizing legislation.

4/ Excludes fellowships and training grants not considered due to pending legislation ($9,515,000).

5/ Includes $9,515,000 for training programs authorized by the continuing resolution.

NOTES: A/ Prior to 1975, the budget was presented on a mechanism basis rather than program. Funds within the appropriations for 1967 through 1974 for aging research are not identifiable and, therefore, are included.

B/ The figures presented in this table have been adjusted to reflect the transfer of some major functions. This permits a more objective comparison of the amount contained in the budget year with amounts in prior years. For example, the responsibility for funding of General Research Support Grants is no longer the function of this Institute. The amounts originally contained in this account in previous years for this particular program have been removed for comparability purposes.

National Institute of Child Health and Human Development

ACTUAL

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
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	73,098,000	80,800,000	76,095,000
1971	93,303,000	94,436,000	94,436,000	94,760,000
1972	103,232,000	109,668,000	126,093,000	116,427,000
1973	127,244,000	130,429,000	160,000,000	130,429,000 1/
1974	106,679,000	125,254,000	135,254,000	125,455,000 2/
1975	124,897,000	120,232,000 3/	145,000,000	141,966,000
1976	106,062,000	126,889,000 4/	126,889,000 4/	136,404,000 5/
1977	129,883,000	140,343,000	150,343,000	145,543,000
1978	155,761,000			

1/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction authorized by P.L. 93-192.

3/ Excludes research and development contracts which were not considered by the House due to expiration of authorizing legislation.

4/ Excludes fellowships and training grants not considered due to pending legislation ($9,515,000).

5/ Includes $9,515,000 for training programs authorized by the continuing resolution.

Justification

National Institute of Child Health and Human Development

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Research for mothers and children	---	$ 71,458,000	---	$ 75,910,000	---	+$ 4,452,000
Population	---	49,707,000	---	52,751,000	---	+ 3,044,000
Intramural research	199	15,224,000	199	17,667,000	---	+ 2,443,000
Direct operations	129	7,848,000	129	8,157,000	---	+ 309,000
Program management	49	1,306,000	47	1,276,000	-2	- 30,000
Total	377	145,543,000	375	155,761,000	-2	+ 10,218,000

General Statement

The National Institute of Child Health and Human Development is founded on the premise that the early phases of the human life cycle offer opportunities for prevention of diseases, disorders, and social handicaps which may affect the individual at any point in his or her life span. The mission of the NICHD is to seek out opportunities for early prevention of disease and disability, using the tools of the biomedical and behavioral sciences, together with demographic, biometric and statistical techniques. Thus, the NICHD fosters a steady expansion of knowledge on child and maternal health, human development, fertility regulation, and the many factors determing the adaptation of individuals and populations to various economic and environmental conditions. In addition, the NICHD serves as the scientific focal point for a number of federal agencies concerned with improved health for mothers and children and with family planning.

Several problem areas have been singled out for special attention by the NICHD in FY 1978. These are areas in which increased funds can be expected to yield major advances in preventive medicine:

1. Adolescent pregnancy. The rising rate of adolescent pregnancy is a major concern not only because of the burden which pregnancy imposes on the very young mother, but also because the age of the mother is a critical factor in determining an infant's chances of survival. Both of the extramural research centers of the NICHD--the Center for Population Research (CPR) and the Center for Research for Mothers and Children (CRMC)---are supporting studies aimed at reducing the incidence of teenage pregnancy and the biomedical risks associated with it.

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2. Diabetes in pregnancy. The diabetic pregnancy represents a formidable challenge to medical science, because the interaction between the diabetic mother and her fetus is relatively inaccessible to study. Both the CRMC and the Intramural Program are planning increased efforts to improve the control of diabetes in pregnant women and to reduce their infants' vulnerability to respiratory distress syndrome and other disorders which now kill about 18 per cent of the infants of diabetic mothers.

3. Developmental dyslexia and other learning disorders. When an intelligent, seemingly well-instructed child is unable to master reading or some other fundamental skill, the result may be ego-damaging frustration for both child and parent. The NICHD is planning a major initiative to clear up the confusion which currently surrounds the subject of developmental dyslexia and other learning disorders.

4. Nutrition. In FY 1978, the NICHD intends to shift funds from studies of undernutrition to studies of nutritional problems which are now known to occur with greatest frequency in the U.S. population. Particularly, the Institute is interested in clarifying the relationship between nutrition and reproductive processes, and the relationship between early nutrition, obesity and diabetes mellitus.

5. Fertility and infertility. When couples lack adequate and acceptable means of controlling their own fertility, the result may be unwanted pregnancy or inability to conceive a wanted child. The NICHD will intensify its support for studies of reproductive processes in order to alleviate infertility and to provide couples with better contraceptive measures.

In addition to increasing its investment in these problem areas, the NICHD will continue its support of research into the causes, prevention and/or amelioration of birth defects, mental retardation, sudden infant death syndrome, respiratory distress syndrome, prematurity, intrauterine growth retardation, and other diseases and disorders which originate in the earliest phases of the human life span. As the Institute fosters a greater understanding of the genetic and/or environmental factors underlying aberrations of development, it will be helping to develop a healthier adult population for the nation.

An increase of $5,000,000 has been provided by the present Administration for studies of the reproductive process, antenatal and infant nutrition, birth defects and adolescent pregnancy.

Research for Mothers and Children

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Pregnancy and Infancy	---	$27,905,000	---	$29,960,000	---	$+2,055,000
Developmental Biology and Nutrition	---	13,689,000	---	15,565,000	---	+1,876,000
Human Learning and Behavior	---	7,690,000	---	7,828,000	---	+ 138,000
Mental Retardation and Developmental Disabilities	---	22,174,000	---	22,557,000	---	+ 383,000
Total	---	71,458,000	---	75,910,000	---	+4,452,000
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	553	$38,165,000	560	$40,967,000	+ 7	$+2,802,000
Competing	190	14,302,000	201	16,142,000	+11	+1,840,000
Special	63	6,916,000	64	6,944,000	+ 1	+ 28,000
Subtotal	806	59,383,000	825	64,053,000	+19	+4,670,000
Training Programs:						
Individual	164	2,490,000	160	2,431,000	- 4	- 59,000
Institutional	286 1/	4,144,000	274 1/	3,893,000	-12 1/	- 251,000
Subtotal	450 1/	6,634,000	434 1/	6,324,000	-16 1/	- 310,000
Research and Development Contracts	40	5,441,000	41	5,533,000	+ 1	+ 92,000
Total		71,458,000		75,910,000		+4,452,000

1/ Full-time equivalents

Introduction

The NICHD pursues a developmental approach to the prevention of disease and disability, dedicated to improving the health and well-being of mothers, infants, and families as the key to assuring a healthy adult population. The programs of Research for Mothers and Children address the special problems of pregnancy and infancy, developmental biology and nutrition, human learning and behavior, and mental retardation and developmental disabilities.

Mechanisms used in this extramural activity are research grants, fellowships, training grants, and research contracts.

Program Plans, 1978

The 1978 level, an increase of $4,452,000 from 1977, will allow for continued efforts in the following activities.

Pregnancy and Infancy--This program promotes research on pregnancy and maternal health, fetal development, and infant health through the first year of life.

High risk pregnancy conditions such as diabetes mellitus, continue to be of major concern, since they contribute heavily to the population of low birth weight infants and babies who suffer lifetime disease and disability. In 1978, emphasis will be given to diabetic control during pregnancy, the most appropriate gestational age for delivery, and early detection of fetal distress. Another important risk factor is pregnancy during the adolescent period, which is associated with high perinatal mortality and prematurity. Research will focus on genetic, physiologic and environmental factors which contribute to pregnancy-induced hypertension in adolescent girls.

Studies supported by the Institute have provided leads to understanding the process of labor and delivery. For example, it has recently been found that calcium works in a series of events involving hormones which affect the onset of labor. Other research suggests that hormones released by the fetus lead to stimulation of uterine contractions. With knowledge of these mechanisms it may be possible to develop better methods to prevent the premature onset of labor. Advances in understanding fetal growth retardation are encouraging. Scientists have learned that decreased oxygen may be a factor in the lower birth weights of infants born to women who smoke. Further research will be supported to determine the role that insufficiency of uterine circulation plays in slowing the growth of the fetus. Also, studies will be supported to develop clinical tests to identify women at risk for premature labor or for delivery of a low birth weight infant.

Congenital defects are present in about 3.5 percent of all live newborns and account for 20 percent of all infant deaths. Studies on this problem will attempt to determine the points during pregnancy at which interference with normal development can result in abnormalities.

The sudden infant death syndrome (SIDS) is still the leading cause of death among infants between one month and one year old. Research has now shown that the cause of the syndrome is not a single mechanism, as previously believed, but that a number of factors are involved. Research will continue on the causes of the syndrome to identify infants at risk and to develop approaches to prevention.

The CRMC will use its new authority for Major Research Programs to create and support multidisciplinary research efforts focused on several of the major health problems mentioned above: diabetes in pregnancy and infancy, prevention of prematurity, adolescent pregnancy, and SIDS.

Developmental Biology and Nutrition--(formerly part of Growth and Development)--This program supports studies on precursors of adult disease, focusing on congenital defects and developmental immunology, nutrition, metabolism, and endocrinology. The goal is to prevent chronic disabilities by understanding their genetic, nutritional, metabolic, and immunologic antecedents.

Research in developmental biology and human genetics is a vital component of preventive medicine which will help lead to reducing birth defects and finding new therapies for genetic problems. In 1978, it is expected that there will be opportunities to exploit new technologies of the study of cells, and recombinant techniques could lead to the synthesis of scarce or presently unavailable hormones, such as human growth hormones and human insulin.

Infectious disease remains a major health problem in the pediatric age group. Currently funded studies have documented a defect in a type of white blood cell in children which contributes to increased susceptibility to infection in the newborn period. Basic and clinical research on the development of a competent host defense system will be continued in 1978.

Hormones and growth factors are important in determining the growth and development of an individual from conception to adulthood. Proper brain development, bone growth, blood pressure, and sexuality are all hormonally dependent. The causes of excesses or deficiencies of certain hormones during crucial phases of growth are subjects of intensive investigation. Basic research is supported that aims to develop a compound which can be synthesized in large quantities and used as a substitute for human growth hormone. In 1978, support will continue for studies on dwarfism and on puberty, including research on mechanisms which control the onset of puberty. A special emphasis is planned for research on diabetes mellitus as this metabolic disorder affects development in children.

In 1978, support of nutrition studies will turn to the problem of overnutrition and obesity. Obesity is a cosmetic problem for children and adults, but its importance for adult health lies in its role as contributor to hypertension and diabetes mellitus. Recent research suggests that dietary control in childhood may decrease adult obesity, while other studies have clarified the relationship between obesity and diabetes mellitus. In 1978, emphasis will be given to studies that explore the relationship of genetics, nutrition, diet, and intermediary metabolism to obesity, insulin resistance, and diabetes mellitus.

Human Learning and Behavior--(formerly part of Growth and Development)--This program is concerned with human intellectual and social development, the ability to acquire knowledge and skills, to communicate effectively, and to interact in a social setting.

The study of learning disorders is a major concern. Of particular interest are children who display learning disorders in school even though they are of normal intelligence and have adequate vision and hearing. Under-achievement in reading, sometimes called developmental dyslexia, is the most prevalent disorder of learning seen in these children. Research has focused on such topics as speech and language acquisition, development of memory, acquisition of reading capability, and effects of attention on learning.

The study of reading disorders is necessarily multidisciplinary, involving education, linguistics, psychology, and the biomedical sciences. In 1978, it is planned to promote a uniformity in methodology so that different disciplines can exchange information to achieve better understanding, improved therapy, or prevention of reading disorders. Development of a reading test which can be used by all scientists interested in reading disorders will help to standardize the methodology used in these divergent fields and perhaps reveal more than one kind of developmental dyslexia.

An equally important domain of human learning involves social and emotional behaviors. The ability to learn and acquire emotional stability is a requirement for the pursuit of personal happiness. A number of projects supported by the Institute focus upon parent/offspring relationships and family interactions during the very early period of an infant's life as well as during childhood. These studies are needed to understand such socially significant problems as alienation, child abuse, motivation, and violent behavior.

In 1978 emphasis will continue on research into contributions of genetic, environmental, and psychosocial factors to parent-offspring relationships and to individual emotional and social development.

Mental Retardation and Developmental Disabilities--(formerly Mental Retardation)--This program supports research into a wide range of biological, behavioral, and social causes of mental retardation.

The problems of mental retardation may have their origin in parental genetics, abnormal fetal growth, birth trauma, prenatal infection, malnutrition, or psychosocial deprivation. Two areas of research merit special emphasis - the impact of social environmental forces on the intellectual and behavioral development of infants and children; and genetic disorders which contribute to mental retardation.

Approximately five million of the estimated six million retarded persons in this country have no demonstrable central nervous system disease. They are heavily concentrated among the poor and come from families further characterized by low intelligence, as measured by I.Q. tests, and poor education of the mothers. The cause of their retardation may be a combination of factors.

Biologically damaged children, particularly those having neurological problems associated with low birth weight, represent another group vulnerable to learning disabilities and other forms of behavioral impairment. The role of biological and social impairments suggests that improving the child's physical condition, socialization, and learning experiences could prevent mental retardation or minimize its disabling effects.

The early identification of children at risk for faulty development is necessary to assure their timely treatment. New research findings highlight the need for studies to determine the potential benefits and risks of various approaches to early treatment. Other studies will be encouraged that can lead to development of techniques for early diagnosis and identification of delayed development and handicapping conditions.

The NICHD will also support studies to learn more about learning and socializing environments for infants with obvious central nervous system damage. An increasing challenge is the growing number of babies being born to young, adolescent single women, since these babies appear to be particularly vulnerable to central and autonomic nervous system damage. Another focal point is the development of tools for the identification of children who are identified as mentally retarded but who are without central nervous system problems and may have the capability to develop marketable skills. In 1978, research in this area will be encouraged, with support planned for studies on improvements in language skills, cognitive development, and social competence in children.

Genetic disorders are the most prevalent cause of biologically-based retardation. The shift toward genetic diseases as a source of disability has become even more pronounced as improved sanitation, nutrition, and therapeutic drugs have decreased infant morbidity from other causes.

The development of amniocentesis and special tissue culture techniques now makes it possible to identify defective fetuses and to prevent their birth through elective, therapeutic termination of the pregnancy. The Institute has supported the development of an automated system for chromosome analysis that will provide a fast, economical, and accurate system of chromosome analysis for use in research and clinical settings. In addition, epidemiologic surveys of large numbers of individuals, such as newborn populations, can now be expedited by this newly developed technology.

In FY 1978 emphasis will be given to research that will contribute to prevention or amelioration of metabolic abnormalities that are often associated with mental retardation.

This program also supports the twelve Mental Retardation Research Centers. The Centers represent a unique resource for multidisciplinary and collaborative research on the complex causes of mental retardation and associated developmental disabilities.

An increase of $3,000,000 has been provided by the present Administration for studies of antenatal and infant nutrition and other factors of poor nutrition as an antecedent to adult disease. Studies of birth defects, with emphasis on genetic bases of congenital malformations; and of adolescent pregnancy as a significant risk factor associated with infant mortality and prematurity will also be initiated.

Population

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivities:						
Contraceptive Development	---	$ 6,640,000	---	$ 6,885,000	---	$+ 245,000
Contraceptive Evaluation	---	5,195,000	---	5,385,000	---	+ 190,000
Directed Behavioral Research	---	3,365,000	---	3,487,000	---	+ 122,000
Research Fundamental to the Population Sciences	---	34,507,000	---	36,994,000	---	+2,487,000
Total	---	49,707,000	---	52,751,000	---	+3,044,000
Budget Mechanism:						
Research Grants:						
Regular:						
Noncompeting	325	22,461,000	333	23,889,000	+ 8	+1,428,000
Competing	118	8,303,000	136	9,595,000	+18	+1,292,000
Special	25	632,000	25	632,000	---	---
Subtotal	468	31,396,000	494	34,116,000	+26	+2,720,000
Training Programs:						
Individual	93 1/	1,378,000	150 1/	1,292,000	+57 1/	- 86,000
Institutional	117 1/	1,733,000	111 1/	1,586,000	- 6 1/	- 147,000
Subtotal	210 1/	3,111,000	261 1/	2,878,000	+51 1/	- 233,000
Research and Development Contracts	159	15,200,000	164	15,757,000	+ 5	+ 557,000
Total	---	49,707,000	---	52,751,000	---	+3,044,000

1/ Full-time equivalents

Introduction

This activity provides for research on (1) methods for fertility regulation; (2) safety and effectiveness of contraceptive methods; (3) population dynamics and reproductive behavior; and (4) fundamental research on reproductive biology.

The population research program is carried out through the mechanisms of research grants, fellowships, training grants, and research contracts.

Program Plans, 1978

The 1978 level, an increase of $3,044,000 from 1977, will allow for continued efforts in the following activities.

Contraceptive Development - This program will continue to involve efforts to find new methods for fertility regulation in both men and women. Research will involve new drugs for the female or male; improved drug administration; vaginal and uterine contraceptives; a long-acting female contraceptive; periodic abstinence; and studies of how specific drugs act.

The rapid advances in contraceptive methods over the past two decades, and their increased usage, have resulted in a number of medical problems which require research. The issue of safety has become more significant than effectiveness. Considerable inroads have already been made toward improved fertility regulation, through clinical trials on (1) drugs that stop sperm production, (2) postcoital contraceptives, (3) teaching women to recognize their fertile periods, and (4) a long-acting injectable contraceptive.

Further progress has been made in laboratory research on new methods of drug administration and on evaluation of new chemicals as possible replacements for currently available drugs.

Contraceptive Evaluation - This program in contraceptive safety emphasizes the identification of risk factors associated with contraceptive use. Studies include evaluation of the adverse medical effects of contraceptive drugs, consequences of induced abortion, safety of intrauterine devices, and health risks associated with sterilization procedures. This research will help lead to the development of safer methods of contraception.

Recent findings indicate that young adult males exposed to diethylstilbestrol (DES) before birth suffer abnormalities of their reproductive system which may result in infertility. The follow-up of vasectomized men to date has revealed no alterations in their physiological status.

Research will be conducted on the major problems of: (1) the relationship of oral contraceptive use to heart attack, various cancers, diabetes, and other diseases; (2) complications related to intrauterine devices; (3) medical effects of vasectomy and tubal ligation; and (4) safety of new methods of contraception which are ready for clinical trial.

Cancer of the breast and reproductive or other organs is the most important unresolved hazard among women using contraceptive drugs. With the widespread use of oral contraceptives having begun in this country about 10-12 years ago, it is timely now to study the relationship between oral contraceptives and cancer. Studies of cancer of the breast, reproductive organs, and other sites, will be started.

Behavioral Sciences Research - Research on population dynamics in the behavioral and social sciences will continue to be concerned with factors in the growth, distribution, and characteristics of people and the impact of population changes on the health and welfare of individuals, families, and society as a whole.

Research will emphasize factors which influence the birth rate and variations in family size, with special attention to motivation for fertility regulation, changes in the structure and functions of the family, use of contraception by both men and women, and the related effects of changing roles in our society, particularly of women.

Efforts will continue on studies of fundamentals influencing variations in the level of fertility and on the social, economic, and pyschological causes and consequences of varying levels of fertility for the population or segments of it. For example, the effects of family size and the timing of births upon the health and welfare of parents and children are important, because public knowledge of such effects can influence decisions made by individuals regarding age at marriage, timing and spacing of births and completed family size. Research findings have documented the correlation between the decline in U.S. fertility and reduced family size, later age of marriage, and increased uses of contraception.

Research Fundamental to the Population Sciences - Fundamental research will continue on high priority aspects of reproductive biology and social sciences of population.

Research on fertility-infertility is supported to gain knowledge required for the development of safe, effective, and acceptable contraceptive measures; and for the alleviation, amelioration or cure of infertility and reproductive diseases or disorders.

A major effort of this research program is aimed at understanding how hormones act in the control of reproductive events such as ovulation, sperm development, and preparation of the uterus for attachment of the developing embryo.

Investigators supported by NICHD have reported remarkable progress in learning information which could lead to the development of new measures of fertility regulation or for the alleviation of reproductive diseases.

Considerable progress has been made in studies of reproductive processes. New knowledge about gonadotropins, the testis and sperm formation, and events leading to fertilization and implantation of the egg may provide a basis for treatment of certain types of human infertility and for the development of contraceptive measures which do not require the use of hormonal drugs.

Adolescent pregnancy and illegitimacy are increasing in the United States. These developments have serious implications for the well-being of the children and their mothers, who are socially, psychologically and economically less well equipped to assume the responsibilities of parenthood than more mature women. Births to such young mothers run a variety of health risks, such as prematurity, birth defects, and problems related to the frequent use of induced abortion. Furthermore, women who have their first births at very young ages tend to bear additional children at a more rapid rate than those who started their childbearing later, bringing additional health risks to both mothers and children.

Research on adolescent pregnancy will involve such specific issues as adolescent sexual behavior, use or non-use of contraception among sexually active adolescents, and factors such as abortion, marriage, adoption, or raising the child out of wedlock. Studies will also deal with the psychological and social consequences of teenage pregnancy.

Research will be conducted on induced abortion and its effects on subsequent pregnancy, to help determine the extent to which any increased risk is related to particular methods of abortion. Studies will also be initiated to determine whether the use of contraceptive drugs by adolescent girls exposes them to special risks, and if the use of oral contraceptives contributes to birth defects and low birth weight. Studies of high risk pregnancy have confirmed an increase in congenital malformations among the offspring of women who have been exposed to contraceptive drugs early in pregnancy.

Nutrition has a direct effect on reproductive performance in various ways, such as influencing the span of reproductive life and infant survival. The research to be emphasized in this area includes involvement of dietary factors in reproductive processes, the relationship between contraceptive use and nutrition, and the role of nutrition in population dynamics. Studies will cover the relationships between nutrition and reproductive potential, nutrition and reproductive outcome, maternal nutrition and breast feeding, and effects of fertility regulation methods on nutrition.

An increase of $2,000,000 has been provided by the present Administration for studies of the reproductive process, including the basic science of sperm formation and fertilization of the egg.

Intramural Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Budget Mechanism:						
Laboratory and Clinical Research..	183	$14,545,000	183	$16,985,000	---	+$2,440,000
Epidemiology and Biometry.....	16	679,000	16	682,000	---	+ 3,000
Total.....	199	15,224,000	199	17,667,000	---	+ 2,443,000

Introduction

The Intramural Research program covers the Institute's own staff and facilities for research on the biomedical and behavioral aspects of human development relating to reproductive biology, population, and maternal and child health, and includes epidemiologic and biometric studies in areas of high priority to the NICHD.

Program Plans, 1978

The net increase of $2,440,000 in Laboratory and Clinical Research, consists of a mandatory decrease of $14,000 for one less day of pay in 1978; offset by a program increase of $700,000, an increase of $119,000 for mandatory increases such as within-grade increases and $1,635,000 for payment for centrally furnished services.

The net increase of $3,000 in Epidemiology and Biometry is for $4,000 in mandatory increases such as within-grade increases; offset by a mandatory decrease of $1,000 for one less day of pay in 1978.

Laboratory and Clinical Research:

Population and reproduction--The intramural program in reproduction research focuses on refinement of our knowledge of the hormonal interactions which are necessary for female and male fertility. This area of study has begun to move rapidly in the past few years, and the information obtained from basic studies has been almost immediately applicable or relevant to field studies. As greater understanding of the structure of hormones and their sites of attachment within receptor cells is gained, investigators have been in a position to learn how to inhibit this attachment. Conversely, through better understanding of the nature of these cell-site receptors, studies of methods to stimulate the formation of these receptors become feasible. Thus,

a new parameter of the control of fertility is opening, and the applications of these findings are already beginning to occur. Additional work on these new leads will be undertaken in 1978.

Institute scientists have completed studies of a condition called anorexia nervosa, which involves a decreased desire to eat and leads to marked emaciation. This condition is of unknown cause and is on the increase worldwide. However, NICHD studies have shown that anorexia nervosa is associated with an imbalance of the hormones necessary for reproduction. The condition thus provides us with a model of altered metabolism which is controlled by the central nervous system through the sex hormones.

Maternal and Child Health--Several laboratories focus on different areas which are important to the improvement of maternal and child health. Pediatric researchers are studying the requirements for optimum nutrition in infants who are abnormally small at birth. They are also studying the mechanisms of lung maturation and function in the newly-born. Geneticists are seeking better methods for diagnosing and treating infants and children with inborn errors of metabolism. Their work includes a study which addresses the genetic susceptibility of the individual to chemicals which cause malformations when the fetus is exposed, and to agents which predispose to cancer later in life. The role of galactose (found in milk sugar) has confounded infant nutritionists for years. It is now becoming clear that galactose plays an important role in improving sugar metabolism, particularly in infants. These basic genetic studies are essential to broaden our understanding of genetic mechanisms which will ultimately lead to the correction of a number of human conditions of genetic origin. Sophisticated neurobiology studies which are under way are important for developing the information which will be required to contribute to the goal of helping all infants and children attain their maximal intellectual potential. The nervous system is particularly difficult to study because of its differences between species, but progress has been gratifying. Research in each of these key areas will continue in 1978.

Epidemiology and Biometry:

The Epidemiology and Biometry Research Program deals with studies on diseases and conditions relevant to all programs of the Institute, particularly those that are quantitative in character. Clinical trials constitute a major area of activity. In addition, research in statistical methodology is undertaken, and consultation to the other staff in the Institute is provided.

Ongoing studies within this program have demonstrated that a history of previous low birth weight or premature births predicts a mother's increased risk of having these problems again in subsequent pregnancies. The extent of this increased risk suggests that previously identified risk factors are not sufficient to explain the problem fully. Now, studies are being initiated to determine additional factors which appear to be related to the repetition of poor pregnancy outcome. Also, in 1978, studies will be initiated in a metropolitan center in which the level of infant mortality is especially high. The role of nutrition and medical care as related to high mortality rates will be investigated.

Clinical trials continue to receive considerable attention. Results of an evaluation of the safety of ultrasound, a procedure used during pregnancy to help diagnose twinning and to determine the location of the fetus and placenta, will be published showing that the procedure is safe. An analysis of the short-term effects of phototherapy, the use of lights to reduce bilirubin levels in the newborn, will be completed. Data management of two other clinical trials, in

cystinosis (a fatal congenital metabolic disorder in children) and on H Influenzae Type B meningitis (the most common cause of mental retardation and other health problems in childhood), will continue.

Comparisons will be made of trends in breast feeding practices among selected groups of the population. Information to be analyzed in this study will be obtained from surveys by the National Center for Health Statistics.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amt.	Pos.	Amt.	Pos.	Amt.
Direct Operations.....	129	$7,848,000	129	$8,157,000	0	+$309,000

The net increase of $309,000 is for $71,000 in mandatory increases such as within-grade increases and $250,000 for payment for centrally funded services; offset by a mandatory decrease of $12,000 for one less day of pay in 1978.

Direct Operations are comprised of staff functions which are necessary to help maintain the Institute's research and research support programs. Included in this activity are the scientific and business management staff who administer extramural grants and contracts and who perform statistical and other analyses of both intramural and extramural programs.

In 1978 extramural staff will give their greatest attention to monitoring research areas requiring coordination between the major programs of Population and Research for Mothers and Children--nutrition, adolescent pregnancy, and diabetes, for example--and to developing new emphasis areas such as dyslexia, congenital malformations, and fertility-infertility. Analytical support will continue to identify trends in patterns of Institute support by scientific disciplines, type of research institutions, and relationships between program areas.

The number of grants and contracts awarded in 1978 is estimated at 1,748 and the dollar amount of these extramural activities is estimated at $123,661,000.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amt.	Pos.	Amt.	Pos.	Amt.
Program Management.....	49	$1,306,000	47	$1,276,000	-2	-$30,000

The net decrease of $30,000 consists of mandatory increases of $14,000, such as within-grade increases; offset by a program decrease of $39,000 and a mandatory decrease of $5,000 for one less day of pay in 1978. Two administrative positions have been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

Program management provides for several staff functions which support the Institute's continuing operations. The activity includes scientific and administrative staff who maintain program direction and management services through the Director's immediate office, provide program planning and evaluation assistance to intramural and extramural staff, and conduct programs for public information and dissemination of research results. In 1978, priority in these functions will be placed on new systems for information dissemination and long-term program planning.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Research for Mothers and Children (Public Health Service Act, Title IV, Parts E and I)

1977 Appropriation Pos.	1977 Appropriation Amount	1978 Authorization	1978 Budget Estimate Pos.	1978 Budget Estimate Amount
---	$71,458,000	A/	---	$75,910,000

Purpose: Research for Mothers and Children covers the health and well-being of mothers, children, and families as the key to assuring a healthy adult population.

Explanation: Research in this field includes the period of life from conception through adolescence and centers on the major problems of pregnancy and infancy, developmental biology and nutrition, human learning and behavior, and mental retardation and developmental disabilities. Objectives are pursued through research grants, fellowships, training grants, and research contracts.

Accomplishments in 1977: Principal accomplishments related to pregnancy and infancy included new leads on the process of labor and delivery, more information about the sudden infant death syndrome, and greater understanding about fetal growth retardation. During this period, more was learned about genetics and birth defects, and about normal development of immunity from infection. Studies on learning have clarified the skills involved in fluent reading and have demonstrated the flexibility of intellectual development. Research findings on mental retardation highlighted the need for studies of treatment methods and diagnostic techniques.

Objectives for 1978: High risk pregnancy conditions, such as diabetes mellitus and adolescent pregnancy, will receive greater emphasis, as will problems of the low birth weight infant. Congenital malformations will continue as a priority, and the focus of nutrition research will turn to overnutrition and obesity as well as studies of antenatal and infant nutrition and other factors of poor nutrition as an antecedent to adult disease. Learning and behavior studies will address a new priority of developmental dyslexia and other learning disorders. In mental retardation, encouragement will be given to development of diagnostic tools and treatment methods for which needs have been identified.

An increase of $3,000,000 has been provided by the present Administration to permit emphasis of the antenatal and infant nutrition studies as well as studies of birth defects and adolescent pregnancy.

A/Title IV, Part E - Indefinite
Title IV, Part I - Legislation is pending

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NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Population (Public Health Service Act, Title IV, Parts E and I and Title X, Section 1004)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$49,707,000	A/	---	$52,751,000

Purpose: Population research comprises the primary Federal effort for biomedical, behavioral, and social science research in the population field.

Explanation: The program covers research on development and evaluation of contraceptives, population dynamics, and fundamental problems of reproductive processes. Objectives are pursued through the funding mechanisms of research grants, fellowships, training grants, and research contracts.

Accomplishments in 1977: In contraceptive development, clinical trials have contributed new information on drugs that stop sperm production, postcoital contraceptives, women's fertile periods, and a long-acting injectable contraceptive. Contraceptive evaluation studies have found higher risk of breast cancer among certain women who use the pill, that males exposed to diethylstilbestrol (DES) before birth may suffer from infertility as adults, and there are no physiological changes in men who have had a vasectomy. Behavioral scientists have documented the decline in U.S. fertility as being correlated to changing attitudes about family size, age at marriage, and use of contraception. Fundamental research has produced new knowledge about reproductive processes in relation to problems of fertility and infertility.

Objectives for 1978: Research on contraceptive development will emphasize new drugs, improved drug administration, vaginal and uterine contraceptives, and periodic abstinence. Contraceptive safety studies will be conducted on the relationship of the pill to various diseases, complications related to intrauterine devices, and new methods of contraception ready for clinical trial. Behavioral/social scientists will address problems of adolescent pregnancy and factors influencing family size and birth rate. Other studies will be directed to problems of nutrition and reproduction.

An increase of $2,000,000 has been provided by the present Administration for studies of the reproductive process, including the basic science of sperm formation and fertilization of the egg.

A/ Title IV, Part E - Indefinite
Title IV, Part I - Legislation is pending
Title X, Section 1004 - Legislation is pending

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Intramural Research (Public Health Service Act, Title IV, Part E and Title X, Section 1004)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
183	$15,224,000	A/	183	$17,667,000

Purpose: Intramural Research includes NICHD scientific staff conducting laboratory and clinical research and epidemiologic and biometric studies.

Explanation: Intramural research addresses the problems of population and reproduction primarily through studies on hormonal interactions necessary for female and male fertility. Maternal and child health research focuses on infant nutrition, lung maturation in the newborn, genetics, and the nervous system. Epidemiology and biometry deal with data on the extent and nature of disease and disability.

Accomplishments in 1977: Hormone studies have provided information on the structure of hormones and how they work, opening new leads for studying the control of fertility and infertility. Studies in pediatrics have produced new information which is basic to our understanding of genetic mechanisms that relate to human conditions of genetic origin. Epidemiologists and biostatisticians have gathered data on a mother's risk of having a baby of low birth weight and demonstrated the safety of ultrasound as a diagnostic technique.

Objectives for 1978: Additional work based on leads from hormone studies will be undertaken. Similarly, accomplishments in the variety of genetic and neurobiology studies in maternal and child health will be used as the base for continued research in 1978. Data research will include a study of factors in high infant mortality rates, completion of an analysis of the use of lights to reduce bilirubin, and continuation of data analysis on a metabolic disorder and the most common cause of mental retardation in children.

A/Title IV - Indefinite
Title X, Section 1004 - Legislation is pending

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Title IV, Parts E and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
117	$7,848,000	A/	117	$8,157,000

Purpose: Direct Operations include staff and their supporting costs of doing business who help maintain day-to-day activities of the Institute's research and research support programs.

Explanation: This activity covers the scientific and business management staff who administer extramural grants and contracts and who perform analyses of intramural and extramural programs.

Accomplishments in 1977: Extramural scientist administrators continued surveillance of established programs and completed efforts to identify new priorities in Population Research and Research for Mothers and Children. Grants and contracts business officers processed the award of some 1,775 grants and contracts.

Objectives for 1978: Population Research staff will emphasize development of new programs in fertility-infertility and adolescent pregnancy, while staff handling Research for Mothers and Children will give priority to new studies on dyslexia, nutrition, and congenital malformations. Both major programs will address their areas of necessary coordination with each other. An estimated 1,748 grants and contracts will be awarded.

A/Title IV, Part E - Indefinite
Title IV, Part I - Legislation is pending

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Title IV, Parts E and I)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
49	$1,306,000	A/	47	$1,276,000

Purpose: Program Management provides for the Institute Director and his immediate staff who maintain program direction and management services.

Explanation: These staff, supported by funds for salaries and other operating costs, provide administrative services, planning and evaluation assistance, and public information services for the several program areas of the NICHD.

Accomplishments in 1977: Normal functions of program guidance and central support services continued throughout 1977. Special efforts were initiated for job classification review in personnel management, and for a long-term program planning process intended to complement existing procedures.

Objectives for 1978: Maintenance of activities for program direction and coordination will continue, but will be supplemented by emphasis on developing new systems for information dissemination and long-term program planning.

A/Title IV, Part E - Indefinite
Title IV, Part I - Legislation is pending

MONDAY, MARCH 14, 1977.

RESEARCH RESOURCES

WITNESSES

DR. THOMAS G. BOWERY, DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
DR. JAMES F. O'DONNELL, DEPUTY DIRECTOR, DIVISION OF RESEARCH RESOURCES
RICHARD L. SHAFER, EXECUTIVE OFFICER, DIVISION OF RESEARCH RESOURCES
BERTIL G. BERGQUIST, BUDGET OFFICER, DIVISION OF RESEARCH RESOURCES
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN F. WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. EARLY [presiding]. The committee will come to order.

I want to welcome you, Doctor. I apologize for the delay. The chairman is tied up in a meeting with the Speaker, so we are going to get started.

We have your statement and biographical sketch which will be inserted in the record.

[The biographical sketch and statement follow:]

BIOGRAPHICAL SKETCH

Name: Thomas G. Bowery.
Position: Director, Division of Research Resources.
Birthplace and date: Bellevue, Pa., December 17, 1921.
Education: B.S., Michigan State University, 1943; M.S., Rutgers University, 1948; and Ph.D., Rutgers University, 1951.
Experience:
Director, Division of Research Resources, 1969 to present.
Acting Director, Division of Research Resources, 1968–69.
Associate Director for Operations, Division of Research Facilities and Resources, National Institutes of Health, 1967–68.
Assistant Chief for Operations, Division of Research Facilities and Resources, NIH, 1965–67.
Extramural Operations and Procedures Office, Office of the Director, NIH, 1964–65.
Special Assistant to the Associate Director for Research Grants, Office of the Director, NIH, 1963–64.
Grants Associate, Division of Research Grants, NIH, 1962–63.
Research professor, Department of Entomology, North Carolina State College, Raleigh, N.C., 1959–62.
Research associate professor, Department of Chemistry, North Carolina State College, Raleigh, N.C., 1953–59.
Research assistant professor, Pesticide Residue Laboratory, Everglades Experiment Station. University of Florida, Belle Glade, Fla., 1951–52.
Research associate in chemistry, Office of the State Chemist, New Jersey Agricultural Experiment Station, New Brunswick, N.J., 1948–51.
Research Fellow, Entomology Department, Rutgers University, New Brunswick, N.J., 1946–48.
Association memberships: American Association for the Advancement of Science, American Chemical Society, and Sigma Xi.
Publications: Author of some 23 publications in 7 journals.

STATEMENT BY THE DIRECTOR

Mr. Chairman and Members of the Committee:

It is again my pleasure to appear before you to discuss the budget request of the Division of Research Resources.

The primary mission of the Division of Research Resources is to develop and make available to awardees of the National Institutes of Health many types of resources that are necessary for the biomedical research effort. These resources include special instruments, clinical and research facilities, experimental animals, trained research personnel, and experimental techniques. As an example, our 83 General Clinical Research Centers, located in hospitals around the country, provide NIH awardees with trained staff and specialized research environments where they study patients with diabetes, hypertension, kidney diseases and many other diseases and disorders.

These resources are not targeted to support the research on one particular disease. Our aim is to design resources that can be used in the study of a wide range of health-related problems; to provide them at a reasonable cost; and to make them available to as many researchers as possible. As part of this key role, the Division is able to lessen the duplication and overlap that would occur if each of the categorical institutes maintained all its own resources.

In order to assure the availability of high quality research resources, we support the development of resources as new research needs are identified. For example, we assumed responsibility for initiating the support of the domestic breeding of nonhuman primates for the NIH extramural

programs when it became apparent there would be a shortage of these experimental animals. Through our six diversified programs, the Division has taken an active role in developing research resources that range from high voltage electron microscopes to utilizing and developing the talent of minority scientists and students.

General Clinical Research Centers Program

Before a new treatment becomes accepted medical practice, it passes through a series of studies from animal experiments to controlled testing in humans. In the latter stages of this complex process where research findings are translated into new treatment approaches, 83 General Clinical Research Centers throughout the country provide special facilities, research equipment and trained staff to support the efforts of over 3,300 clinical investigators. In a typical ten bed General Clinical Research Center investigators may be studying patients with diabetes, kidney disease, cataracts, or any number of other disorders. As part of such a Center, the Division supports nurses and other health professionals skilled in research techniques, a laboratory that can perform tests a normal hospital laboratory is not equipped to handle, and usually a diet kitchen with staff to prepare diets for the study of metabolic related disorders.

In the coming year we will continue to encourage use of the Centers for outpatient research studies. Since the Division began an outpatient program in 1970, 60 percent of the Centers have adapted their facilities to accommodate ambulatory patients. Not only has this resulted in savings of hospitalization costs, but has, in turn, allowed the Centers to support more research studies and more patients for each study.

As the NIH moves forward on clinical trials, we will be working with the staffs of our Centers and the categorical Institutes to develop the

additional capability to support such trials. One aspect of this is a joint activity by the staffs of our General Clinical Research Centers Program and Biotechnology Program in collaborating on a project called CLINFO. Its intent is to automate the collection, analysis and sharing of research data for clinical investigators. We expect such automation to pay off with a substantial shortening of the time it takes from the initial study of a new lead to its validation as a safe and better method to prevent or treat an illness. Through a set of contracts we are currently collaborating a computer organization and investigators at three General Clinical Research Centers in the testing of a multi-user desk-top computer specially designed to collect, analyze and make more easily available research data. By making possible and encouraging this kind of collaboration, we hope to assist in the development of special resources that will facilitate the clinical trials process.

Biotechnology Resources Program

Everywhere we turn we see examples of how technology has touched our day-to-day activities. We watch TV programs that are beamed through satellites circling the earth. We drive up to a bank at 3 A.M. and have a computerized teller withdraw money from our checking account. There are countless examples of how technology has been harnessed to speed up communication and to create quicker, easier, more convenient and more accurate ways of doing things. Our Biotechnology Resources Program is serving a similar role for the biomedical research community. Developments in the fields of physics, chemistry, mathematics and computer science are being used for applications to biomedical problems. In workshop settings we continue to bring medical specialists such as

internists, cardiologists and neurosurgeons together with technology experts such as electronic engineers and computer specialists to bring about such application.

The electron probe microanalyzer, initially funded in collaboration with the National Heart, Lung, and Blood Institute, and currently funded by the Division of Research Resources is an extraordinary new instrument capable of ascertaining the elemental chemical content of human fluids, cells or tissue. The instrument can quantitatively measure the location and amounts of the major chemical elements of the human body such as sodium, phosphorus, calcium and sulphur. By analyzing large collections of red blood cells, investigators can observe composition changes as they relate to age, sex, or disease states. This could be used in the study of leukemia, sickle cell anemia, diseases of the bone marrow and many other disease areas. In effect, we have given the biomedical research community one of the sharpest probes available to search for answers at the point where it all begins.

Another newly developed National resource is a cell culture machine that is capable of producing large numbers of cell cultures, and of screening 100 million cultures at one time to detect mutant cells. Its phenomenal screening speed becomes somewhat more comprehensible when you compare it with what the microwave oven has done to conventional cooking time. Up until now, testing for cancer-causing chemicals and drug-induced birth defects has been a protracted and tedious process. This machine promises to accelerate that process so that drugs which cause birth defects as well as chemicals with carcinogenic properties can be identified quickly. Early detection will allow for swift intervention, possibly saving lives and preventing unnecessary suffering and

disability. Cell biologists throughout the country are being invited to use this machine for screening carcinogens, genetic mapping and other research applications.

Chemical/Biological Information-Handling Research Program

Through the Chemical/Biological Information-Handling Program, we have supported the development of special computer tools for scientists to study how drugs and other chemicals affect human patients and experimental animals. The heart of the Program is the PROPHET System, a National computer resource. It consists of a centrally stored collection of powerful, yet easy-to-use computer procedures, accessible from anywhere in the Nation by remote terminals and telephone lines. Our staff is making this service available to an increasing number of NIH awardees. Currently, emphasis is being placed on the use of PROPHET to study the molecular basis of immunity, and to a wide range of other studies such as antifertility drugs, the control of blood pressure and the inhibition of tumor growth. During the coming year we expect to extend PROPHET services to over 140 scientists at 20 institutions in 11 states.

Laboratory Animal Sciences and Primate Research Programs

When a researcher decides to use experimental animals in a study, the choice of a particular kind of animal depends on how useful that animal is as a model for the disorder being studied. Through the Laboratory Animal Sciences Program, the Division continues to support the development of such animal models so that researchers will have available the best possible alternatives short of using human subjects. For instance, we recently supported the development of diabetic mice that have unique advantages over mice which were previously used in diabetes research; cats that exhibit a disorder similar to Tay-Sachs disease in

humans; and rats that can be used to study some allergic disorders. In addition to encouraging the development of new animal models, the Program supports animal colonies of unusual and special value for biomedical research.

As part of this responsibility, our staff has initiated contracts to develop a supply of domestically-bred nonhuman primates. In recent years foreign countries have restricted the exportation of wild-caught primates, causing a shortage of these animals for research studies. Because of their close similarity to humans, these primates are essential to the study of many human diseases and disorders. It is projected that within three to four years, Division-supported contractors will be able to supply 1,900 rhesus monkeys and 400 squirrel monkeys annually. This will represent approximately one-third of the primates needed by the extramural investigators.

The seven Primate Research Centers supported by the Division are also breeding nonhuman primates for use in research conducted at these Centers. Through their breeding efforts, they have been able to produce approximately 50 percent of their annual requirements. These Centers continue to make significant contributions to the study of nonhuman primates in the areas of reproductive biology, lung diseases, infectious diseases, nutritional and metabolic diseases and the behavioral sciences.

Because research on nonhuman primates is in many cases the final step before undertaking human clinical research, our staff has encouraged efforts to disseminate this information to the scientific community. Through a Division-supported Primate Information Center, the world's literature on research using primates is catalogued and indexed. In

the past year, this Center responded to over 800 scientists who wrote for specific bibliographic, abstract and tabular information.

Minority Biomedical Support Program

We consider the development of human resources as one of our most important responsibilities. Through the Minority Biomedical Support Program, we are tapping the talent of ethnic minorities and institutions in an effort to bring their scientists and future scientists into the mainstream of American biomedical research. Currently, 81 colleges and universities with significant ethnic minority student enrollments participate in this Program. One indicator of the success of this Program can be seen in the number of undergraduate participants who are motivated to pursue graduate studies in the health sciences. In 1976, approximately 74 percent of MBS graduates chose advanced studies in biomedical fields, in comparison to only 18 percent of all non-MBS graduates at these institutions.

A necessary step to full participation in the biomedical research community is the publication of research findings in scientific journals. Our staff will continue to encourage and create opportunities for MBS participants to publish their research findings in scientific journals and to present their papers at meetings of professional organizations. Through arrangements made by our staff, one of the Nation's top biomedical journals recently published a special section on the MBS Program that included eight scientific papers by senior faculty scientists and their undergraduate students. This exposure to the research process from experiment to publication in a major scientific journal was a "first" for many of these MBS participants.

In the coming year, our staff will explore the possibility of awarding MBS grants to two-year colleges with special efforts directed toward community colleges serving American Indian students.

Research Resources Information Center

In order to assure that our resources are used as widely as possible and to encourage closer collaboration among scientists who use our resources, we have established a Research Resources Information Center. Through the contract mechanism, our staff is collaborating in the design of an information exchange network that should promote widespread sharing of available resource services, and new analytical research techniques and technologies. Initial projects include the publication of a regular newsletter and the development of a directory of available resource services.

Future Plans and Budget

In 1978 we will continue to support our established resources and to develop selected additional resources as new needs are identified.

The budget request for the Division of Research Resources for FY 1978 is $102,074,000, a net reduction of $35,426,000 below the FY 1977 appropriated amount of $137,500,000. I will be happy to answer any questions and provide whatever additional information you require for the record.

GENERAL RESEARCH SUPPORT PROGRAM

Mr. EARLY. Doctor, your budget eliminates the part for biomedical research support, formerly the general research support grants. Now, we briefly touched on this matter with Dr. Fredrickson. However, I think we should cover it in more detail with you today.

First: How many years have you proposed to eliminate this program?

Dr. BOWERY. I think this is the fourth year that the recommendation has been made to eliminate this program.

Mr. EARLY. With the new administration agreeing with you, I get the feeling the executive branch knows something we don't know. Suppose you take us through the steps that led you to decide to eliminate this program. Dr. Fredrickson, if you want to comment, feel free.

Dr. FREDRICKSON. Thank you.

I think I should point out that this decision is partly due to the necessity to determine a level of priorities within the total NIH budget. It is in this area that NIH has had to make difficult decisions and has chosen to suggest this deletion in the budget of the Division of Research Resources.

But it does eliminate that kind of support for all the Institutes since this is the only place in the NIH budget which supports this type of activity.

Mr. EARLY. Does it eliminate paperwork or just shift laterally to the program?

Dr. FREDRICKSON. Its purpose is to protect other aspects of the NIH program, particularly the ability to maintain our commitments on research grants and the ability to fund new ones. Those abilities would be impaired if we tried to make up this $41 million item by taking it from grant support funds in each of the Institutes.

USES OF BIOMEDICAL RESEARCH SUPPORT FUNDS

Mr. EARLY. Last year you gave us an example of the work supported under this program. You identified the work of a young investigator at the Mayo Clinic on the effects of chenic acid on dissolving gallstones. On page 194 of your budget material I see the same example. If this is the only example of outstanding work that you can point out, then maybe OMB is correct, in saying that the payoff is not worth the investment.

Would you like to try and give some examples and restore my faith in this program?

Dr. BOWERY. That was just one of many examples that showed how a pilot project that was initiated with a fairly small amount of biomedical research support money was then supported by one of the Institutes to become a major factor in developing a large scale clinical trial conducted by one of the categorical Institutes. Some 3,000 pilot projects per year through some 400 institutions are funded through this program. Biomedical research support moneys are used to encourage a number of innovative and creative ideas by young investigators to gather some preliminary data before they submit a full-blown project application to the NIH.

These funds help to assure continuity of funding where a temporary lapse in funding occurs. That is, an investigator has received approval from NIH but for the moment has not received sufficient funds to proceed. This allows the investigator's institution to make an onsite determination to tide the investigator over for a while until the project receives funds from an Institute.

These funds provide opportunities for investigators to pool some of the money that is made available to them by their institution for selected pieces of equipment that may not be easily justified on a single research project grant.

Biomedical research support funds are often used by an institution to help maintain their high standards of laboratory animal care, or to help pay for some computer services that may be needed for a number of investigators, or to help pay for the early stages of designing new instruments. None of these uses requires the full-blown application procedure back through the NIH which would take both time and additional NIH staff energy and additional paperwork.

Now within that context we would be pleased to submit a number of additional specific examples for the record of those general activities.

Mr. EARLY. All right.

Dr. FREDRICKSON. As you know, these grants are awarded by formula to institutions depending upon their ability to compete for research grant and contract support for specific projects. It is, in a sense, a measure of their capability for doing research which allows them to receive these awards.

Several years ago the rules governing the expenditure of these funds were made more stringent by the Division of Research Resources. I have investigated in detail how certain large institutions in the country have been using these funds. I find that the records maintained by the Division of Research Resources are very detailed and permit an experienced scientist and administrator to make a judgment of his own about how effectively this money may have been used to maintain the stability of the research activities in our institution.

I must say I am very much impressed by the quality of decision and the value that I believe was derived from an institution's having these funds to maintain its research enterprise.

Mr. EARLY. Doctor, would you list the outstanding work you have supported within the last 3 years under the biomedical research support program? By "oustanding" I mean projects that have contributed significantly to understanding a particular problem and have significantly contributed to new scientific knowledge. Just supply that for the record.

Dr. BOWERY. I would be happy to.

[The information follows:]

EXAMPLES OF OUTSTANDING WORK SUPPORTED BY
BIOMEDICAL RESEARCH SUPPORT FUNDS

Biomedical Research Support (BRS) funds provide direct or indirect support for much of the research supported by the National Institutes of Health through grants or contracts. Examples of that support in important scientific work are listed below. Also included are profiles of two BRS recipient institutions' use of their grant funds.

Initial Support for Research on Blood Clot Formation

At the Beth Israel Hospital in Boston, Biomedical Research Support (BRS) funds were instrumental in the development of Dr. Robert Rosenberg's research on understanding the mechanism of blood clot formation. Initial findings supported by BRS funds allowed Dr. Rosenberg to compete successfully for more substantial amounts of funding. The clinical implications of Dr. Rosenberg's research are two-fold. First, by determining how the anticoagulant, heparin, blocks the events leading to clotting, it may be possible to tailor an individual's dosage of this drug. Secondly, low doses of heparin may become a widely used therapy in preventing pulmonary embolisms in patients undergoing surgery. If BRS funds were not available, the research supported by this program would not have been given the thrust forward toward getting further support for knowledge aimed at solving this important health problem.

Pilot Project Support in Diabetes Research

The University of Minnesota used some of its Biomedical Research Support (BRS) funds for studies that explored pancreas cell transplants as a potential treatment for diabetes. These studies were instrumental in obtaining additional support from the National Institute of Arthritis, Metabolism and Digestive Diseases. Supported by BRS funds, an investigator demonstrated that when the insulin-producing pancreas cells of newly-born rats were transplanted to diabetic rats, the diabetes was completely reversed and the rats remained symptom-free for more than 18 months. These findings may have important implications for the treatment of human diabetes. With further progress on the problems of human tissue compatibility, pancreas cell transplants may some day provide a significant advance in diabetes treatment.

Support of a Young Investigator's Cancer Research

A young investigator who joined the Georgetown University Lombardi Cancer Research Center in 1975 received start-up support from a Biomedical Research Support (BRS) award. This support enabled him to establish his laboratory research program immediately and produce preliminary data on new anti-tumor compounds. Since this initial study, he has competed successfully for substantial funding from the National Cancer Institute and the American Cancer Society. Without BRS funds providing the initial opportunity to demonstrate his mettle, this young investigator would have experienced delays and some difficulty in attracting support from the traditional sources. Because of the impetus the investigator received from early BRS funding, significant progress has occurred in a short period of time. By the spring of 1976, the young investigator had developed the drug, chlorozotocin, that is both effective against malignant tumors and does not damage vital bone marrow which produces normal blood cells. The drug is

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now in its initial clinical stages and is being tested on 35 volunteer cancer patients. It is hoped that this new drug will permit more intensive chemical treatment of cancer.

Interim Support for Hepatitis Research

Biomedical Research Support (BRS) funds were used to support an epidemiological study of Hepatitis B Virus during its second year when funding from a regular research grant was delayed. The first year of a field study had been conducted when regular funding was temporarily interrupted as a result of relocation of the principal investigator. During the interim BRS funds were used, allowing the study to proceed without interruption. Currently, the longitudinal study is receiving grant support from NIGMS. The investigator is studying the Hepatitis B Virus (HBV) among natives of the Solomon Islands in order to learn more about how the HBV is transmitted and what factors, such as heredity, culture, and environment, affect its transmission. The native population provides an excellent group for studying this problem because the prevalence of symptom-less carriers is 100-fold higher among them than among the U.S. population and extended families are available for studying hereditary influences.

Development of an Epilepsy Animal Model

Biomedical Research Support (BRS) funds were used to develop a strain of gerbils that are now being used in studies of epilepsy. An investigator at UCLA undertook a selective breeding program and produced a strain of gerbils that exhibits brain wave activity characteristic of grand mal seizures. As a result of this BRS-funded effort, the gerbil has been established as a viable model for the study of epilepsy.

Interim Support for Rabies Research

Funds from a Biomedical Research Support (BRS) award to the Wistar Institute for Anatomy and Biology, Philadelphia, sustained the field test of a rabies vaccine when a delay occurred in renewal support for the study. The delay in funding placed the study in jeopardy because large batches of the vaccine would have been lost. BRS funds were the only available support to tide the project over without interruption. In cooperation with the World Health Organization, investigators from the Wistar Institute conducted a field test of the rabies vaccine in Iran. Results showed that the vaccine successfully protected 45 persons who were bitten by rabid dogs and wolves. None of the vaccinated persons suffered adverse side effects. This is the first successful treatment for rabies infection, and it was the BRS Program that provided support at a critical point in the study.

Initial Support for Research in Cellular and Molecular Biology

In the past three years Biomedical Research Support (BRS) funds have supported a series of exciting scientific accomplishments in cellular and molecular biology. Dr. Jonathan King, a young virus researcher, received Biomedical Research Support Grant "start-up" funds when he arrived at the Massachusetts Institute of Technology in Boston for studying how viruses, the tiniest of all parasites, are assembled. Recent studies from his laboratory, now supported by the National Institute of General Medical Sciences, have shown that an "assembly protein" which has a "scaffolding function" is required for this process. Dr. Paul Sypherd, of the University of California at Irvine, is also interested in how ribosomes, the cellular machines which translate information from DNA into functional proteins, are assembled. With the assistance of BRS funds, Dr. Sypherd has identified a protein which is necessary for ribosome assembly which is similar to that of viruses. BRS funds were vital to Dr. Sypherd to generate other sources of NIH funding. Dr. Michael Rossman, a young investigator, received Biomedical Research Support Grant funds to equip and supply his new laboratory at Purdue University at Lafayette, Indiana, and to develop his program on the three-dimensional structure of the enzyme, lactic dehydrogenase. This enzyme plays a key role in cell metabolism; it is, for example, the key step in the utilization of blood lactate as a source of energy for the heart muscle. Dr. Rossman has not only determined the spatial architecture of this molecule but has also shown that one of the basic dogmas of protein chemistry, that the sequence of amino acids determines how a protein is folded, is no longer tenable. Initial BRS funds allowed Dr. Rossman to generate enough data to justify applying for traditional funding. All of these studies on basic cell research are necessary because most diseases of the body are associated with abnormal cellular function and an understanding of the structure and function of viruses, ribosomes and enzymes can provide clues to the processes that result in the malfunction of these components in various forms of diseases. In each of the above cases, the availability of BRS funds allowed new faculty members to embark on their research efforts almost immediately without having to wait for a year or two before obtaining funding from the traditional grant review process.

Supplemental Support for Dental Research

In 1974 and 1975, at the Forsythe Dental Center in Boston, Biomedical Research Support (BRS) funds helped to support research on the cause of periodontosis, a severe destructive disease leading to a rapid loss of tooth-supporting bone in adolescents which usually results in tooth loss before 25 years of age. BRS funds provided partial salary support for a team of scientists, who using new techniques to culture microbes which are sensitive to air, quickly demonstrated that the disease was caused by a hitherto unidentified bacteria and could be controlled by antibiotic therapy. Although only a small amount of BRS funds was needed to supplement other sources of funding, it accelerated the research program to such an extent that in a short span of time a dramatic change occurred in the knowledge concerning this previously untreatable disease.

Pilot Project Support for Cancer Research

The Sidney Farber Cancer Institute, Boston, used its Biomedical Research Support (BRS) award to develop and launch a new drug treatment program for a common type of bone cancer in children. The BRS award was the only available support that the institution, which has little or no unrestricted endowment, could use for developing such a program. The BRS funds were specifically

used for:

- pre-clinical studies on the proposed drugs,
- routine clinical tests to assess appropriate drug dosages, and
- development of new treatment protocols.

Having laid the groundwork with BRS funds, the investigators at the Sidney Farber Cancer Institute applied to the National Cancer Institute and subsequently attracted grant and contract support.

These investigators have pioneered in the specialized treatment of bone cancer patients with high doses of the drugs, methotrexate, citrovorum factor "rescue" and adriamycin. This drug therapy has had a major impact on survival and limb preservation. In one study, the drugs were given to 32 newly diagnosed patients after removal of the primary tumor by amputation. In 60 percent of the patients, this has prevented spread of the disease to the lungs, in contrast to the norm of 20 percent in non-treated patients. Additionally, this treatment was given to 21 patients with advanced disease affecting the lungs, and 15 have been diagnosed free of the disease. New investigations raise the possibility of preserving rather than amputating useful, functioning limbs.

BRS funds are currently supporting a study to produce new variations of the drug adriamycin which exhibit greater anti-tumor activity and reduced toxicity.

Development of Central Research Resources

The Massachusetts Institute of Technology Research Laboratory of Electronics used Biomedical Research Support (BRS) funds toward the purchase of apparatus (quadrapole mass spectrometer and multichannel residual gas analyzer) for the development of the molecule microscope. Three varieties of the instrument are being developed: a scanning pinhole molecule microscope, a cold surface molecule microscope, and a scanning desorption molecule microscope. These instruments differ from other microscopes, microprobes, and other charged particle instruments in that there is negligible penetration so that surfaces of biological structures can be studied in a unique way. Molecule microscopes can detect neutral molecules, which leave the surface without having to overcome attraction forces experienced by charged molecules.

New instruments such as these provide information about processes of health and disease not previously available. In some instances they provide information more reliably and quickly, and often at less cost than by previously available techniques.

BRS funds were used by an investigator at the Massachusetts Institute of Technology to purchase and adapt microwave equipment for the detection of breast cancer. The use of microwaves is a promising alternative to the use of X-ray thermography with its attendant risks. BRS funds also provided salary support for a graduate student and technician who worked on the project. In the coming year, a second-generation radiometer that should permit detection of tumors at greater subsurface depths will be ready for testing.

The Community Blood Council of Greater New York, Inc. used a part of its BRS award to set up an automated system for planning and controlling the distribution of blood among 30 hospitals in Long Island, New York. These hospitals transfuse approximately 60,000 units of whole blood and

packed cells each year. A review of the system after its first year in operation showed an improved availability of blood within this region and a reduced loss of blood supplies through outdating.

Support for Central Research Resources

The Institute of Medical Research, Camden, New Jersey, maintains cultures of 1,500 mutant human cells that are used extensively by investigators throughout the country who are studying human genetic diseases and other problems such as aging. Biomedical Research Support (BRS) funds were used to establish a computer storage and retrieval system for data on the cultures. As a result, this national resource has increased its value and usefulness.

BRS funds were used by the National Magnet Laboratory at Massachusetts Institute of Technology for initial costs of recruiting an expert on pulsed, high-frequency nuclear magnetic resonance spectrometry. This expert completed a team of scientists who will develop a new complex instrument system that will apply highly advanced knowledge of physics to the understanding of the fundamental molecular basis of human disease. The system will be available to any and all qualified researchers, regardless of their institutional affiliation.

At Washington University School of Medicine, St. Louis, BRS funds provided partial support for a mass spectrometer facility. This facility has been used extensively in studies of infants to learn how the immature individual converts protein to carbohydrate and to study disorders of such conversion that cause seizures as a result of abnormally low levels of carbohydrates. Use of the mass spectrometer facility makes it possible to perform these and many other varied clinical studies without the administration of radioactive compounds.

Profiles of Two Biomedical Research Support Recipient Institutions' Use of Their Grant Funds

City of Hope Medical Center

BRS Award - 1976	$149,926	(6.3% of entitlement)
Entitlement (PHS research grants)	$2,376,948	

Summary of Latest Annual Progress Report

13 Projects Awarded	$48,558
Average support per project	$3,735
Range $311 - $14,423	
Animal Facilities	$55,151
Instrument Shop	$6,575

Project Support

Interim salary support for investigation on synthesis of mammalian trisomics.

Supplies for subsequently funded development of technique to transfer nuclei between cells.

Interim support for subsequently funded resubmission of competing renewal application for study that demonstrated insulin requirement for embryonic cell differentiation in Drosophila, and that hydroxyurea causes developing nerve and muscle cells to differentiate into giant cells with functioning axons that transmit electrical impulses across synapses to elicit contraction in the muscle cells.

Videotape recorder for use by two investigators.

Immunologist recruited to collaborate with a clinical investigator in developing new approaches to cancer immunotherapy.

Partial start-up salary for basic scientist to synthesize radioactive-labelled compounds for investigations throughout the hospital.

Pilot study produced preliminary data on cerebellar correlates of motor performance that greatly strengthened application for other funding.

Temporary salary support for a research technician during delay in grant funding prevented interruption in subsequently funded research on nuclear and mitochondrial RNA and protein synthesis in brain.

Establish tissue culture procedures for research on the development of electrophysiologic excitability of cells and tissues pending resubmission of grant application that was approved and funded.

Partial salary support of investigator for three months to permit completion of a project in lipid research.

Animal Facilities

Parial support for a Large Animal Facility and a Vivarium.

Developed technical skills of animal care personnel in dissection and surgery that resulted in improved progress of research projects using animals and more productive use of research technicians.

Department of Electronic Instrumentation

Repair and calibration of instruments purchased by research project grants.

Develop and adapt instruments for greater effectiveness and new more useful applications.

Shared use of instruments was achieved.

Case Western Reserve University School of Medicine

BRS Award - 1976	$261,305 (3.7% of entitlement)
Entitlement (PHS research grants)	$6,983,875

Summary of Latest Annual Progress Report

28 Research Projects Supported (includes 16 pilot projects)	$84,368
Average support per project	$3,013
Range $174 - $9,880	
Computer Facility	$47,703
Central Shared Research Equipment	$73,612
Medical Student Research Assistance	$8,400

Computer Facility

A high speed line printer greatly increased the available services and number of users served by the Biometry Computer Laboratory.

A disc memory controller increased 20 fold the size of the data base that can be manipulated and has led to solution of problems that previously could not be addressed.

A graphic display reduced the time required for graphic output from 80 minutes to one minute and has resulted in interaction between the user and the computer not possible previously.

Over 125 research projects throughout the Medical School have used these new computer capabilities.

Central Shared Research Equipment - most new shared equipment was funded partially from the BRS grant.

Counting Equipment

1. Beta counter
2. Gamma counter
3. Liquid scintillation counter

Fluorescent Photo-microscope

Tricarb Sample Oxidizer

NMR Spectrometer

Role of the Biomedical Research Support Mechanism

As can be seen from the samples listed above, Biomedical Research Support (BRS) funds have served as financial resources to assist current and future NIH-supported investigators to carry on their important scientific work. Usually that work is reported through the accomplishments of all of the NIH Institutes, for BRS funds have provided some direct or indirect support to many of those projects. BRS funds rarely support the entire cost of a major research project--that is the purpose of the NIH regular research project mechanism. Like most other Division of Research Resources' resource grants which provide critical resource support, many important scientific research projects either could not be completed at all, or would cost considerably more time or money to complete in the absence of BRS funds.

Mr. EARLY. You state in your budget justification that these funds are used to pay other research costs not normally met by Public Health Service grants. Will you explain this to the committee? What kind of costs?

Dr. BOWERY. In examining the flexibility with which the institutions have used these funds, we have found expenditures in pilot projects, for example, ranging from in one instance a minimum of $11 to a maximum of some $83,000.

Mr. EARLY. What I am trying to get to, more specifically, is that the justification sounds like it is justifying the establishment of a slush fund.

Dr. BOWERY. It is not a slush fund. The key here is that the biomedical research support program allows the institution to quickly make determinations onsite when something is needed.

Certainly an expenditure of $11 would indicate that probably an investigator needed to purchase a tube or two for a radioisotope counter.

Mr. EARLY. What would be the maximum? Would $11 be one of the minimum commitments? What would be the maximum commitment that could be made within this flexibility?

Dr. BOWERY. We have seen examples where institutions have used the money to recruit a new investigator and sometimes a new cadre of staff members to develop a whole new department that was developing in that institution. The only alternative to using biomedical research support funds would be to put together a half dozen individual research projects in an application for an NIH grant. Such a process could delay the development of that new thrust by many months or years. It is not a slush fund. There is a review group within the institution that works closely with the Chief Administrator or Dean.

DOLLAR RANGE OF BIOMEDICAL RESEARCH SUPPORT GRANTS

Mr. EARLY. How much is the average biomedical research support award and how many institutions receive these awards?

Dr. BOWERY. The average in 1976 was around $96,000.

Mr. EARLY. What are the maximum and minimum awards?

Dr. BOWERY. The minimum runs around $15,000 and the maximum goes as high as about $260,000.

Of over 400 institutions that received the funds last year, 63 percent of those awardees received funds in the range from $15,000 to $100,000 a year. In the upper limits there were only 12 percent of the institutions in the eligible group that received funds from a range of $200,000 to $250,000.

Mr. EARLY. So, therefore, the other 25 percent is between $100,000 and $200,000?

Dr. BOWERY. That is right.

BIOMEDICAL RESEARCH DEVELOPMENT PROGRAM

Mr. EARLY. Now, you also support a biomedical research development award. How does this differ from the regular biomedical research support grant?

Dr. BOWERY. Because Congress had expressed concern about institutions that were not eligible for the biomedical research support award program, that is, institutions which receive less than $200,000 of active Public Health Service research support, it was requested that some type of a competitive program should be launched for institutions that are new, small or developing. The biomedical research development program, which we developed in response to that request, was announced in late 1976 and currently we have 65 applications in hand for review. Awards will be made from the fiscal 1977 budget.

Mr. EARLY. Is this to make a catch-all in order to make everyone eligible?

Dr. BOWERY. No, it is to seek out from among eligible institutions those that have promise for developing increased biomedical research capability. Most of our applications are coming in from the newer health professional schools and the smaller schools that have been established with Federal and State funds and are already in the process of generating new capabilities in the field of biomedical research.

Mr. EARLY. But doesn't that make it so broad that there are no restrictions, that we are giving no incentives to be good in the business, but that we are going to catch everyone?

Dr. BOWERY. Well, the difference between the biomedical research support award and the biomedical research development award is that the latter one is highly competitive. Out of the 65 applications, we probably will only fund 12 institutions.

Mr. EARLY. But isn't it competitive only among those programs that were not eligible for the other grants?

Dr. BOWERY. Competition will be among those groups that feel they fall within the instructions that the Congress gave us regarding assisting the new, smaller, and developing institutions.

Mr. EARLY. How many institutions receive this award and what is the average amount of these grants?

Dr. BOWERY. We have not made any of those grants as of yet. The program was initiated under fiscal 1977 funds. We probably won't be making actual awards until later in this calendar year.

Mr. EARLY. Has a range been set for the size of these grants?

Dr. BOWERY. The range will be approximately $100,000 a year for 3 years, possibly with one renewal for 3 years. But we have not yet made that final decision.

GENERAL CLINICAL RESEARCH CENTERS

Mr. EARLY. Doctor, there is one area of major increase in your budget, namely, the clinical research centers. Suppose you tell us why you need an additional $8 million for this program.

Dr. BOWERY. Basically that breaks down into three components: $4 million of the $8 million would be used to cover the increased cost in maintaining the present operations of the 83 centers. This program has had an unusually high inflationary rate, particularly in the area of hospitalization and personnel costs.

With the increase of $4 million we would hope to stabilize the activities of the 83 centers.

An additional $3 million would be used to bring the research patient occupancy up to the optimal level. It has been recommended by our National Advisory Council that we fund approximately 200,000 patient days rather than the current allocation of 173,000 patient days. We will use part of that $3 million to increase the activities in our out-patient program which is currently running about 40,000 out-patient visits. We would like to increase to approximately 75,000 out-patients.

Mr. EARLY. Are you attempting to shift some of the work of these centers to an out-patient basis?

Dr. BOWERY. Yes. Some 60 percent of the 83 centers have out-patient capability and we are trying to increase that capability.

Mr. EARLY. So you are trying to shift to a greater emphasis on an out-patient basis?

Dr. BOWERY. Moving in that direction, yes, sir.

The final $1 million of the $8 million increase would be used to expand what we call our CLINFO project. This is a project in which we are adapting computer technology to make the clinical research process more efficient and to tailor computer hardware and software specifically to clinical research centers.

Mr. EARLY. In your statement there was a lot of talk, emphasis, and concentration on computers. Is all that going to be done for just an additional $1 million?

Dr. BOWERY. We have been supporting this program at a level of a little over $600,000 for the past several years. Those initial funds were used to develop the prototype and develop the dialog between the computer technologists and the clinical researchers. These additional funds would be used to try to expand this computer tool into several other clinical research centers throughout the country, not just the three or four centers in which they are currently being used.

Mr. EARLY. So you need $1 million to develop that?

Dr. BOWERY. Yes. Within that amount we would be doing two things, making the design better and moving these new special tools into other clinical research centers throughout the country.

Mr. EARLY. I have several other questions, Doctor, but the chairman has imposed the 10-minute rule, so we are going to go by the rules. I will supply these questions for the record.

Mr. EARLY. Mr. O'Brien?

BUDGET DECREASE

Mr. O'BRIEN. Maybe Mr. Early covered this, but from a look at your budget could it be argued that the need for research resources is decreasing?

Dr. BOWERY. Most of the decrease comes out of specifically one program and that is the biomedical research support program.

Mr. O'BRIEN. You have two rather interesting illustrations in that area. It seems strange to me that maybe you would not continue the program.

Dr. BOWERY. Well, certainly, in looking at the development of this particular budget it has been recognized by my Division, by the National Institutes of Health, by the Public Health Service, and recently by the Secretary that the BRS program is valuable.

I think the final decision was made on the basis of the priorities afforded to a general institutional support program versus using the funds for more specific categorical-targeted research project grants.

LABORATORY ANIMAL SCIENCES AND PRIMATE RESEARCH PROGRAM

Mr. O'BRIEN. I think you mentioned in your statement that the primate research centers have been able to develop about 50 percent of the need.

Dr. BOWERY. That is correct, sir. This budget calls for a decrease of approximately $2 million in the overall Laboratory Animal Sciences and Primate Research program. With that decrease we would have to reduce the Primate Research Centers activities by about $1 million which would certainly slacken their primate breeding capabilities, eliminate 15 major research programs; terminate 15 scientist positions and approximately 50 technician positions.

We would also have to terminate two of our primate breeding contracts which would reduce that effort by about $500,000. The balance of that $2 million reduction would be taken up by eliminating some nine research grants that are used to help institutions that receive NIH research project grants to meet requirements of the Animal Welfare Act.

Mr. O'BRIEN. Thank you, Doctor.

Thank you, Mr. Chairman.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. EARLY

REDUCTION IN ANIMAL RESOURCES PROGRAM

Mr. EARLY. You are proposing a level of funding for the experimental animal program about 10 percent below last year's level. Almost everybody we talk to says there is a tremendous shortage of high-grade animals. Why, then are you cutting back?

ANSWER. The decision was made because we identified additional support for general clinical research centers as the highest priority in 1978. Expansion of clinical resources is essential to meet the growing requirements of the categorical Institutes as a result of their increased research efforts in such areas as diabetes, arthritis, nutrition, cystic fibrosis, and genetics.

You are correct that there is a tremendous shortage of high-quality research animals. The 10-percent reduction will have its impact in three areas. First, there will be a cutback in our awards to research institutions to help them improve the quality of their animal care programs. Some research institutions do not have facilities, caging, or animal care staffs that enable them to meet all the requirements of the Federal Animal Welfare Act. Second, we will reduce our domestic primate breeding programs. The programs are designed to supply high grade research primates and were initiated because of critical shortages of wild-caught imported animals. Third, there will be a reduction in the research program of our primate research centers. These centers conduct human health related research in reproductive biology, nervous system diseases, heart and vascular diseases, cancer, the effects of air pollutants, and infectious disease using man's closest relatives in the animal kingdom. The reduction in the primate centers budget will result in the layoff of up to 15 scientists and 50 technical personnel.

Mr. EARLY. Would NIH researchers be forced to increase its purchase contracts at a higher cost if this cut were accepted?

ANSWER. There will not be an immediate influence on the cost of animal purchase contracts. Over a number of years the reduction will increase the cost of research itself because research on poorly cared for animals is unreliable

and inefficient. Shortages of primates have already resulted in three- to five-fold price increases. Additional price increases are likely, however, domestic production will not result in lower cost animals because it is expensive itself.

USE OF PRIMATES

Mr. EARLY. Is there any control placed on the scientists at NIH regarding the use of the more advanced animal models such as the rhesus monkey. Does anybody review the use of these resources if they are so scarce?

ANSWER. Yes; the InterAgency Primate Steering Committee of which NIH is the lead agency has developed criteria for the use of primates. The criteria are: That the research proposed can be done best with primates, that is, no other known system or other kind of animal could produce comparable results; that the species of primate proposed is the most appropriate, and that some other more plentiful species would not be adequate; that the number of primates proposed is the minimum that will produce acceptable scientific results; that the primates will not be sacrificed during or at the end of the study except in those cases requiring termination as part of the investigation: that, if sacrifice is deemed necessary, positive action will be taken to share body material when feasible.

NIH is revising its grant application form requiring the investigator to submit specific justification when a scarce or expensive animal such as a primate is used.

REDUCTION TO THE MINORITY BIOMEDICAL SUPPORT PROGRAM

Mr. EARLY. Doctor, there is a tremendous amount of support for increasing the amount of money we put into the minority biomedical support program. Even your own statement indicated you are planning to expand into the 2-year schools. Why then are you proposing to cut funding by almost $1 million? It doesn't seem to make any sense.

ANSWER. This decision was made because we identified additional support for general clinical research centers as the highest priority for 1978. Clinical resources are necessary to meet the increased requirements of the categorical Institutes because of their expanded research efforts in the areas of diabetes, arthritis, nutrition, cystic fibrosis, and genetics. Although this is a serious reduction to this very important program, it will be partially offset by a small increase in the cooperative agreements we have negotiated with the other Institutes.

OTHER NIH SUPPORT TO MINORITY INSTITUTIONS

Mr. EARLY. How much work do you do with the rest of NIH in encouraging support to minority institutions from the regular grant cycle? The $776,000 you talk about is not very impressive for a group with a $2.5 billion research budget?

ANSWER. Prior to the inception of the minority biomedical support program, the number of National Institutes of Health grants awarded to present minority biomedical support investigators was practically nil with the exception of Howard University and Meharry Medical College. None of the other minority institutions was able to compete for regular NIH grants. This situation is improving as a result of the minority biomedical support program. We have established cooperative agreements with a number of the NIH categorical Institutes, whereby they support projects that are relevant to their research missions. In 1976 two Institutes provided approximately $1.2 million of support for minority biomedical support projects. In 1977 and 1978 it is estimated that over $2 million of support will be provided by five of the Institutes.

INTENDED USE OF MINORITY BIOMEDICAL SUPPORT FUNDS BY INSTITUTIONS

Mr. EARLY. You now provide grants to schools with "significant" minority enrollment in addition to the all-black institutions. How do you insure that this money all goes for "minority biomedical support"?

ANSWER. During the review of an institution's application for a minorty biomedical support grant particular attention is paid to the institution's track record of encouraging and assisting minorities to pursue careers in biomedical research. After the grant is awarded it is closely monitored by program staff. Since we cannot require the institutions to discriminate in the selection of

student participants, a few disadvantaged nonminority students have been supported by this program. From data available for the first 4 years of this program, approximately 870 Hispanics and 110 American Indian students have been supported at nonblack institutions. Of those institutions receiving MBS grants, there have been no instances where the intent of the program has not been carried out.

PAYMENT OF INDIRECT COSTS

Mr. EARLY. Doctor, what is your position on the matter of paying indirect costs associated with the minority support program? Do you feel there is justification for excluding these?

ANSWER. I feel that recipients of minority biomedical support grants are being discriminated against and should receive indirect costs payments. They are competitive institutional grants composed of individual research projects similar to other NIH grants which do pay indirect costs. I do not feel there is justification for excluding indirect costs to MBS grantees, since they incur overhead costs the same as grantees of the other Institutes.

Mr. EARLY. GAO has suggested several approaches if we wished to pay these associated costs. Which alternative would you prefer if the committee were so disposed?

ANSWER. We feel that the best alternative would be to change the language of future appropriation acts to exempt the minority biomedical support program from the prohibition against payment of indirect costs on grants for the general support of research.

Mr. EARLY. What would be the percent added onto the funding which would be necessary if these costs were allowed? Is the 16 percent which GAO talks about accurate?

ANSWER. The GAO reviewed indirect costs foregone by recipients of MBS grants for the fiscal years 1974 through 1976. They reported that an additional 16 percent funding would have been required to pay indirect costs in fiscal year 1976. That figure was based upon their study of sample institutions and means that in 1976, an estimated additional $1.2 million would have been needed.

Since 1976, the cost of administering research grants at institutions has risen approximately 2 percent per year which alone would require about 20 percent additional funding to meet indirect costs in 1978. In addition, passage of the National Research Service Award Act of 1974 added the stipulation that financial support for students participating on new MBS research projects would be paid salary and wages rather than stipends. Since the base for computing indirect costs is salaries and wages the increase of this base increases indirect cost payments for the MBS program. The indirect cost rate is set and does not fluctuate as the base is changed. The result is that in fiscal year 1978, an estimated additional 30 percent funding will be required in the MBS program to pay indirect costs, an amount slightly lower than the overall NIH average indirect cost payment.

MINORITY BIOMEDICAL SUPPORT SYMPOSIUM

Mr. EARLY. What is the costs of the MBS Symposium which you sponsor?

ANSWER. The cost of the present symposium sponsored by Xavier University in New Orleans, is built into the total MBS program award made each year to Xavier University. Because of the increase in the number of papers presented, participants attending each year and inflation, the costs have increased each year.

The costs have escalated from $9,000 in 1972 to about $15,000 in 1977, not including the salary of the program director, and other Xavier University staff who assist in the tasks associated with planning and conducting the symposium.

We have an application in house that requests $25,000 for fiscal year 1978. It should be pointed out that this amount does not include the expenses (travel and per diem) for the students and faculty attending. They use travel funds from their own respective MBS grant, institutional funds or a combination thereof.

INCREASING USE OF CLINICAL CENTERS

Mr. EARLY. Now we have talked to you in the past about improving utilization of your clinical centers. Can you tell me what progress you are making in getting more investigators to use the centers?

ANSWER. Several actions are being taken to improve utilization. The first involves physical changes in the general clinical research centers to make them available or suitable to more investigators. Investigators were reluctant to study patients in centers which were isolated from the other patient care facilities, which were located on open wards, or had inflexible arrangements for segregation of sexes and ages. Several of these have been moved or modified. Centers which were operating inefficiently because they were split between several locations have been combined, sometimes with provision of scatter beds. Centers with low occupancy rates were closed, and two new ones opened.

A long-range action to increase the number of investigators carrying out research with patients is the accelerated development of the clinical associate physician (CAP) program. This program supports physicians, who have already completed clinical postdoctoral training, for work experience in a clinical research center which then allows them to initiate a clinical research project.

Within NIH, a coordinating committee composed of clinical research program staff and representatives of the categorical Institutes recommended closer collaboration and information exchange between the Division of Research Resources and various programs of the National Institutes of Health which fund grants for research requiring hospital beds. As a way of apprising various programs of the categorical Institutes of the availability of DRR resources, the Division has initiated a series of "interfacing sessions" with Institute representatives. Finally, the recent organization of clinical research program directors has received DRR support and encouragement as a possible way of encouraging intercenter collaboration and resource sharing which should result in a more widespread use of beds and laboratories.

NUMBER OF INVESTIGATORS USING THE CENTERS

Mr. EARLY. We asked you to insert a table in the record last year showing the number of investigators using the centers—we would like you to update that table?

ANSWER. Last year we showed the number of investigators using these centers in fiscal year 1975 and estimated the number of investigators who would be expected to use the centers in 1976. Due to the new fiscal year dates, the actual data for fiscal year 1976 will not be reported to us until after April 1, 1977. Thus, at this time we have no information to update our estimate for fiscal year 1976. However, that information will be made available to the committee by early summer.

OVERALL OCCUPANCY RATES FOR CLINICAL RESEARCH CENTERS

Mr. EARLY. What was the overall occupancy rates for the centers in fiscal 1976? How does that compare with 1975?

ANSWER. The overall occupancy rate for the clinical research centers was 71 percent in 1975. In 1976 the overall estimated occupancy rate was 80 percent.

Mr. EARLY. Suppose you insert a table in the record showing the number of beds for each center and the occupancy rate for fiscal years 1974, 1975, 1976, and the estimated occupancy rate for 1977.

[The table follows:]

CLINICAL RESEARCH CENTERS
BEDS AND OCCUPANCY

	FY 1974 1/		FY 1975 1/		FY 1976 2/		FY 1977 2/	
	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds.	% of Occ.	No. of Beds	% of Occ.
Duke University	17	83.6	15	99.8	15	80.0	15	100.0
University of Alabama	10	85.9	10	110.1	10	85.0	10	79.1
Ohio State University	10	52.9	10	50.0	8	75.0	8	80.0
Johns Hopkins	21	69.4	16	85.1	16	75.0	16	80.0
Washington Univ.-St. Louis	33	65.4	33	55.6	33	76.2	33	59.8
Univ. Washington-Seattle	16	41.0	12	58.9	12	85.0	15	78.8
Emory University	12	90.8	10	103.3	10	100.0	10	96.4
University of Pennsylvania	10	46.2	10	52.8	8	60.0	8	75.0
University of Michigan	15	86.0	15	88.6	15	96.7	10	100.0 3/
Univ. of Southern California	10	73.2	10	74.5	10	75.0	10	80.0
University of Rochester	8	94.7	8	95.9	8	95.0	8	93.7
University of North Carolina	12	58.9	12	66.3	12	60.0	12	72.8
Cornell University	12	83.2 3/	12	94.5 3/	14	95.7	14	81.0
Northwestern University	8	80.4	8	60.2	8	80.0	8	100.0
Albert Einstein	12	65.0	8	79.2	8	95.0	8	95.0
University of Colorado	18	83.2	18	87.9	18	85.0	18	86.1
Johns Hopkins University	8	50.8	8	52.7	6	80.0	6	70.0
Montefiore Hospital	16	61.9	16	60.6	12	90.0	12	90.0
New England Med. Center	14	55.3	10	79.5	10	75.0	10	95.9
University of Chicago	10	49.2	10	61.3	8	80.0	8	75.0
University of Pittsburgh	10	60.2	10	61.7	8	93.8	8	85.0
Medical College of Wisconsin	10	61.3	7	97.8	7	80.0	7	90.0
University of Iowa	12	101.1	12	84.6	12	90.0	12	90.0
Georgetown University	10	59.4 3/	6	57.8 3/	6	90.05/		
University of Oklahoma	8	88.0	8	66.4	8	85.0	8	80.5
University of Puerto Rico	12	64.5	12	47.6	12	57.0	6	90.0
University of Utah	15	62.2	15	61.8	10	100.0 3/	9	100.0 3/
Virginia Commonwealth Univ.	7	75.4	7	82.0	7	100.0 3/	7	100.0 3/
University of Cincinati	6	77.8	6	108.6	9	80.0	9	80.0
University of Colorado	6	70.6	6	81.8	6	90.0	6	98.7

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CLINICAL RESEARCH CENTERS
BEDS AND OCCUPANCY

	FY 1974 1/		FY 1975 1/		FY 1976 2/		FY 1977 2/	
	No. of Beds	% of Occ.	No. of Beds	% of Occ.	No. of Beds.	% of Occ.	No. of Beds	% of Occ.
Stanford University	16	51.1	12	57.5	12	80.0	12	70.0
Mt. Sinai	9	72.8	9	78.6	9	80.0	9	72.2
University of Texas	10	74.8	10	72.6	10	85.0	10	84.0
St. Christopher's Hosp.	8	79.3	8	66.9	8	75.0	8	77.5
Univ. of California, S.F.	18	72.9	18	60.6	12	103.3	15	81.3
Univ. Hosp. of Cleveland	6	67.3 3/	6	71.5 3/	6	100.0 3/	6	100.0 3/
Stanford University	6	55.3	6	66.1	6	75.0	6	91 9
Univ. of Florida	7	77.4	7	78.4	7	90.0	7	81.0
Univ. of California, S.F.	9	45.7	9	34.3	7	75.0	7	70.0
Child. Hosp. - Pittsburgh	6	55.0 3/	6	60.0 3/	6	75.0	6	68.1
Child. Hosp. - Los Angeles	6	71.4	6	62.8	4	87.5	4	75.0
MIT	12	64.8	10	79.9	10	78.1	12	68.5
Vanderbilt University	21	70.4	21	67.3	21	90.0	21	76.5
New York University	13	87.7	13	89.4	13	80.0	13	88.9
Rockefeller University	30	91.2	30	83.0	30	91.3	30	83.2
Philadelphia Gen. Hospital	8	43.8 5/	-	-	-	-	-	-
University of Vermont	6	57.5	6	50.5	6	65.0	6	70.0
Children's Hospital-Cinncinati	8	60.5	8	60.0	8	65.0	8	60.0
Yale University	15	62.7	14	59.9	14	89.3	14	67.5
Child. Hosp. Med. Ctr.-Boston	10	67.6	10	73.8	10	80.0	10	80.0
University of Washington	6	69.8	6	67.3	4	100.0 3/	-	-
Baylor University	6	93.1	6	74.6	6	52.5 5/	-	-
Baylor University	6	70.2	6	61.4	6	75.0	6	80.0
Child. Mem. Hosp.-Chicago	6	76.9	6	66.5	3	100.0 3/		
Case Western Reserve	8	88.2	8	104.8	8	86.4	8	90.0
University of Tennessee	6	79.3	6	72.9	6	100.0	6	98.7
SUNY-Syracuse	10	68.3	6	77.1	6	100.0	4	80.0
Child. Hosp.-Philadelphia	8	58.4	8	50.8	6	75.0	6	92.0
University of Miami	14	72.6	10	85.8	10	90.0	10	77.9
Health Research, Inc.	10	149.5	10	155.7 5/	-	-	-	-
Child. Hospital, D.C.	5	53.4	5	44.8	3	91.3 4/		
Univ. of Missouri	9	48.1	9	48.4	9	75.0	9	66.1
University of Chicago	6	47.2	6	52.4	4	100.0	4	65.0

CLINICAL RESEARCH CENTERS
BEDS AND OCCUPANCY

	FY 1974 1/		FY 1975 1/		FY 1976 2/		FY 1977 2/	
	No. of Beds	% of Occ.	No. of Beds.	% of Occ.	No. of Beds.	% of Occ.	No. of Beds.	% of Occ.
SUNY-Downstate	8	72.0	8	80.6	6	100.0	6	80.0
University of Pennsylvania	3	96.1 5/	-	-	-	-	-	-
University of Oregon	4	72.5	4	65.1	4	85.0	4	100.0 3/
Bowman Gray	4	55.0	4	64.8	4	70.0	-	-
Temple University	8	75.7	8	71.8	8	75.0	8	70.5
Baylor University	12	74.7	13	78.2	13	90.0	12	75.1
Univ. of Minnesota	8	73.7	10	92.7	10	77.6	10	76.9
Harbor General Hospital	8	67.0	8	78.7	8	75.0	8	80.0
Boston University	8	51.6	8	74.3	8	80.0	8	92.3
Mayo Foundation	12	52.0	12	80.3	10	60.3	10	98.6
University of Mississippi	5	66.3	5	52.4	5	80.0	5	63.7
Children's Hospital-Buffalo	5	59.7 5/	-	-				
University of Texas	12	69.8	12	69.5	12	90.0	12	74.2
Columbia University	4	79.9	8	75.6	12	86.6	12	100.0 3/
University of Arizona	2	94.0	2	49.7 4/	-	-	-	-
Johns Hopkins Univ. 6/	-	-	-	-	-	-	-	-
Albany Medical College	6	47.4	6	47.9	6	70.0	6	86.5
Indiana University	8	61.1	8	59.9	8	75.0	8	71.3
U. of Calif.-San Diego	8		8	64.6	8	80.0	8	78.7
Kansas U. Medical Center	5	113.5 3/	5	115.3 3/	5	100.0	5	100.0 3/
Scripps Clinic	6		6	67.3	6	85.0	6	70.3
University of Virginia	7	59.6	7	71.3	7	80.0	7	70.0
Univ. of California, L.A.	8	77.4	8	92.8	8	100.0	8	100.0 3/
Peter Bent Brigham	16	70.9 3/	16	60.3 3/	18	80.0	18	98.6
Univ. of New Mexico	-	-	-				5	75.0
Beth Israel Hosp.	14	40.8	10	55.2	10	75.0	8	85.0
Univ. of South Carolina	-	-	-	-	-	-	7	76.5

1/ Fiscal Years 74'-75' - Actual % of Bed Occupancy including research and nonresearch patients except for Footnote 3. Excludes outpatients.
2/ 76'-77' - Awarded Occupancy except for footnote 3.
3/ Nonresearch patients are excluded in these estimates. These centers have special characteristics which permit operation of over 100% using nonresearch patients to help offset the costs.
4/ Converted to Scatter Bed Unit.
5/ Phase out year.
6/ Johns Hopkins - Outpatient Unit.

RATIONALE FOR VACANT BEDS

Mr. EARLY. On a separate table show us how much it costs you in fiscal years 1974, 1975, 1976 for the support of empty beds—and give us an estimate for fiscal year 1978?

ANSWER. Optimal occupancy for a clinical research center is 70 percent to 85 percent depending on the size and type of center, and on the nature of the research being conducted. A few centers which have adjacent overflow capacity may exceed 100 percent of the nominal capacity although some beds may remain vacant on other occasions. General hospitals admit patients because of their medical needs; research centers, however, are small wards which admit patients on the basis of their significance as research subjects irrespective of their general health status. The cost of such periods of vacancy is an integral part of the cost of operating a center, that is, it is the cost of doing business. The cost of such vacancies has not been separately accounted for, but is built into the overall cost of center bed space.

Payment for center bed space is negotiated either on the basis of the institution's cost for the space, or as a per diem rate. The choice of the method of payment is that which minimizes the cost per patient-day. For example, in large centers, where the patient load is high, a negotiated flat rate for center space can achieve a lower cost per patient-day, though it may appear to include a "payment" for vacancies.

THIRD-PARTY PAYMENTS

Mr. EARLY. We also have talked in the past about third-party reimbursements under the centers program—how much will you collect in 1977 and 1978?

ANSWER. We estimate that third-party reimbursements will amount to $5.7 million in 1977 and $6.1 million in 1978. These moneys pay for hospital care required apart from costs of the research.

In some centers, an occasional nonresearch patient is admitted through careful administrative control. Such control is necessary to assure that center personnel are not diverted from their research tasks. Consequently, the centers will not admit acutely ill nonresearch patients.

The ratio of third-party reimbursements to the appropriated level will not change significantly in 1977 and 1978.

MR. CONTE

PRIMATE BREEDING

Mr. CONTE. What success have you achieved in increasing the availability of nonhuman primates for research purposes?

ANSWER. The first animals produced from our domestic breeding contracts were distributed for research use in 1976. These included about 100 rhesus monkeys and 40 squirrel monkeys. In our primate research centers program over 1,000 animals were produced for research use in 1976. Most of the breeding programs started in recent years are now nearly stocked with breeders. Altogether, primate breeding projects in this country will produce 6,600 animals for research and other biomedical uses within a few years; this is 15 to 20 percent of the number used in the United States. The importance of primate breeding is emphasized by the fact that all primate species have been listed as either endangered or threatened by the Convention on Trade in Endangered Species of which the United States is a signatory. With moderate expansion breeding can be targeted on critical needs and essential U.S. requirements can be met.

OUTPATIENT RESEARCH

Mr. CONTE. I am pleased to see that you will be encouraging the use of your clinical research centers for outpatient research studies. About how many ambulatory patients did you accommodate last year? What sorts of studies are underway for which you can use outpatient participants?

ANSWER. Based on our latest information, we estimate that approximately 50,000 outpatient visits were accommodated during fiscal year 1976. Studies currently underway that are using outpatient participants include trials of new diagnostic and therapeutic measures in patients with chronic diseases such as coronary artery disease, high blood pressure, and diabetes; and studies of new treatment methods for genetic diseases in children.

BIOTECHNOLOGY PROGRESS

Mr. CONTE. Can you provide some additional examples of successful projects from your biotechnology program?

ANSWER. The following are examples of successful projects from our biotechnology research program:

A mass spectroscopy resource established at Washington University, St. Louis, is being used to measure the levels of antidepressant drugs in hospital patients in order to determine what are the most effective dosages; to measure the amounts of plasticizers that build up in tissue following intravenous feeding using a plastic catheter; and to study placental drug transfer of local anesthetics during childbirth.

Researchers at a mass spectrometry resource have developed a new method to diagnose the disorder neuroblastoma, a cancerous tumor of the nervous system, before clinical manifestations are apparent by separating and identifying a large number of metabolites present in the patient's urine. The usefulness of this technique as a more general diagnostic method is being evaluated.

Investigators at a computer resource have developed a novel technique to measure the extent of injury caused by heart attack in an intact heart accurately, safely, and noninvasively, and to provide diagnostic information needed for selecting and evaluating therapy, using a newly developed instrument called a positron-emission transaxial tomograph.

Investigators at another computer resource have developed a technique, employing ultrasound tomography and computerized ultrasound image analysis which will detect breast cancerous tissue more accurately and safely than current X-ray techniques. This new method may offer a more cost effective and safer approach for mass screening for early detection of breast cancer.

Mr. CONTE. How widely disseminated are the results of the biotechnology program?

ANSWER. Results from resources supported by the biotechnology research program are disseminated to researchers through an ongoing series of workshops on biotechnology topics, through a contract-supported information exchange network for users of the Division's resources, and through the scientific publications channel.

Mr. CONTE. Do you have examples of developments from that program which are in general usage today?

ANSWER. The biotechnology program's successful collaboration with private industry has resulted in commercial development of a radiation treatment planning system, an arrhythmia monitoring system, and a continuous positive airway pressure system for treating infants with respiratory illness. These systems have been and are being sold to hospitals and clinics in this country and abroad.

DISTRIBUTION OF BIOMEDICAL RESEARCH SUPPORT AWARDS

Mr. CONTE. Doesn't the biomedical research support program also help get away from the tendency for Federal biomedical research grants to go to institutions which are already receiving such grants?

ANSWER. In order to be eligible for a biomedical research support award, an institution must receive a minimum of three PHS research support awards for a total of $200,000. However, the proration factors that are used to compute the biomedical research support awards decrease as an institution's PHS research support funds increase. The resulting effect is that institutions receiving smaller amounts of PHS research support receive biomedical research support awards that are up to eight times as much proportionately as those institutions receiving larger amounts of PHS research support.

BIOMEDICAL RESEARCH DEVELOPMENT AWARDS

Mr. CONTE. What institutions have received biomedical research development grants? How much funding will the biomedical research development (BRD) program receive in 1977? Assuming that we continue this program, what would be an appropriate level of funding to maintain the 1977 level and provide for new grants in about the same amount?

ANSWER. The first biomedical research development awards will be made later in fiscal year 1977. We are in the process of reviewing 65 applications from which we will make 12 awards. In 1977, the biomedical research development program

will award approximately $1.2 million. Should the program be continued, $2.4 million would be required in fiscal year 1978 to maintain the awards made in 1977 and provide for 12 new awards.

FUNDS NEEDED FOR CONTINUATION OF THE BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. CONTE. If it were decided to maintain the biomedical research support program at current levels, providing for all continuations and reasonable numbers of new starts, how much would be needed?

ANSWER. If it were decided to maintain the biomedical research support program at current levels, $44,600,000 would be needed in fiscal year 1978. This would include $2.4 million for the biomedical research development program, providing for 12 continuation and 12 new awards.

REQUEST TO OMB FOR BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. CONTE. What was your request to the Office of Management and Budget for the biomedical research support program?

ANSWER. Our request for the biomedical research support program was $47,730,000.

ELIMINATION OF THE BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. CONTE. Aside from O.M.B.'s constraints, in your professional judgment is this proposed elimination justified?

ANSWER. It is extremely difficult to justify the elimination of the biomedical research support program when one sees the kind of results we have already cited. There is no other program at NIH that provides support to research institutions with the type of flexible guidelines that allow them to provide interim support to research projects when lags occur between funding periods; to provide centrally shared resources that no single grant project could justify; to explore new research leads through pilot projects; and, to select and support new investigators. The biomedical research support program has been successful in meeting one of its major objectives, that is, serving as a stabilizing force within the biomedical research community. However, this is not the kind of program where once the objective has been achieved, there is no longer a need for its existence. There is an ongoing need for a program that will provide institutions with support that covers research costs not normally met by PHS research grants. If the biomedical research support program is terminated, institutions will have to find other funding sources to cover these research costs or simply forgo such things as the support of new investigators, the purchase of centrally shared equipment, pilot and feasibility studies, et cetera.

DECREASE IN MINORITY BIOMEDICAL SUPPORT PROGRAM

Mr. CONTE. Why are you proposing a decrease in support for the minority biomedical support program?

ANSWER. The rationale for decreasing the minority biomedical support program was that additional support was needed for the general clinical research centers program in order to keep pace with the increased demands placed on the centers by expanded research efforts in the areas of diabetes, arthritis, nutrition, cystic fibrosis, and genetics. Because of the tight budget situation, the only way the division could be responsive to the need for more clinical research resource support was to reallocate a portion of the funds from nonclinical programs such as the minority biomedical support program.

INDIRECT COSTS FOR THE MINORITY BIOMEDICAL SUPPORT PROGRAM

Mr. CONTE. If we were to decide that the payment of indirect costs to recipients of MBS grants was appropriate, how much additional funding would be required? Does such a decision require a change in the authorizing legislation?

ANSWER. The minority biomedical support program would require an additional $3 million to pay indirect costs. This represents approximately a 30 percent increase in funding. This estimate was developed using the current NIH average ratio of indirect-to-direct costs which is 35 percent. The authorizing

legislation does not have to be changed to allow the minority biomedical support program to pay indirect costs. It can be accomplished by changing the language of future appropriation acts to exempt the minority biomedical support program from the prohibition against payment of indirect costs on grants for the general support of research.

MR. MICHEL

CLINICAL RESEARCH CENTERS

Mr. MICHEL. Are the 83 General Clinical Research Centers receiving any of their funds from other Institutes, and if so, to what extent?

ANSWER. The centers do not receive any direct support from the other Institutes. Eleven centers do, however, have collaborative arrangements whereby the Institutes support specialized beds adjacent to or contiguous with the General Clinical Research Centers. These arrangements generally provide for the sharing of personnel and facilities for research patient care.

Mr. MICHEL. How are patients chosen for these centers?

ANSWER. Patients are admitted to centers based on their suitability for study in approved scientific projects and their willingness to participate. To admit patients to the center, the clinical investigator must submit a detailed project plan to the institution scientific review committee. After approval by this committee, the project is forwarded to a separate Institutional Review Board which reviews the project for appropriateness for human studies and the adequacy of the procedure for obtaining informed consent. Following approval of the project, an investigator may then admit patients to the center for study on that project.

ELECTRON PROBE MICROANALYZER

Mr. MICHEL. Has this electron probe microanalyzer been perfected as yet, or is it still in the development stage?

ANSWER. Electron probe microanalyzers are commercially available both in the United States and abroad. They have been used for many years in the examination of metals, mineral specimens, and other materials and were used, for example, to characterize the rocks and soil returned from the Moon. Use of the instruments in biology and medicine is more recent and experiments in the area of sample preparation and the construction of stages for handling frozen hydrated samples are in progress. Changes in concentrations of calcium, sodium, potassium and phosphorus are sensitive indicators of biological function, and electron probe instruments should make it possible to extend the observations of electron microscopy into areas of physiology and function in both normal and diseased cells.

Mr. MICHEL. Is that a sizable, expensive piece of equipment?

ANSWER. The instrument, with accessories, costs approximately $250,000. Computer controls and automatic systems for data storage and processing add $50,000 to $100,000 onto this cost.

BIOMEDICAL RESEARCH SUPPORT PROGRAM

Mr. MICHEL. Last year we were told that the schools receiving the most Research Resources funds were the same schools receiving the most regular research funds. Is that still the case?

ANSWER. Yes, that is still the case. However, those institutions receiving smaller amounts of PHS research support receive biomedical research support awards that are up to eight times as much proportionately as those institutions receiving larger amounts of PHS research support. The proration factors that are used to compute the BRS awards decrease as an institution's PHS research support funds increase.

Mr. MICHEL. Are you still restricting eligibility for funding under your program to schools receiving at least $200,000 in regular research funds?

ANSWER. Yes. Under the policy guidelines of the biomedical research support program, in order to be eligible an institution must have received a minimum of three PHS research support awards for a total of $200,000.

Mr. MICHEL. How many schools are receiving research resources funds?

ANSWER. It is estimated that 462 biomedical research support awards will be made in 1977. This number includes 12 biomedical research development awards.

PEDIATRIC CLINICAL RESEARCH CENTERS

Mr. MICHEL. What is the present occupancy rate for your child research centers?

ANSWER. There are 11 pediatric units, 5 combined adult and children units, and 1 maternal-child unit. The average estimated occupancy rate of these centers for fiscal year 1977 is 78 percent.

DISCONTINUED SUPPORT OF CLINICAL RESEARCH CENTERS

Mr. MICHEL. Have any centers been discontinued during the past year because of a low benefit-cost ratio? If so, which ones?

ANSWER. Yes. There were six clinical research centers that received phase-out grants in 1976: University of Washington; Health Research—Roswell Park; Baylor College of Medicine; Bowman Gray School of Medicine; Children's Hospital of Buffalo; and Children's Memorial Hospital, Chicago. In 1977 three more centers received phase-out awards: Albany Medical College; Georgetown University; and University of Puerto Rico.

SHORTAGE OF PRIMATES

Mr. MICHEL. What is the current shortage of primates that exists, and at what rate are you closing the gap?

ANSWER. The current minimum requirement for nonhuman primates for bioscientific activities in the United States is about 34,250 animals anually. An optimum supply would be about 48,000 animals, which was approximately the number of primates being used before the shortages began occurring in 1973. This is contrasted with a current supply of about 30,000 animals annually. We have underway domestic primate breeding projects that will produce about 6,600 animals annually. We should close the gap for the minimum need for most species within 2 or 3 years, provided that there is no further reduction in the supply of wild caught animals from foreign countries. However, we are fearful of further supply reductions because all primates are now on appendix II (potentially endangered) of the International Convention on Trade in Endangered Species of which the United States is a signatory. In addition to domestic breeding we are working to stabilize our supply from foreign countries by supporting surveys of primate populations and recommending management procedures.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Research Resources

Amounts Available for Obligation[1/]

	1977	1978
Appropriation.....	$137,500,000	$102,074,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $2,594,000; 1978 - $2,071,000.

Research Resources

Budget Mechanism

	1977			1978		
	No.	FTE[1/]	Amount	No.	FTE[1/]	Amount
Grants						
Special						
Clinical Research.....	83		$ 46,677,000	83		$ 54,658,000
Biotechnology Research....	50		12,413,000	52		12,385,000
Laboratory Animal Sciences and Primate Research.....	78		18,738,000	69		17,194,000
Biomedical Research Support.....	462		40,873,000	--		---
Minority Biomedical Support.....	74		9,711,000	70		8,772,000
Subtotal.....	747		128,412,000	274		93,009,000
Training						
Individual						
Noncompeting.....	4	4	48,000	8	8	103,000
New.....	4	4	56,000	--		---
Subtotal.....	8	8	104,000	8	8	103,000
Institutional						
Noncompeting.....	2	8	136,000	5	18	342,000
Competing.....	--		---	1	4	70,000
New.....	4	14	275,000	--		---
Subtotal.....	6	22	411,000	6	22	412,000
Total Training.....	14	30	515,000	14	30	515,000
Research and Development Contracts.....	25		4,692,000	23		4,367,000
Direct Operations.....	--		3,152,000	--		3,393,000
Program Management.....	--		729,000	--		790,000
TOTAL.....			$137,500,000			$102,074,000

1/ Full time equivalents

DHEW - National Institutes of Health

CROSSWALK - 1977 Column of 1978 Justifications

Research Resources
(Dollars in Thousands)

Program Activity	MECHANISM												
	Research Grants												
	Regular Program		Special Programs		Training Programs								
	Non-Comp.	Comp.	Multi-discip. Centers	Other	Indiv.	Instit.	Res. & Develop. Contracts	Intra-mural, Labs & Clinics Research	Direct Oper.	Program Mgmt.	Disease Control	Cancer Constr.	Program Total
Clinical Research.....				$ 46,677			$ 400						$ 47,077
Biotechnology Research...				12,413			400						12,813
Laboratory Animal Sciences and Primate Research.....				18,738	$104	$411	2,802						22,055
Biomedical Research Support.....				40,873									40,873
Minority Biomedical Support.....				9,711									9,711
Chemical/Biological Information-Handling Research.....							1,090						1,090
Direct Operations.....									$3,152				3,152
Program Management.....										$729			729
Total Obligations...				$128,412	$104	$411	4,692		$3,152	$729			$137,500

DHEW - National Institutes of Health

CROSSWALK - 1978 Column of 1978 Justifications

Research Resources
(Dollars in Thousands)

Program Activity	MECHANISM												
	Research Grants				Training Programs		Res. & Develop. Contracts	Intramural, Labs & Clinics Research	Direct Oper.	Program Mgmt.	Disease Control	Cancer Constr.	Program Total
	Regular Program		Special Programs										
	Non-Comp.	Comp.	Multi-discip. Centers	Other	Indiv.	Instit.							
Clinical Research.....				$54,658			$ 450						$ 55,108
Biotechnology Research...				12,385			450						12,835
Laboratory Animal Sciences and Primate Research.....				17,194	$103	$412	2,302						20,011
Biomedical Research Support.....				--									--
Minority Biomedical Support.....				8,772									8,772
Chemical/Biological Information-Handling Research.....							1,165						1,165
Direct Operations.....									$3,393				3,393
Program Management.....										$790			790
Total Obligations...				$93,009	$103	$412	$4,367		$3,393	$790			$102,074

Summary and Explanation of Changes

1977 Estimated Obligations	$137,500,000
1978 Estimated Obligations	102,074,000
Net Change	-35,426,000

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Increases:				
A. Built-in:				
1. Direct Operations				
a. Within-grade pay increases	--	$ 1,064,000	--	+$29,000
b. Federal Employees Compensation Fund	--	5,000	--	+3,000
c. Service and Supply Fund	--	64,000	--	+7,000
d. Payment for centrally furnished services	--	413,000	--	+38,000
Standard Level User Charge		(47,000)		(+15,000)
2. Program Management				
a. Within-grade pay increases	--	689,000	--	+6,000
Subtotal				+83,000
B. Program:				
1. Research Grants				
a. Special Programs				
(1) Clinical Research	--	46,677,000	--	+7,981,000
2. Training				
a. Institutional				
(1) Noncompeting grants converted from competing status and associated increased costs	--	136,000	--	+275,000
(2) Noncompeting grants converted to competing status	--	275,000	--	+70,000
b. Individual				
(1) Noncompeting grants converted from competing status and associated increased costs	--	48,000	--	+86,000
3. Research and Development Contracts				
a. Clinical Research	--	400,000	--	+50,000
b. Biotechnology Research (CLINFO Program)	--	400,000	--	+50,000
c. Chemical Biological Information-Handling Research	--	1,090,000	--	+75,000
4. Direct Operations	--	3,152,000	--	+188,000
5. Program Management	--	729,000	--	+56,000
Subtotal				+8,831,000
Total, increases				+8,914,000

	1977 Base		Change from Base	
	Pos.	Amount	Pos.	Amount
Decreases:				
A. Built-in:				
1. Direct Operations				
a. One less day of pay	--	$ 1,064,000	--	-$5,000
2. Program Management				
a. One less day of pay	--	689,000	--	-1,000
Subtotal				-6,000
B. Program:				
1. Research Grants				
a. Special Programs				
(1) Biotechnology Research	--	12,413,000	--	-28,000
(2) Laboratory Animal Sciences and Primate Research	--	18,738,000	--	-1,544,000
(3) Biomedical Research Support	--	40,873,000	--	-40,873,000
(4) Minority Biomedical Support	--	9,711,000	--	-939,000
2. Training				
a. Institutional				
(1) Competing grants converted to noncompeting	--	275,000	--	-275,000
(2) Noncompeting grants converted to competing	--	136,000	--	-69,000
b. Individual				
(1) Noncompeting grants completed	--	48,000	--	-31,000
(2) Competing grants converted to noncompeting	--	56,000	--	-56,000
3. Research and Development Contracts				
a. Laboratory Animal Sciences and Primate Research	--	2,802,000	--	-500,000
4. Direct Operations				
a. Decrease of 1 position	49	1,064,000	-1	-19,000
Subtotal			-1	-44,334,000
Total, decreases			-1	-44,340,000
Total, net change			-1	-35,426,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
185	Clinical Research...	--	$ 47,077,000	--	$ 55,108,000	--	+$8,031,000
187	Biotechnology Research.....	--	12,813,000	--	12,835,000	--	+22,000
190	Laboratory Animal Sciences and Primate Research...	--	22,055,000	--	20,011,000	--	-2,044,000
193	Biomedical Research Support.....	--	40,873,000	--	---	--	-40,873,000
195	Minority Biomedical Support.....	--	9,711,000	--	8,772,000	--	-939,000
198	Chemical/Biological Information-Handling Research..	--	1,090,000	--	1,165,000	--	+75,000
200	Direct Operations...	49	3,152,000	48	3,393,000	-1	+241,000
	Standard Level User Charge.....		(47,000)		(62,000)		(+15,000)
201	Program Management..	28	729,000	28	790,000	0	+61,000
	Total Obligations..	77	137,500,000	76	102,074,000	-1	-35,426,000
	Standard Level User Charge.....		(47,000)		(62,000)		(+15,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions	77	76	-1
Full-time equivalent of all other positions	6	6	0
Average number of all employees	85	84	-1
Personnel compensation:			
Permanent positions	$ 1,640,000	$ 1,621,000	$ -19,000
Positions other than permanent	103,000	103,000	--
Other personnel compensation	10,000	10,000	--
Subtotal, personnel compensation	1,753,000	1,734,000	-19,000
Personnel benefits	220,000	220,000	--
Travel and transportation of persons	142,000	185,000	+43,000
Transportation of things	18,000	20,000	+2,000
Rent, communications and utilities	87,000	91,000	+4,000
Printing and reproduction	70,000	70,000	--
Other services			
Project contracts	4,692,000	4,367,000	-325,000
Payment for centrally furnished services	413,000	451,000	+38,000
Other	1,119,000	1,369,000	+250,000
Supplies and materials	24,000	28,000	+4,000
Equipment	35,000	15,000	-20,000
Grants, subsidies and contributions	128,927,000	93,524,000	-35,403,000
Total obligations by object	137,500,000	102,074,000	-35,426,000

Authorizing Legislation

Legislation	Amount Authorized	1978 Budget Request
Public Health Service Act, Title III, Part A. Section 301 -- Research and Investigation in general.....	Indefinite	$102,074,000
Title IV, Part I -- National Research Service Awards Act.....	---1/	---

1/ Authorization expires September 30, 1977. Extension legislation is pending.

Research Resources

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$142,841,000	$142,841,000	$156,141,000	$142,841,000
1969	148,200,000	143,419,000	155,523,000	145,509,000
1970[1/]	130,398,000	134,358,000	145,358,000	137,358,000
1971[2/]	109,678,000	126,901,000	127,501,000	126,901,000
1972	117,269,000	127,160,000	136,648,000	135,648,000
1973	99,013,000	135,767,000	143,694,000	135,767,000[3/]
1974	88,626,000	133,316,000	133,994,000	126,935,000[4/]
1975	82,700,000	124,370,000[5/]	130,000,000	127,200,000
1976	81,093,000	129,100,000[6/]	132,000,000[6/]	130,265,000[7/]
1977	92,342,000	136,299,000	142,299,000	137,500,000
1978	102,074,000			

1/ Excludes Office of International Research, portions of which were transferred to the National Institute of Allergy and Infectious Diseases and the John E. Fogarty International Center.

2/ Excludes the Division of Computer Research and Technology incorporated into the "National Institutes of Health Management Fund" in 1971 and appropriation title changed to "Research Resources".

3/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

4/ Appropriation after reduction as authorized by P.L. 93-192.

5/ Excludes $1,430,000 for contract funds excluded in House Allowance due to lack of authorizing legislation.

6/ Excludes fellowships and training grants--not considered due to pending legislation ($334,000).

7/ Includes $334,000 for fellowships and training grants authorized by the continuing resolution.

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Research Resources

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$ 81,141,000	$ 81,141,000	$ 84,641,000	$ 81,141,000
1969	87,500,000	82,719,000	86,900,000	84,809,500
1970[1/]	69,698,000	73,658,000	79,658,000	63,565,000
1971[2/]	63,701,000	66,201,000	66,801,000	66,320,000
1972	68,069,000	71,948,000	75,948,000	74,981,000
1973	75,009,000	75,073,000	83,000,000	75,073,000[3/]
1974	88,632,000	133,322,000	134,000,000	129,426,000[4/]
1975	82,700,000	124,370,000[5/]	130,000,000	127,200,000
1976	81,058,000	129,065,000[6/]	132,065,000[6/]	130,265,000[7/]
1977	92,342,000	136,299,000	142,299,000	137,500,000
1978	102,074,000			

1/ Excludes the Office of International Research, transferred to the National Institute of Allergy and Infectious Diseases and the John E. Fogarty International Center in 1970.

2/ Excludes the Division of Computer Research and Technology incorporated into the "National Institutes of Health Management Fund" in 1971 and appropriation title changed to "Research Resources".

3/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

4/ Appropriation after reduction as authorized by P.L. 93-192.

5/ Excludes contracts not considered by the House due to lack of authorization.

6/ Excludes fellowships and training grants--not considered due to pending legislation ($334,000).

7/ Includes $334,000 for fellowships and training grants authorized by the continuing resolution.

Justifications

Research Resources

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Clinical Research.....	--	$ 47,077,000	--	$ 55,108,000	--	+$8,031,000
Biotechnology Research.....	--	12,813,000	--	12,835,000	--	+22,000
Laboratory Animal Sciences and Primate Research.....	--	22,055,000	--	20,011,000	--	-2,044,000
Biomedical Research Support.....	--	40,873,000	--	---	--	-40,873,000
Minority Biomedical Support.....	--	9,711,000	--	8,772,000	--	-939,000
Chemical/Biological Information-Handling Research.....	--	1,090,000	--	1,165,000	--	+75,000
Direct Operations.....	49	3,152,000	48	3,393,000	-1	+241,000
Program Management....	28	729,000	28	790,000	0	+61,000
Total Obligations...	77	137,500,000	76	102,074,000	-1	-35,426,000

General Statement

The Division of Research Resources provides the resources for the investigation of a broad range of health problems. These resources include: research animals; technologies, equipment and instruments; highly sophisticated centers for conducting clinical research; a program for the support of institutionally identified research; and a program which supports opportunities for ethnic minorities to participate in biomedical research.

The primary mission of the Division is the development and maintenance of research resources for the use of grantees of the National Institutes of Health. These resources are often developed as part of the investigation of a health problem so that the resource, whether it is a new computer application, a sensitive monitoring instrument, an experimental animal or a specialized clinical environment, can be an important, even a critical factor, in discovering more about diabetes, heart disease, sudden infant death syndrome, glaucoma, cancer or whatever disorder is being investigated.

The Division programs are not targeted to a single categorical disease. The full range of human health problems comes within its purview as it serves the resource needs of all the Institutes. In this role, the Division has developed expertise in the planning, initiation and management of research resources. Its goal is to provide not only the best possible resources, but also to provide them at a reasonable cost and make them available to as many researchers as possible. To accomplish its mission, the Division administers six programs: Clinical

Research, Biotechnology Research, Laboratory Animal Sciences and Primate Research, Biomedical Research Support, Minority Biomedical Support, and Chemical/Biological Information-Handling Research.

Clinical Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Clinical Research.....	88	$47,077,000	88	$55,108,000	0	+$8,031,000
Budget Mechanism:						
Research Grants:						
Special.....	83	46,677,000	83	54,658,000	0	+7,981,000
Research and Development Contracts.....	5	400,000	5	450,000	0	+50,000
Total.....	88	47,077,000	88	55,108,000	0	+8,031,000

Introduction: The General Clinical Research Centers (GCRC) Program establishes and maintains special clinical facilities as resources for clinical investigation to increase knowledge of the cause, progression, prevention and control of human disease. The Program supports 760 dedicated research beds in 83 GCRCs, located in the teaching hospitals of medical schools throughout the Nation. They are staffed by 1,660 full-time research-trained personnel, including physicians, nurses, dietitians, technicians and social workers. Scientists using the GCRC beds for research receive support for their projects through the National Institutes of Health extramural research programs. Investigations on the GCRCs cover the medical research spectrum, including cancer therapy, organ transplantation, obesity, diabetes, disorders of growth, heart disease, high blood pressure, mental retardation and drug metabolism. About 40 percent of research conducted on the GCRCs consists of initial clinical trials of new diagnostic, therapeutic or preventive measures. Through publications, meetings and teaching rounds, these Centers function as major channels for the communication of new medical advances to the biomedical research community, students, hospital staff physicians and community practitioners.

The following summary describes some of the significant facts about the GCRC:

--More than seventy-five percent of the cost of dedicated grant supported research beds awarded by NIH is supported by the GCRC Program.

--More than 1,500 investigators, supported by an estimated $200,000,000 in grants and contracts from the NIH categorical Institutes programs, as well as by 605 grants from industry and private sources, use the GCRCs.

--Approximately 15 percent of the NIH regular and special research grants (totaling $1.4 billion) involve investigators who use the GCRCs.

--A total of about 3,300 biomedical researchers use the GCRCs.

--Just under 3,000 scientific papers and 1,500 abstracts are published each year reporting work performed in the GCRCs. One quarter of these publications concern studies on outpatients. An increasing number of publications over a six-year period of stable budgets and contracting bed resources attests to an increasing efficiency of Center utilization.

During 1977, the Program supported 83 clinical research Centers in roughly 60 percent of the teaching medical institutions of the Nation. Although these Centers can accomodate both children and adults, 20 percent of them focus on pediatric problems.

Program Plans: The amount requested for 1978 will provide support for approximately 83 Centers, including three new Centers which have reached a high level of clinical research activity. Additional funds will be used to increase research patient occupancy and to restore approximately 150 research personnel so that these Centers can operate at levels consistent with their scientific capacity. New funds will be used to expand outpatient research staffing, especially for new clinical trials activities, and to automate research patient records. An outpatient research program was started in 1970 to reduce the costs of research performed in the GCRCs. About 60 percent of the GCRCs have modified their facilities in order to include ambulatory subjects as research patients. The use of outpatients has enlarged the area of research and allowed a greater number of patients to be studied, treated, and maintained as a control group, providing additional research opportunities at lower costs.

In 1978, efforts to apply new technology to clinical research such as mass spectroscopy will be expanded. Computer systems that aid clinical research will be further tested with a view toward wider use on a competitive basis. Increased efforts to encourage scientific collaboration between Centers will be fostered.

	1976 (est.)	1977 (est.)	1978 (est.)
Research Inpatients	184,000	175,000	200,000
Research Outpatient Visits	47,000	40,000	75,000

About 41 percent of the funds supporting the 1,500 NIH-supported investigators using the GCRCs come from the National Heart, Lung and Blood Institute; 18 percent from the National Cancer Institute; 19 percent from the National Institute of Arthritis, Metabolism and Digestive Diseases; 7 percent from the National Institute of Neurological and Communicative Disorders and Stroke; 7 percent from the National Institute of General Medical Sciences; 5 percent from the National Institute of Child Health and Human Development; and smaller fractions from the National Institute of Allergy and Infectious Diseases, the National Institute of Dental Research, the National Eye Institute, and the Alcohol, Drug Abuse and Mental Health Administration.

Biotechnology Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Biotechnology Research.....	53	$12,813,000	55	$12,835,000	+2	+$22,000
Budget Mechanism:						
Research Grants: Special.....	50	12,413,000	52	12,385,000	+2	-28,000
Research and Development Contracts.....	3	400,000	3	450,000	0	+50,000
Total.....	53	12,813,000	55	12,835,000	+2	+22,000

Introduction: The Biotechnology Research (BR) Program supports the development and assures the availability to biomedical investigators of technologies and tools that give them research capabilities previously inaccessable to them. Developments in the fields of physics, chemistry, mathematics, engineering and especially computer science have been applied to biomedical problems, making possible studies that at one time were very impractical or even impossible. High voltage electron microscopes produce sharp and nearly intact pictures of cellular material. Computers not only store research data but serve as powerful analytical tools that allow researchers to compress the time it takes to test and draw conclusions from their studies. Minaturized measuring devices allow investigators to monitor more accurately changes that occur in specific systems or organs of the body. Through its grants and contracts, the BR Program plays a major role in the development of these technologies, and an equally important role in maintaining and making these resources widely available to the biomedical research community.

The following table gives a picture of the diversity of the support received by investigators who use the biotechnology resources to conduct their studies. The data comes from 40 resources supported by the BR Program.

Users of Biotechnology Resources
by Organization Supporting the Research Projects

Organization	Number of Research Projects
National Institute on Aging	1
National Institute of Allergy and Infectious Diseases	28
National Institute of Arthritis, Metabolism and Digestive Diseases	57
National Cancer Institute	99
National Institute of Dental Research	6
National Institute of Environmental Health Sciences	2

Cont.

Users of Biotechnology Resources
by Organization Supporting the Research Projects

Organization	Number of Research Projects
National Eye Institute	5
National Institute of General Medical Sciences	90
National Institute of Child Health and Human Development	43
National Heart, Lung and Blood Institute	89
National Institute of Neurological and Communicative Disorders and Stroke	57
Division of Research Resources	44
National Library of Medicine	3
Health Resources Administration	24
Food and Drug Administration	3
Alcohol, Drug Abuse and Mental Health Administration	67
Other Government Agencies	27
Other Non-Government Organizations	7

Program Plans: At the requested funding level, the BR Program will support approximately 52 resource grants and three contracts. Efforts will be directed toward establishing more national resources and toward exploring new technologies that hold promise of developing into widely-used resources.

Recognizing the high cost of complex technologies and the relatively scarce talent that is available to exploit them, the BR Program initiated and promoted resources that can serve scientists on a national or a broad regional basis. Seven such national resources are in operation. They consist of:

-two one-million volt electron microscopes
-a 360 megahertz nuclear magnetic resonance spectrometer
-a computer with "artificial intelligence" capabilities, i.e., a computer capable of reaching decisions and solving problems through analysis and reasoning similar to functions of the human brain
-a biomedical engineering resource in microelectronics
-large-scale production of mutant cells
-a supply of radioisotope-labelled compounds.

A recently established national resource is the cell culture machine developed by Nobel Prize winner, Dr. Donald A. Glaser, University of California. This machine produces large numbers of cell cultures under rigidly controlled conditions and is capable of screening 100 million cultures at once for mutant cells. Similar to the way the microwave oven has compressed cooking time, this cell culture machine has significantly accelerated the study of certain cancers, drug-induced birth defects and some viral diseases. Cell biologists throughout the country are encouraged to use this machine for screening possible cancer-causing compounds, genetic mapping, virus essays and many other research applications.

The CLINFO project has moved into its second phase. The objective of this project is to adapt computer technology to the special needs of the clinical researcher. Should the CLINFO project be adaptable to widespread use, investigators will be able to significantly shorten the time it takes to complete their studies and publish their results. Through the contract mechanism, the BR Program will continue to fund a computer organization and investigators at three General Clinical Research Centers to test a multi-user, minicomputer system for the handling and analysis of research data. The BR Program will continue to sponsor

workshops in order to disseminate information about the availability of resources and to generate ideas for future technological developments.

These workshops bring together biomedical investigators and experts in the development and use of technologies such as mass spectrometry, electron microscopy, nuclear magnetic resonance and computer applications. The intent of these workshops is to encourage wider use of the available resources, to produce an interplay among the biomedical investigators and technology experts with the hope that new research applications can be found, and to provide the BR Program with possible areas for future development.

Laboratory Animal Sciences and Primate Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Laboratory Animal Sciences and Primate Research....	107	$22,055,000	96	$20,011,000	-11	-$2,044,000
Budget Mechanism:						
Research Grants:						
Special.....	78	18,738,000	69	17,194,000	-9	-1,544,000
Training:						
Institutional:						
Noncompeting.....	2	136,000	5	342,000	+3	+206,000
Competing.....	--	---	1	70,000	+1	+70,000
New.....	4	275,000	--	---	-4	-275,000
Supplemental.....	--	---	--	---	--	---
Subtotal.....	6	411,000	6	412,000	0	+1,000
Individual:						
Noncompeting.....	4	48,000	8	103,000	+4	+55,000
Competing.....	--	---	--	---	--	---
New.....	4	56,000	--	---	-4	-56,000
Supplemental.....	--	---	--	---	--	---
Subtotal.....	8	104,000	8	103,000	0	-1,000
Total Training.....	14	515,000	14	515,000	-2	0
Research and Development Contracts.....	15	2,802,000	13	2,302,000	-2	-500,000
Total.....	107	22,055,000	96	20,011,000	-11	-2,044,000

Introduction:

The Laboratory Animal Sciences (LAS) and Primate Research (PR) Programs assure that biomedical scientists have optimal animals available for use in health-related research. Special emphasis is given to those animal resource activities that affect broad segments of NIH-supported researchers. The two programs are administered through grants and contracts. Training in laboratory animal sciences and medicine is also supported.

Program Plans:

At the requested funding level, the LAS and PR Programs will fund 69 research grants, 9 less than in 1977; 14 National Research Service Awards; and 13 contracts, 2 less than in 1977. The Programs will continue to support similar types of resources and activities as currently funded, but at a reduced level.

Laboratory Animal Sciences:

The LAS Program assists institutions in developing and improving animal resources for biomedical research and training. Currently, the Program supports animal colonies of unusual and special value for research; studies directed at finding animal models which are needed for research on human disease; projects to assist institutions to comply with the legal and policy requirements for care of laboratory animals; laboratories for the diagnosis and control of disease in laboratory animals; research related to improving health care and determining environmental requirements of animals used in research; reference and information centers; domestic breeding of nonhuman primates; and research training of specialists in laboratory animal medicine.

The exploration and development of animal models continued to advance during the past year. Examples include the development of:

--a diabetic mouse that has unique advantages over mice that have previously been used for studies of this disease;

--a cat that exhibits a disorder similar to Tay-Sachs disease in humans;

--a strain of rat that can be used to study allergic disorders.

Through LAS support of diagnostic laboratories, in-depth studies of animal disease problems resulted in over 70 publications and presentations during the past year. In addition, severl of these laboratories have worked closely with commercial producers of laboratory animals to identify and control disease problems.

Because foreign countries have restricted the exportation of wild-caught primates, the LAS Program has undertaken support for the domestic breeding of nonhuman primates. In fiscal year 1976, 600 rhesus monkeys and 12 squirrel monkeys were produced by domestic breeders. Within four years it is projected that the contractors will be able to supply 1,900 rhesus monkeys and 400 squirrel monkeys annually.

The following table summarizes the number and types of activities supported by the LAS Program:

Laboratory Animal Sciences--Fiscal Year 1976

Resources Supported	Number of Projects
Resource-Related Research	10
Animal Models and Special Colonies	24
Basic Improvement of Institutional Animal Resources	21
Animal Disease Diagnostic and Investigative Laboratories	13
Reference and Information Centers	5
Primate Breeding Contracts	7
Animal Resource Contracts	8
Institutional National Research Service Awards	6
Individual National Research Service Awards	4
Total Projects Supported	98

Primate Research:

The Primate Research Centers Program provides specialized facilities and unique research environments for conducting many types of biomedical research using nonhuman primates as animal models. Seven Primate Research Centers are supported at the following locations: Seattle, Washington; Beaverton, Oregon; Davis, California; Covington, Louisiana; Atlanta, Georgia; Madison, Wisconsin; and Southborough, Massachusetts. These Centers continue to make significant contributions to biomedical primatology in the areas of reproductive biology, lung diseases, infectious diseases, nutritional and metabolic diseases and behavioral sciences.

The following table summarizes the personnel and activities supported at the Primate Research Centers:

Primate Research Centers Program--Fiscal Year 1976

Core Staff Scientists	176
Total Core Staff	806
Visiting Scientists	25
Collaborating Scientists	437
Graduate Students	171
Scientists Provided Biological Specimens	291
Papers Published	778
Books Published	12
Primates produced for research	1,100
Projects Supported--Core Staff Scientists	88
Projects Supported--Collaborating Scientists	99

Research using nonhuman primates is often the final step before undertaking human clinical research or clinical trials. In order to make knowledge gained from such research readily available to the scientific community, the Program supports a Primate Information Center. This activity catalogs and indexes the world's literature on research using primates. They do literature searches and produce current bibliographies. They also extract baseline data on primates from the literature and compile it for ready use by the scientific community. During the past year, the Center responded to over 800 scientists who wrote for specific bibliographic, abstract, and tabular information.

Biomedical Research Support

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Biomedical Research Support.....	462	$40,873,000	--	---	-462	-$40,873,000
Budget Mechanism:						
Research Grants: Special.....	462	40,873,000	--	---	-462	-40,873,000

Introduction: The Biomedical Research Support (BRS) Program provides awards to institutions based on a formula applied to the total amount of Public Health Service (PHS) grants received by the institutions. The formula is designed so that institutions with the smaller total of PHS-supported research receive up to eight times as much, proportionately, BRS support as institutions that receive the largest amounts of PHS research support.

The BRS awards are used by the institutions to support pilot and regular research projects; specialized or central resources such as animal facilities or expensive instruments; and other research costs not normally met by PHS grants. Approximately 70 percent of the BRS funds are used to support regular research grants and pilot studies, some of which are later able to compete for regular research grant support from one of the PHS agencies.

In the past year, BRS funds were allocated to institutions that include health professional schools, hospitals, research organizations and research universities. From 1964 to 1975, BRS funds supported at least 18,700 pilot studies and 37,000 research projects. About 25 percent of BRS funds supported central research facilities, providing investigators with services, instruments, equipment and expertise.

The Biomedical Research Development (BRD) Program was established as a new sub-program in 1977 within the BRS Program. It is designed specifically for new, small and developing institutions that have demonstrated a potential for supporting a viable research base, and it will help them to develop and sustain high quality biomedical or behavioral research programs.

In fiscal year 1977, an estimated 462 BRS awards will be made. The BRD Program will make 12 new awards to eligible institutions.

Program Plans: The broad general institutional support provided by grants of this program has accomplished the original objectives of building institutional strength. The best use of research funds in the future is to focus research project grants in targeted priority biomedical research areas. Therefore no funds are requested for the BRS program in 1978.

The following is an example of a pilot project supported with BRS funds. In 1971, a new, young investigator at the Mayo Clinic in Rochester, Minnesota, received $10,000 in BRS funds for a feasibility study to see whether chenic acid could dissolve gallstones. The original pilot study showed that after six months of treatment, half the patients had gallstones reduced in size, and in those patients where gallstones disappeared, no surgery was needed. Currently, the National Cooperative Gallstone Study is recruiting 1,000 gallstone patients in ten major medical centers as the final step in testing chenic acid. Chenic acid shows promise of a nonsurgical therapy for gallstones which would help some 475,000 Americans to avoid the surgeon's knife each year, and would alter the suffering of another 16 to 20 million people who are prone to gallstone attacks.

The following is an example of how BRS funds are used to meet special equipment needs. An investigator at the Children's Hospital in Pittsburgh is developing a mass screening program to detect thyroid hormone deficiency in newborn infants with an aim to prevent permanent mental retardation. In 1972, BRS funds were used to purchase an automatic gamma counter with computer connections, a sophisticated instrument not justifiable by his regular research grant, but necessary for measuring thyroid stimulating hormone rapidly and accurately. To date, this group has detected eight infants with thyroid hormone deficiency, started treatment at an early age and found that all infants have had normal growth and mental development. This investigator has recently received a four-year grant from the Department of Health, Education, and Welfare to continue his studies.

Minority Biomedical Support

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Minority Biomedical Support.....	74	$9,711,000	70	$8,772,000	-4	-$939,000
Budget Mechanism:						
Research Grants:						
Special.....	74	9,711,000	70	8,772,000	-4	-939,000

Introduction: The purpose of the Minority Biomedical Support (MBS) Program is to increase the numbers of ethnic minority faculty, students, and investigators engaged in biomedical research by broadening the opportunities for their participation in biomedical research and by providing appropriate settings in which these goals can be accomplished. The MBS Program is the major focus and effort of the NIH to involve minorities in biomedical research.

Currently, 81 colleges and universities with significant ethnic minority student enrollments participate in this program. The grantees include 57 schools with a predominance of Black students, 17 schools with a large Hispanic student enrollment, 5 schools with a significant number of American Indian students and 2 schools with significant numbers of Hawaiian/Pacific Island students.

The following table summarizes some significant MBS Program accomplishments:

MBS ACCOMPLISHMENTS FOR FY 1976

Number of Participants - 1976

Faculty	514
Other Staff	103
Undergraduates	970
Graduate Students	176
Postdoctoral	3
TOTAL	1,766

Career Choices of Graduates - June 1976

Number of Student Participants Graduated	399
To Advanced Training:	
Number of Student Participants Admitted to Medical School	116
Number of Student Participants Admitted to Dental School	22
Number of Student Participants Admitted to Graduate School	120
Number of Student Participants Admitted to Other Health Related Schools	39
	297*

Research Results

Total Projects Supported	412
Number of Publications	163
Number of Papers Presented (Including Abstracts)	609

Other Grant Support Generated as Result of MBS Program

Number of applications submitted	204
Number of applications approved in 1976 only	127

1976 Grant Support from Sources Other than MBS**

	Number	Amount
NIH	34	$ 776,385
Other Government	66	$2,339,566
Non-Government	37	$ 532,545
		$3,648,496

* Approximately 74 percent of MBS graduates have chosen to do advanced studies in comparison to only 18 percent of all non-MBS graduates at these institutions.

** It has become clear that MBS monies are acting as "seed" funds to channel research projects and personnel into the mainstream of American biomedical research.

Program Plans: At the requested level for 1978, the MBS Program will fund approximately 70 grants, four less than in 1977. Program staff will explore the possibility of awarding MBS grants to two-year colleges with special efforts directed toward community colleges on American Indian reservations.

Because the MBS Program was authorized as part of the General Research Support Program, it is not allowed to pay indirect costs to its grantees. The appropriation language specifically prohibits the use of any appropriated funds for the payment of indirect costs to recipients of general research support grants. Because of this authorization, MBS grantee institutions must pay a larger share of biomedical research costs than institutions receiving support from regular research or program project grants. The General Accounting Office has conducted a study as requested by the House Appropriations Committee on the economic impact on the MBS recipient institutions of the policy of not paying indirect costs. This report may be used to determine if indirect costs should be paid to MBS grantees. If the decision is made by the Congress to authorize payment of indirect costs to recipients of MBS grants, additional funds will be required.

Cooperative agreements with the National Cancer Institute (NCI) and the National Heart, Lung and Blood Institute (NHLBI) have resulted in support for 45 individual projects relevant to the NCI and NHLBI missions. Currently, the National Institute on Aging, the National Institute of Dental Research and the National Institute of Allergy and Infectious Diseases are initiating similar cooperative agreements. In fiscal year 1978, these cooperative efforts will continue and the possibility of extending such agreements to the other categorical Institutes will be explored.

In 1978, the Program staff will continue to encourage and create opportunities for its participants to publish their research findings in scientific journals and present their papers at meetings of professional organizations. Through arrangements made by the Division, one of the nation's top biomedical journals recently published a special section on the MBS Program that included eight scientific papers by senior faculty scientists and their undergraduate students. This exposure to the research process from experiment to publication in a major scientific journal was a "first" for these MBS participants. In addition, an annual symposium for MBS participants has shown a dramatic increase in the numbers attending and the papers presented:

	1973	1974	1975	1976
Numbers Attending	250	470	900	1,300
Papers Presented	76	165	280	370

Chemical/Biological Information-Handling Research

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	No.	Amount	No.	Amount	No.	Amount
Subactivity:						
Chemical/Biological Information-Handling Research.....	2	$1,090,000	2	$1,165,000	0	+$75,000
Budget Mechanism:						
Research and Development Contracts.....	2	1,090,000	2	1,165,000	0	+75,000

Introduction: The Chemical/Biological Information-Handling (CBIH) Program is part of the NIH-wide effort to develop new drugs and make better use of old ones. The Program provides special computer tools to scientists who study how drugs and other chemicals affect human patients and experimental animals. With these computer tools, laboratory and clinical investigators can carry out projects that would be impractical, if not impossible, to do by manual means alone. By helping scientists probe in new and deeper ways into the mechanisms by which specific chemical substances bring about their biological effects, the Program is expanding the knowledge base from which tomorrow's drug therapies will be derived.

The heart of the CBIH Program is the PROPHET System--a national computer resource especially designed for the study of drug action mechanisms and other chemical/biological interrelationships. PROPHET is an integrated collection of powerful yet easy-to-use computer procedures which is based in a central facility, accessible from essentially anywhere in the nation via remote terminals and telephone lines, and supported by a staff strongly oriented toward assisting those life science investigators who are inexperienced in the use of computers. PROPHET is the most nearly comprehensive collection of information-handling capabilities for the study of chemical/biological interactions ever to be synthesized into a single computer system and made available as a service to the life science community in national competition.

In addition to these scientific and technological features, important administrative and economic advantages accrue from the way PROPHET is designed and operated. Because a time-shared computer is employed, all remote installations may be active simultaneously, thereby helping scientists tailor their computer usage to to the needs of their research rather than the other way around. Because a dedicated computer is involved, PROPHET services are available 7 days per week for a minimum of 15 hours per day, and often around the clock. By having investigators at many different geographically separate sites share the resource, users gain access to capabilities they can justify only collectively, and unnecessary duplication of expensive equipment and special expertise is avoided.

Program Plans: During FY 1977 the number of satellite installations supported by the central PROPHET computer is to be increased to 15. This will make PROPHET services available to over 120 users at 17 institutions in 9 states.

Emphasis on use of PROPHET to study the molecular basis for immunity is continuing. A unique collection of data has been accumulated on the structures of

antibodies. Statistical analyses of these data are producing new insights into antibody specificity. This data base also has been generated in hard copy form and distributed within the immunology research community. It is being up-dated on the computer for use in further studies.

Staff of the National Institute of Child Health and Human Development (NICHD) is using the PROPHET system in the management of its contraceptive drug development activities. Files of molecular structure data and biological test results from studies of potential new antifertility agents are collected in the computer and analyzed extensively in a search for substances which are both efficacious and safe.

The System continues to be applied to a wide range of other studies related to drug development in such areas as the control of blood pressure, the inhibition of tumor growth, and central nervous system effects.

During FY 1978 the number of satellite installations supported by the central PROPHET computer is to be increased to 17. This will make PROPHET services available to over 140 users at 20 institutions in 11 states.

In addition to continuing support for projects begun during FY 1977 and previously, emphasis will be placed on computer applications in the area of cancer chemotherapy. Efforts also will be made to employ a commercial computer-based telecommunications network in the interest of reducing data transmission costs.

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Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivity:						
Direct Operations....	49	$3,152,000	48	$3,393,000	-1	+$241,000
Budget Mechanism:						
Direct Operations....	49	3,152,000	48	3,393,000	-1	+241,000

Introduction: This activity supports the Division's extramural program staff who administer and manage the research resource grants, training grants, and research and development contracts. There are no matching fund requirements. The staff of the six programs are responsible for short and long term planning and development of the programs. Because the Division supports research resources in contrast to individual research projects, the staff has expertise in the management of costly and long-term research resources. Considerable effort is directed toward making these resources widely available to the biomedical research community. The staff also is responsible for the review of grant applications prior to review by the National Advisory Research Resources Council. They provide assistance and act as liaison with applicants and grantees. They are responsible for the management of all active resource grants.

Program Plans: An estimated 747 grants, 25 contracts and 14 training awards will be made in 1977. Program staff will continue to administer, manage and review the grants and contracts. Planning and development efforts will continue to assure that the Division's programs are responsive to the needs of the biomedical research community. Division's staff also will continue to participate in the InterAgency Primate Steering Committee as it develops plans to provide an adequate supply of non-human primates for biomedical research.

An estimated 274 grants, 23 contracts and 14 training awards will be made in 1978. The decrease of 473 grants from the 1977 level includes the elimination of the Biomedical Research Support Program.

One administrative position has been removed in 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Subactivity:						
Program Management....	28	$729,000	28	$790,000	0	+$61,000
Budget Mechanism:						
Program Management....	28	729,000	28	790,000	0	+61,000

Introduction: This activity provides the general administration, planning, direction, and coordination of the Division's Programs.

Program Management funds the Office of the Director and its related staff, the Office of Program Analysis, and the Office of Science and Health Reports. The six programs administered are Clinical Research, Biotechnology Research, Laboratory Animal Sciences and Primate Research, Biomedical Research Support, Minority Biomedical Support, and Chemical/Biological Information-Handling Research.

Program Plans: The Division will continue to support, under contract, the development of a Research Resources Information Center. This Center is designed to be an information exchange network for users of Division-supported resources. It is intended to promote a more widespread sharing of available resource services, new analytical or research techniques and technologies. Initial projects include the publication of a regular newsletter and the development of a directory of available resource services.

The Division will continue its "interfacing" meetings with the officials of the categorical Institutes to acquire information about the current needs and the future plans of the Institutes, and to assure that the Division's Programs are responsive to the needs of investigators supported by the NIH.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Clinical Research (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$47,077,000	Indefinite	--	$55,108,000

Purpose: The General Clinical Research Centers Program provides the Nation's clinical investigators with the specialized clinical research resources and facilities needed to increase medical knowledge and to translate the latest laboratory discoveries into improved care for patients.

Explanation: Applications for General Clinical Research Center awards are submitted by public and nonprofit private medical schools, research hospitals, and other medical institutions capable of carrying out well-designed studies in any preclinical or clinical science working with human patients. Applications are reviewed by the General Clinical Research Centers Advisory Committee, program staff, and the National Advisory Research Resources Council. Priorities of awards are based on the nature of the proposed research described in the application. Project grants are awarded in yearly increments for periods from three to five years. There are no matching fund requirements.

Accomplishments in 1977: In 1977, it is estimated that 83 project grants will be awarded, four less than in 1976. Of these, 82 will be continuations of previously funded grants and one new grant which will receive support for the first time.

Objectives for 1978: The estimate for 1978 provides for 83 awards, of which 80 will be continuations and three will be new. Rising hospital-related costs have forced reductions in staff and services available to support patients, resulting in loss of patient days of research over the past several years. The additional funds will permit restoration of patient days of research, thereby increasing the occupancy levels in existing centers. New clinical trial activities and applications of new technologies to clinical research such as mass spectroscopy also will be expanded.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Biotechnology Research (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$12,813,000	Indefinite	--	$12,835,000

Purpose: The Biotechnology Research Program interfaces the knowledge of the physical sciences, mathematics, and engineering to biology and medicine for the advancement of biomedical research. The Program's resources combine the use of sophisticated and expensive instruments and equipment, complex methodologies, and unique human expertise to aid in the solution of important biomedical problems.

Explanation: The Program has an array of diverse resources, all designed to meet one or more specific technological needs of biomedical research scientists. Emphasis is placed on the use of digital computation, mass spectrometry, nuclear magnetic resonance spectroscopy, and electron microscopy in biomedical research. As new, advanced technological tools become pertinent to health research, the Program makes these tools available to other biomedical research personnel in order to accelerate the solutions to biomedical health problems. The trend is for resources to be specialized to specific research needs rather than to have general biomedical research application. The Program's grants are awarded in yearly increments for a project period up to five years and are eligible for renewal. The grant applications are reviewed by several study components (one for each technology in the Program). Contracts are also used to support research. No matching funds are required.

Accomplishments in 1977: In 1977, it is estimated that 50 grants and 3 contracts will be issued. Of these, 46 will be for continuation of ongoing grants and 4 for new grants. There will be 3 renewal contracts issued. The awards will be distributed among the following categories: computer resource grants, biomolecular characterization resource grants, biomedical image and image processing resource grants, biomedical engineering, clinical research data management and analysis development contracts, and other categories.

Objectives for 1978: The estimate for 1978 provides for 52 grants and 3 contracts. Of these, 50 will be continuations and 2 will be for new grants. Three renewal contracts will be awarded. The total funds available will provide for the continued development and shared use of sophisticated equipment in areas such as digital computation, mass spectroscopy, nuclear magnetic resonance spectroscopy, and electron microscopy as tools to be used to improve biomedical research.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Laboratory Animal Sciences and Primate Research (Public Health Service Act, Sections 301 and 412)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$22,055,000	Indefinite	--	$20,011,000

Purpose: The Laboratory Animal Sciences and Primate Research Program supports resource projects that provide, or enable biomedical scientists to use effectively, animals in human health related research. Special attention is given to those animal resource activities that are broadly supportive of the missions of the various NIH components.

Explanation: Grants are made to seven Primate Research Centers which are located in different parts of the Nation. These Centers provide specialized environments where research with these expensive and difficult to handle animals can be conducted in an efficient manner. Nonhuman primates are valuable research subjects because they are biologically more similar to humans than are other animals. The Primate Centers are heavily engaged in research on infectious diseases, reproductive biology, cancer, heart disease, and the nervous system. No matching funds are required.

Project grants and contracts for Laboratory Animal Sciences are made to institutions for the following: support for animal colonies of unusual and special value for research; studies directed at finding animal models which are needed for research on human diseases; projects to assist institutions to comply with the legal and policy requirements for care of laboratory animals; laboratories for the diagnosis and control of disease of laboratory animals; research related to improving control of disease of laboratory animals; research related to improving health care and determining environmental requirements of animals used in research; reference and information centers dealing with selected problems; for domestic breeding of nonhuman primates, and research training of specialists in the field of laboratory animal medicine. No matching funds are required.

Accomplishments in 1977: In 1977 it is estimated that 78 grants will be awarded. Of these, 60 will be continuations of previously awarded grants and 18 will be new grants. It is estimated that 15 contracts will be awarded of which 10 will be renewals of existing contracts and 5 will be new contracts. In addition there will be 6 institutional training grants awarded including 4 new grants and 8 individual grants awarded of which 4 will be new grants.

Objectives for 1978: The estimate for 1978 provides for 69 continuation grants. It is estimated that 6 continuing institutional training grants and 8 continuing individual grants will be awarded. There will also be 13 contracts awarded, 10 renewals and 3 new. Emphasis will continue in the area of primate breeding to meet the increased demand for these animals in biomedical research and to offset the restrictions of exportation of primates.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Biomedical Research Support (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$40,873,000	Indefinite	--	--

Purpose: The Biomedical Research Support Grant Program strengthens, balances and stabilizes Public Health Service supported biomedical and behavioral research programs by providing grants-in-aid to public or nonprofit universities, hospitals, laboratories, and other institutions for the general support of their research and research training programs.

Explanation: This Program provides funds to eligible institutions. They determine the emphasis, scientific direction, and content of their research activities. Approximately seventy percent of the funds support regular research and biomedical research pilot projects. Some of these successful pilot projects have been able to compete for regular long term research grants from one of the PHS components. About twenty-five percent of the funds support centrally shared equipment and facilities such as laboratories, instruments, computers and animal facilities which are used by the several grantee recipients of research grants within each institution. The remaining funds support unforeseen research needs and opportunities. All of these awards are funded as formula grants. No matching funds are required.

Accomplishments in 1977: In 1977, it is estimated that 462 grants will be made. There will be 450 continuations and 12 new grants awarded. These funds will provide support to approximately 462 health professional schools, other academic institutions, hospitals, health departments and other nonprofit research organizations. The new subprogram, Biomedical Research Development, will make 12 new awards to smaller institutions in order to help them improve their potential research capability so that they can contribute their effort to solving national biomedical health problems.

Objectives for 1978: No funds are provided in the 1978 President's budget for this program because other biomedical and behavioral research activities have a higher priority at this time.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Minority Biomedical Support (Public Health Service Act, Section 301)

1977 Appropriation		1978	Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$9,711,000	Indefinite	--	$8,772,000

Purpose: The purpose of the Minority Biomedical Support Program is to increase the number of ethnic minority faculty, students, and investigators engaged in biomedical research by broadening the opportunities for their participation in biomedical research and by providing appropriate settings in which these goals can be accomplished.

Explanation: Since the Program began in 1972, it has encouraged the involvement of ethnic minority students and faculty in the biomedical sciences and in health professions to enable our Nation to benefit from this untapped human resource. Some of the institutions now eligible to receive grants from this Program include two-year colleges, and colleges and universities having a large number of ethnic minority students, in addition to the traditional ethnic minority colleges, universities and health professional schools. Only funds for the direct costs are awarded for a period of up to five years and are issued in yearly increments. There are no matching funds required.

Accomplishments in 1977: In 1977, it is estimated that there will be issued 74 grants supporting minority institutions. Of this, there will be 72 continuations and 2 new grants awarded.

Objectives for 1978: The estimate for 1978 provides for 70 grants which is a decrease of 4 grants from 1977. There will be 68 continuations and 2 new grants awarded. The funds will continue to support institutional research programs involving minority scientists in biomedical research and to increase the exposure of minority students to the challenges and opportunities of biomedical research.

Because the MBS Program was authorized as part of the General Research Support Program, it is not allowed to pay indirect costs to its grantees. The appropriation language specifically prohibits the use of any appropriated funds for the payment of indirect costs to recipients of general research support grants. Because of this authorization, MBS grantee institutions must pay a larger share of biomedical research costs than institutions receiving support from regular research or program project grants. The General Accounting Office has conducted a study as requested by the House Appropriations Committee on the economic impact on the MBS recipient institutions of the policy of not paying indirect costs. This report may be used to determine if indirect costs should be paid to MBS grantees. If the decision is made by the Congress to authorize payment of indirect costs to recipients of MBS grants, additional funds will be required.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Chemical/Biological Information-Handling Research (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
--	$1,090,000	Indefinite	--	$1,165,000

Purpose: The Chemical/Biological Information-Handling Research Program assists the biomedical research community to employ modern computer-based information-handling concepts and methods in its efforts to place knowledge about chemical/biological interactions on an improved theoretical base.

Explanation: By focusing interest on computer-oriented methods for organizing, representing, and communicating biomedical information, the Program encourages research by those who wish to advance our predictive capabilities and to lay the scientific and technological groundwork for future information systems. The Program's strategy is (1) to develop standardized yet flexible computer-based tools with which laboratory and clinical investigators can represent, organize, manipulate, and communicate their research data and other information in the most scientifically meaningful ways; (2) to make these tools available to qualified members of the national community of scientists who are studying the mechanisms of chemical drug action and analogous phenomena; and (3) to collaborate with the users of these tools to refine existing methodologies and identify needs for new ones.

Accomplishments in 1977: It is estimated that two renewal contracts will be issued. The number of satellite installations supported by the central PROPHET computer is to be increased to 15. This will make the PROPHET services available to over 120 research investigators at 17 institutions in 9 states. Emphasis on the use of PROPHET to study the molecular basis for immunity is to be continued. A unique collection of data has already been accumulated on the structures of antibodies. Statistical analyses of these data are producing new insights into antibody specificity. This data base has also been generated into hard copy and has been distributed within the immunology research community. The data will continue to be updated on the computer for future studies.

Objectives for 1978: The estimate for 1978 provides for two renewal contracts. The number of satellite installations supported by the central PROPHET computer is to be increased to 17. This will make PROPHET services available to over 140 users at 20 institutions in 11 states. In addition to continuing to support projects begun during FY 1977 and previously, emphasis will be placed on computer applications in the area of cancer chemotherapy. Efforts will also be made to employ a commercial computer-based telecommunications network in order to reduce data transmission costs.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
49	$3,152,000	Indefinite	48	$3,393,000

Purpose: The Division's special programs of resource and center grants, training grants, research and development contracts, and formula grants are administered by this activity.

Explanation: The staff of this activity administers and manages the research resource grants, training grants and contracts, of its six extramural programs including the formula grants of the Biomedical Research Support Program. There are no matching fund requirements. The staff of each Program is responsible for planning and developing activities which will best serve the various health missions of both its Program and those of the NIH. They review and evaluate the grant applications for presentation to the National Advisory Research Resources Council. They also provide assistance and act as liaison between applicants and grantees, and provide continued monitoring of the grants. Scientific and technical reviews of each of the grants are provided to assure that the scientific mission of the Programs of the Division of Research Resources and those of the NIH are fulfilled.

Accomplishments in 1977: In 1977, it is estimated that 747 grants, 25 contracts, and 14 training awards will be made. Of the 747 grants to be awarded, 710 are continuations and 37 are new grants. Of the 25 contracts to be awarded, 19 are renewal and 6 are new contracts. This activity will provide assistance to the grantees and applicants. It will act as liaison between the applicants and grantees and continue to provide the proper monitoring of the grants and contracts that they issue. The activity will continue to participate with the InterAgency Primate Steering Committee, which is developing plans for the provision of adequate primate supplies for both the NIH's extramural and intramural research.

Objectives for 1978: In 1978, it is estimated that 274 grants, 23 contracts, and 14 training awards will be issued. There will be a decrease of 473 grants because no funds were requested for the 462 grants of the Biomedical Research Support Program in fiscal year 1978. Of the 274 grants to be awarded, 267 are continuations and 7 are new grants. There will be 23 renewal contracts issued. The staff will continue to administer and manage the research resource grants, contracts, and training grants of the Division's six extramural programs. The staff also will continue to be responsible for the planning and development of their programs in order to serve the various health missions of both their programs and those of the NIH.

NATIONAL INSTITUTES OF HEALTH

Research Resources

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Section 301)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
28	$729,000	Indefinite	28	$790,000

Purpose: This activity manages and provides the general administration, planning, direction, and coordination of the Division's Programs.

Explanation: Program Management funds the Office of the Director and its related staff, the Office of Program Analysis, and the Office of Science and Health Reports. They provide the overall direction, management, administration, and coordination of the Division's Programs which are Clinical Research, Biotechnology Research, Laboratory Animal Sciences and Primate Research, Biomedical Research Support, Minority Biomedical Support, and Chemical/Biological Information-Handling Research.

Accomplishments in 1977: The Division will continue to support, under contract, the development of a Research Resources Information Center. This Center is designed to be an information exchange network for users of Division supported resources. It is intended to promote a more widespread sharing of available resource services and new analytical research techniques and technologies. Initial projects include the publication of a regular newsletter and the development of a directory of available resource services.

The Division will continue its "interfacing" meetings with the officials of the categorical Institutes to acquire information about the current needs and the future plans of the Institutes, and to assure that the Division's Programs are responsive to the needs of the research investigators supported by the National Institutes of Health.

Objectives for 1978: This activity will continue to provide the overall direction, management, administration and coordination of the Division's Programs.

MONDAY, MARCH 14, 1977.

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

WITNESSES

DR. MILO D. LEAVITT, JR., DIRECTOR
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
GEORGE E. PRESSON, EXECUTIVE OFFICER, JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
NORMAN D. MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN F. WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

JOHN E. FOGARTY INTERNATIONAL CENTER

Mr. FLOOD [presiding]. We now have the National Institutes of Health, the John E. Fogarty International Center for Advanced Study in the Health Sciences.

The presentation will be made by Dr. Milo D. Leavitt, Jr., the Director.

We have your biographical sketch, Mr. Leavitt, which we will place in the record at this point.

[The biographical sketch follows:]

BIOGRAPHICAL SKETCH OF 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.S.; and 1958–59, Harvard University, M.P.H.

Experience:

Director, John E. Fogarty International Center for Advanced Study in the Health Sciences, NIH, 1968 to present.

Member, U.S. Delegation to 25th, 26th, 27th, and 29th World Health Assemblies, Geneva, 1972–76.

Acting Director, Office of Program Planning, NIH, 1967–68.

Deputy Director, Office of Program Planning, NIH, 1967.

Deputy Assistant Secretary for Science and Population, DHEW, 1966–67.

Science Policy Coordinator, OS–ASH, DHEW, 1966.

Head, Special International Programs Section, Office of International Research, NIH, 1962–66.

Assistant Chief, Prenatal Research Branch, National Institute of Neurological Diseases and Blindness, NIH, 1960–62.

Chief, Project Services Branch, Collaborative Research, NINDB, NIH, 1959–60.

Postdoctoral Public Health Trainee, Harvard School of Public Health, Boston, Mass., 1958–59.

Clinical Assistant Professor Medicine, Medical College of Pennsylvania, Philadelphia, Pa., 1949–58.
Fellow, Internal Medicine, Mayo Clinic, Rochester, Minn., 1945–49.
Captain, U.S. Army Medical Corps, 1942–45.
Rotating Internship, Philadelphia General Hospital, Philadelphia, Pa., 1940–42.

Association memberships: American Medical Association, Philadelphia County Medical Society, Society of the Sigma Xi, American Diabetes Asociation, Association of American Medical Colleges, New York Academy of Sciences, American Asociation for the Advancement of Science, Industrial Medical Association, Alumni Asociation of the Mayo Foundation, American Public Health Association, and fellow, College of Physicians of Philadelphia.

BIOGRAPHICAL SKETCH OF GEORGE E. PRESSON

Position: Executive Officer, Fogarty International Center, NIH.
Birthplace and date: June 15, 1912—Weir, Kans.
Education: 1935–38, Columbus University, Washington, D.C., B.C.S.; 1938–39, Columbus University, Washington, D.C., M.C.S.; and 1941–42, George Washington University.
Experience:
Executive Officer, Fogarty International Center, NIH, 1968 to present.
Chief, Conference and Administrative Management Branch, Fogarty International Center, NIH, 1968.
Head, Management Operations Section, OIR/NIH, 1963–68.
Staff Assistant, Office of International Research, NIH, 1962–63.
Executive Officer, Division of International Health, PHS, 1957–62.
Administrative Officer, Division of International Health, PHS, 1951–57.
Budget Officer, Division of Administrative Management, PHS, 1947–51.

Mr. FLOOD. We also have your statement which we will place in the record.

[The statement follows:]

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

National Institutes of Health

Statement by the Director, Fogarty International Center

on

Fogarty International Center

Mr. Chairman and members of the Committee:

I appreciate the opportunity of appearing before you to present the programs of the Fogarty International Center.

Since the establishment of the Fogarty International Center nearly nine years ago, we have endeavored to promote, foster, and support the concept of the Center as the visible and tangible embodiment of the nation's devotion to the use of science for peaceful purposes and the good of mankind. The Center's programs encourage interaction, study, cooperation and collaboration within the international biomedical community and provide opportunities for discussion of significant research, public health, medical and biomedically related social and economic issues.

ADVANCED STUDY

The Advanced Study program plays a key role in the Center's activities, serving as an important channel for the acquisition and communication of research knowledge and as an instrument for the transfer of technology. Its conferences

provide opportunities to U.S. and foreign scientists to improve their understanding of international biomedical research problems and serve as an effective forum for the exchange of research information and for enhancing international collaboration.

Maintaining its role as a Center for Advanced Study we will continue to conduct, with scientific and funding collaboration from the NIH institutes, selected scientific meetings. These conferences will include such subjects as the Recombinant DNA experimentation, Tropical Medicine, Viral Immunity and Hepatitis.

Concurrent with its conferences, the Center is studying a communication technique of informal scientific memoranda in an attempt to shorten the time between the completion of a research experiment and the availability of the data via formal publication in a scientific journal. The informal nature of the project stimulates the exchange of brief summaries of completed experiments, research progress reports, discussion of research problems and an analysis of research results. This project involves research scientists in 48 countries who are investigating, among other things, hepatitis, interferon, leprosy and liver cancer.

Another communication technique being examined, with the cooperation of the National Aeronautics and Space Administration, is the use of two-way radios transmitting through satellites to permit direct communication between research investigators.

GEOGRAPHIC HEALTH STUDIES

The Fogarty International Center is also conducting studies of the health systems and activities of other countries. An analysis of these foreign health-related activities and programs may provide U.S. Government health administrators with new insights in solving some of the complex problems relating to the improvement of health in the United States. Hence these studies are made available to public and private sectors which may influence the decision-making processes in the United States. This information is also available to the medical communities and governments of other countries and international organizations. The specific objectives of these studies are: (1) to advance U.S. knowledge of health practices in different geographic regions or individual countries; (2) to publish selected documents covering all phases of medicine and health in different regions; and (3) to improve cooperation between clinicians, health scientists, and health administrators in the United States and other geographic areas.

FOGARTY SCHOLARS-IN-RESIDENCE

The Fogarty Scholars-in-Residence Program has played an important role in the development of the Fogarty International Center as a center for advanced study in the health sciences by bringing distinguished scholars from the U.S. and abroad representing various disciplines to the Center to pursue their scholarly interests and to contribute to the academic interests of the NIH. Through their individual scholarship, interaction

with leading scientists, promising young investigators and science administrators at NIH and other biomedical research institutions, major achievements have been made in areas of contemporary importance in research. Assessment of the environmental, ethical and social implications of contemporary biomedical research is a major feature of the Scholar's program. Clusters of scholars are selected to consider advanced topics of fundamental importance to biology and medicine, to assess the evolutionary impact of medical technology, and in general, to perform the technological assessment of biomedical research.

INTERNATIONAL EXCHANGE PROGRAM

Activities under the International Exchange Program have as their basic purpose the expansion and dissemination of scientific knowledge through the promotion of collaborative relationships between U.S. scientists and laboratories and their foreign counterparts. Such collaboration may include the joint conduct of research projects of significance in host laboratories, the acquisition of special skills and experience, and the application of research findings in other field settings.

INTERNATIONAL RESEARCH FELLOWSHIPS

International Research Fellowships are awarded annually by the Fogarty International Center to promising young foreign scientists at the postdoctoral level to enable them to pursue biomedical research projects at NIH and other U.S. institutions.

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The Program is designed to promote collaborative relationships between U.S. and foreign scientists in research studies of mutual interest and significance through participation of the Fellows while in the U.S. and through their enhanced research capability after return to their countries of origin.

The Program presently involves approximately 35 participating countries. We are, however, receiving many requests from individuals in non-participating countries for inclusion in this program. Plans are, therefore, under consideration to increase the participation by other countries, including Thailand, Pakistan, and additional countries in Latin America.

SENIOR INTERNATIONAL FELLOWSHIPS

The Senior International Fellowship Program was initiated in 1975 to provide the opportunity to mid-career faculty members of U.S. schools of medicine, osteopathy, dentistry and public health who have demonstrated productive scholarship and recognized stature in their profession, to go abroad to study and to share their expertise.

The response to the initiation of the Program has been encouraging and reflects an evident need within the U.S. biomedical academic community for this type of support.

INTERNATIONAL COOPERATION

The program of formal intergovernmental agreements for cooperation has gained momentum and acceptance. A number of biomedical cooperative projects have been proposed and exchanges

of American and foreign scientists have been accomplished. Perhaps the most widely known of these agreements is that between the United States and the Soviet Union. Through the current agreement between these two countries, especially in the health field, a number of specific problem areas, cancer, heart disease, arthritis, and the environment, are being explored on a mutual basis. In addition, exchanges of individual scientists have provided cooperation in many other biomedical areas.

Other bilateral agreements have been negotiated with Egypt, France, the Federal Republic of Germany, Iran, Italy, Japan, Romania, Spain and Yugoslavia.

The diminution of foreign currency under the Special Foreign Currency Program has made it necessary to take measures to alleviate the impact of the loss of these funds upon the biomedical research community in those countries. One measure has been the development of bilateral agreements providing for collaborative funding by the countries involved. These agreements establish "institution-to-institution" collaboration between U.S. and foreign institutions. These new bilateral agreements with excess currency countries will be directed toward maintaining existing biomedical science collaboration and developing new research projects.

GORGAS MEMORIAL INSTITUTE

This institution was founded in 1921 as a memorial to Major General William Crawford Gorgas, whose efforts in

environmental sanitation led directly to the successful construction of the Panama Canal and to the eventual eradication of yellow fever from the great urban centers of tropical America. With continuous support from Congress since 1929, the Gorgas Memorial Institute has operated the Gorgas Memorial Laboratory (GML) in Panama City, Republic of Panama.

The Laboratory is a uniquely situated resource for the conduct of research and research training in tropical medicine. It has adequate facilities to undertake a sophisticated level of research and has field conditions readily at hand. It conducts a diversified program of research in tropical disease of importance to the United States, Panama, and Central America. Particular emphasis is placed upon viral and parasitic diseases, and the effects of environmental change on the transmission of infectious diseases and their vectors. In the latter category, major studies are underway to assess the ecologic effects of hydroelectric dam construction and resulting water impoundment.

With the increase authorized by Congress in 1974 and an appropriation level now at $1.4 million, the period ahead affords an opportunity to reinvigorate the Laboratory's programs and to refocus its major research priorities, eliminate those activities of marginal value, and to play an important role in an expanding international cooperative endeavor.

In addition to these specific activities, the Center is responsible for the administrative support and management of the

NIH Visiting Program, the International Visitors Center and the programming of foreign health professionals sponsored by the Pan American Health Organization and the World Health Organization.

For these programs and activities, the Fogarty International Center is requesting $8,369,000.

I shall be pleased to reply to any questions of the Committee.

Mr. FLOOD. You may want to present your assistant with you here.

Dr. LEAVITT. Mr. Presson, my executive officer, accompanies me.

Mr. FLOOD. Of course.

Now, Doctor, your overall increase this year is a relatively modest one, about 4 percent as we calculate it here. Would you prefer to say this is pretty much a status quo budget right down the line?

Dr. LEAVITT. Yes, sir, it is.

GORGAS MEMORIAL INSTITUTE

Mr. FLOOD. Now, you are asking for $1,400,000 for the Gorgas Memorial Institute. What portion of the total operating budget out there is expected to fund that appropriation?

Dr. LEAVITT. The total allocation?

Mr. FLOOD. What portion?

Dr. LEAVITT. It would come from the Fogarty appropriation in total; $1.4 million is included in the total Fogarty appropriation.

Mr. FLOOD. What part of the total operational budget? Is that total as well? I mean for Gorgas.

Dr. LEAVITT. The funds provided through the Fogarty International Center budget represents 82 percent of the total operational budget of Gorgas.

Mr. FLOOD. Has there been any financial support to the Institute at all from any other countries from the Pan American Health Organization, anything at all?

Dr. LEAVITT. Yes, sir. Small amounts have been made available from the Pan American Health Organization and the Government of Panama.

Mr. FLOOD. What about to the Institute?

Dr. LEAVITT. The Institute is the incorporated body that provides the support to the laboratory.

Mr. FLOOD. Has there been any increase to the Institute from any other countries or from the Pan American Organization?

Dr. LEAVITT. Very small support from the Pan American Health Organization, but not from other countries that I am aware of, sir, other than the Government of Panama.

Mr. FLOOD. Last year, by the way, you provided a breakdown for us of the amount of funds that the Institute gets from the other Public Health Service programs; will that support remain relatively stable next year?

GORGAS MEMORIAL LABORATORY—RESEARCH

Dr. LEAVITT. I would expect it to, sir.

Mr. FLOOD. Can you describe for us two or three of the most important projects, research projects, now being conducted at Gorgas?

Dr. LEAVITT. Yes, sir. The one——

Mr. FLOOD. When were you down there last?

Dr. LEAVITT. I have not been there for 3 years. However, the Fogarty Center did sponsor a site visit to the Gorgas Memorial Laboratory last October. This included scientists from U.S. universities, NIH and other Federal agencies, as well as administrative personnel from NIH.

Mr. FLOOD. Pick out two of the most important research projects.

Dr. LEAVITT. Yes; the first is the Bayano River project which has been set up to determine ecological effects of hydroelectric dam construction in a particular area as the waters rise and change the ecology of the area. This gives us some idea of what may happen to wildlife and the diseases they carry in a particular area.

Mr. FLOOD. That is one.

Dr. LEAVITT. The other important activity that I think is important to the United States and to Panama is the research and maintenance of the surveillance of virus diseases such as yellow fever, Venezuelan equine encephalitis, influenza, and other diseases. The Gorgas staff conducts this surveillance on an ongoing basis.

YELLOW FEVER

Mr. FLOOD. Was there a sign of yellow fever up there a couple of years ago?

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. Upcountry?

Dr. LEAVITT. Yes. They did expect that yellow fever was going to carry across the Panama Canal and pose a threat to the United States. However, through the efforts of the Gorgas Memorial Laboratory staff, preventive and control measures were instituted and as a result, the disease was contained.

Mr. FLOOD. How much money did you spend on each one of those?

Dr. LEAVITT. I am not sure I could break that down for you at this point, but we will provide it for the record.

Mr. FLOOD. Fine.

[The information follows:]

Cost of selected projects at Gorgas	*Estimate 1977*
Virology program (including yellow fever)	$248,000
Bayano—core support	156,785
Additional grant support	175,000

RELATIONS WITH GORGAS MEMORIAL INSTITUTE

Mr. FLOOD. We have spoken about your attempts time and again to bring this Gorgas facility more directly under your control. Has that taken place finally? You made quite a thing about that last year.

Dr. LEAVITT. We are not eager to bring the Gorgas Memorial Laboratory under the immediate control of the Fogarty Center, but we think it is important to support it and to help strength it.

Mr. FLOOD. You did tell us about your attempts to bring Gorgas more directly under your control.

Dr. LEAVITT. Only as far as the administrative and financial arrangements are concerned.

Mr. FLOOD. Has that taken place?

Dr. LEAVITT. Yes, sir, it has taken place. As a result of the site visit made last October I think a better understanding has developed between the two organizations.

Mr. FLOOD. I have heard something about the Panama Canal through the years. More generally, has the current political uncer-

tainty in the Canal Zone affected in any way the operations of the Gorgas Laboratory?

Dr. LEAVITT. I believe not, really. In fact, I am very pleased to report the recent additions to the staff of the Gorgas Memorial Laboratory. There is going to be a new Director very shortly and five American scientists will also join the staff who will further strengthen its scientific capability.

So I really believe that in the overall view their scientific capability will be enhanced.

Mr. FLOOD. One last question on Gorgas.

You talked about this a few minutes ago. A study of the ecological impact of this hydroelectric project, now that seems very worthwhile, it may be a very worthwhile program. But why is it the responsibility of this program? Why should that be in this program? It may be very worthwhile research, sure.

Dr. LEAVITT. The staff was eager to learn what would happen to diseases and to the animals located in an area that is going to be flooded and what happens with the spread of disease as a result of that flooding and the creation of a lake.

Mr. FLOOD. That is part of the program at Gorgas?

Dr. LEAVITT. Yes, it has been part of the program since it came under the Fogarty budget in 1970.

ADVANCED STUDY

Mr. FLOOD. Tell us how much money do you plan to spend during the fiscal year of 1978 on what is known as the advanced study program?

Dr. LEAVITT. Our scholars' program includes all fellowships, Mr. Chairman, which is budgeted at a level of $3.4 million in 1978. From the International Center, activity which is budgeted at $3.3 million in fiscal year 1978, we fund the advanced study program which includes conferences, as well as other direct operations of the Center.

Mr. FLOOD. How are the topics selected for the conferences you hold under the advanced study project?

Dr. LEAVITT. Topics are selected through meetings of my top executive staff; results of study section deliberations; initiatives that are set forth by the Congress; initiatives that are discussed at National Advisory Council meetings; and conferring with our scientific colleagues in the Institutes at NIH.

DNA RECOMBINANT RESEARCH

Mr. FLOOD. In your statement you talk about the upcoming conference on the recombinant DNA program. There are several such conferences being planned that we have heard about and read about, including the one last week at the Institute of Medicine.

What will your conference accomplish that these other meetings we hear about won't do?

Dr. LEAVITT. In this particular upcoming conference we want to consider the risks, the biohazards of recombinant DNA research.

Dr. FREDRICKSON. Mr. Chairman, I might add, that this is not the sole intent of these forthcoming conferences that the Fogarty Inter-

national Center will help us hold. We are now engaged in looking at other potential biohazards in research that extend beyond the vary narrow question of recombinant DNA to other problems.

Mr. FLOOD. But I was talking about the recombinant DNA conference to be held by this group, why is it different than the one last week or the others we heard about?

Dr. FREDRICKSON. This conference will concentrate on bringing together experts on enteric organisms and diseases. This type of bacteria is used for the host in some recombinant DNA research. We need to bring together people who have experience and ask many questions about the use of these hosts. This will be important in getting on the record what is known.

Mr. FLOOD. This will be part of a series on recombinant DNA?

Dr. FREDRICKSON. Yes, it will be part of the series.

INTERNATIONAL HEALTH SYSTEMS SURVEYS

Mr. FLOOD. How many international health surveys are planned during the next year?

Dr. LEAVITT. There are about three.

Mr. FLOOD. Also in your statement you talked about the value of these international studies to U.S. Government administrators. Can you give us two examples of how these studies have been useful to the United States?

Dr. LEAVITT. We have recently completed such a survey of the health service system in Sweden as well as in Denmark. This information has been made available to medical schools, schools of public health and to congressional staff and Members of the Congress upon request.

We feel that we can learn something from the experience of other countries in avoiding some of the pitfalls that may confront us in the years ahead, particularly in the matter of national health insurance.

Mr. FLOOD. That could be timely.

Dr. LEAVITT. Yes, sir.

SCHOLARS PROGRAMS

Mr. FLOOD. Now you are proposing to increase the award for these various scholarship programs that you have. Can you tell us what is the average grant for each program and also how much of an increase do you propose?

Dr. LEAVITT. We propose, Mr. Chairman, an increase of about $2,000 per award during 1978.

Mr. FLOOD. What is the average grant?

Dr. LEAVITT. The International Research Fellowship program will be $16,000. At the present it is $14,000. The senior program, the Magnuson Fellowship program, the awards will go to $20,000 from $18,000. The Fogarty scholars-in-residence whose present award is in the range of $30,000 will be increased to $39,000.

Mr. FLOOD. How many scholars are you going to support by these programs?

Dr. LEAVITT. This past year we were able to support 20 such scholars in the Fogarty scholars-in-residence program. In the coming year we should be able to support an equal number.

Dr. FREDRICKSON. That is not the total number for the Fogarty Center programs.

Dr. LEAVITT. Yes, there will be 188 awards in the scholars program in 1978.

Mr. FLOOD. How are American students selected for the senior international fellowship program?

Dr. LEAVITT. Faculty members at midcareer in schools of medicine, osteopathy, dentistry and public health apply formally to the National Institutes of Health. The application is reviewed by a special study section set up by our Division of Research Grants which then makes recommendations to the Fogarty Center concerning those applications which should be supported.

Mr. FLOOD. Under the program for the American scholars that go abroad, do we pay the entire cost or does the host institution pay anything at all?

Dr. LEAVITT. We pay for the round-trip transportation, a stipend and a small allowance for research support.

Mr. FLOOD. What about the home institution?

Dr. LEAVITT. The home institution usually supports the faculty member through the provision of sabbatical funds so that our awards simply augment the salary that he gets on sabbatical.

EXCESS FOREIGN CURRENCY PROGRAMS

Mr. FLOOD. Here is something also in your statement. You talk about the problem created by a diminished supply of the excess foreign currency.

Dr. LEAVITT. Yes, sir.

Mr. FLOOD. What do you mean by that?

Dr. LEAVITT. In countries such as Israel, the excess foreign currencies were exhausted 4 to 5 years ago. In Poland where we had many active projects, the excess foreign currencies have also diminished. However, that program is still viable. In Yugoslavia, on the other hand, our resources have been exhausted.

Mr. FLOOD. So what? What are the problems?

Dr. LEAVITT. We found that the use of these foreign currencies did generate some excellent biomedical research projects and we were very eager to continue them. They were certainly relevant to the NIH mission.

Mr. FLOOD. What happens now?

Dr. LEAVITT. In the case of Israel, a binational foundation has been set up to which the United States and Israel both have contributed equal sums and the interest on those funds which amounts to a little over $2 million a year is used to fund those meritorious projects that have been underway for a number of years as well as new projects.

Mr. FLOOD. Is Israel the only place?

Dr. LEAVITT. In Yugoslavia a joint fund was established, however, the small balance was fully committed and is now used up. Now, the investigator who wishes to set up a project in Yugoslavia applies to

NIH for support under the regular grant research program, either for total or for one-half support for the project. The other half of the support comes from Yugoslavian funds. We are trying to maintain the excellent scientific research under this program.

Mr. FLOOD. Is there any reaction from Poland at all?

Dr. LEAVITT. Yes, sir. They have been very eager to make a monetary contribution themselves as well as depending on the United States for program support. I should point out that a joint fund has also been established in Poland. There has been a very viable program in Poland, particularly in the neurosciences and oncology.

Mr. FLOOD. Mr. O'Brien?

Mr. O'BRIEN. I have nothing.

Mr. FLOOD. Mr. Early?

INTERNATIONAL HEALTH SYSTEMS STUDIES

Mr. EARLY. The Fogarty International Center is also conducting these studies of the health systems in other countries. How long have they been going on?

Dr. LEAVITT. Approximately 8 years, Mr. Early.

Mr. EARLY. What have we gotten out of the studies?

Dr. LEAVITT. We distribute these studies to health administrators, developers of health policy, major libraries in the United States and abroad. We feel that these documents will be of vital interest and value in the development of U.S. policies in health. They have also been transmitted to international organizations such as the World Health Organization.

Mr. EARLY. Will this research have any import to the implementation of a national health program here in the United States?

Dr. LEAVITT. It is our belief that the documents will provide information on questions which must be considered in developing a national health program in the United States.

FELLOWSHIP ACHIEVEMENTS

Mr. EARLY. On page 4 you say that there have been many major achievements that have been made in the area. Can you identify a couple of these?

Dr. LEAVITT. I am not sure I follow you.

Mr. EARLY. You say that through interaction with leading scientists, promising young investigators, and science administrators at NIH and other biomedical research institutions have made major achievements in areas of contemporary importance in research.

Can you identify the areas?

Dr. LEAVITT. Yes.

At Stanford one of our young postdoctoral fellows has made an important contribution in seriological studies of the Epstein-Barr virus, the probable cause of infectious mononucleosis in humans, particularly younger people. This may assist us in developing a much better method for diagnosing infectious mononucleosis.

Mr. EARLY. You say it may. Has it?

Dr. LEAVITT. Yes, it is being developed right now so that we finally may have a very good serologic test for infectious mononucleosis.

At the Salk Institute another investigator has developed a methodology which permits the measurement of brain hormones in the blood which have an effect on the pituitary gland which affects human growth.

So these are two examples of rather important medical contributions that these young scientists have made who have come to us from abroad.

Mr. EARLY. And there have been others?

Dr. LEAVITT. Yes, we will supply them for the record.

[The information follows:]

FOGARTY INTERNATIONAL CENTER FELLOWSHIP ACHIEVEMENTS

A British research fellow at the University of California at Los Angeles has studied the "Zollinger-Ellison Syndrome," a gastro-intestinal disorder in which extreme stomach acidity is associated with a pancreatic tumor and intractable peptic ulcer formation. Several years ago the discovery and synthesis of gastrin, a polypeptide hormone secreted by the pyloric antrum, led to new information concerning the etiology and diagnosis of this syndrome. It has since been demonstrated that gastrin may exist in several forms in the human body. The detection of these forms and their analysis by sensitive laboratory techniques developed by the young investigator at U.C.L.A. will greatly assist the practicing physician who must accurately diagnose different types of peptic ulcer before he may effectively treat them.

A young endocrinologist from Scotland, working in a major U.S. medical center, has devoted the past 2 years to investigating the control of thyroid gland function by a hormone secreted by the human brain. This hormone directly regulates secretion of thyroid-stimulating hormone releasing factor (TRF) by the pituitary or "master" gland. Since thyroid disorders affect several million Americans every year, the development of sensitive and accurate tests for thyroid function is extremely important for diagnosis and management of thyroid dysfunction.

A Chilean investigator devoted his fellowship to an investigation of the relationship of adrenocortical hormones to high blood pressure. Using sensitive laboratory methods for determining the concentration of the hormones in blood, he developed the relationships between the blood level of desoxycorticosterone (DOC) and the establishment of hypertension. He then demonstrated that lowering the DOC level to normal resulted in a reduction of blood pressure levels to within normal limits.

A young Swedish pediatrician, during his research training at the University of North Carolina, conducted studies on testicular feminization. On the basis of his investigations he concluded that the cause of this endocrine disease in human beings, called pseudohermaphrodism, is most likely due to unresponsiveness of the target cells, that is, the testis itself, to male sex hormone. This research fellow utilized animal tissues in his research, including the coxcomb which has been used extensively in studies of androgen effect.

An Indian research fellow at the University of Wisconsin, employing laboratory techniques for the measurement of vitamin D and parathyroid hormone, studied the development of rickets in malnutrition. If children are deprived of adequate protein in the diet, defective bone growth characteristic of rickets still develops despite exposure to sunlight (ultraviolet radiation). This young investigator therefore studied the metabolism of vitamin D in rats on controlled low protein diets to develop methods for identifying disturbances in the normal metabolism of vitamin D. His findings should greatly assist in identifying malnourished children at special risk of developing rickets.

INTERNATIONAL FELLOWS

Mr. EARLY. Do you feel these are productive as far as research?

Dr. LEAVITT. Yes, I believe they are. We have some of the best young talent coming to us from abroad. They are very carefully reviewed by an in-country committee which submits the applications of their very

best candidates. The NIH conducts a second review under the scientific review system. Final selections are made from the best of those applications.

Mr. EARLY. Did you reply to the chairman that there were 188 such scholarships?

Dr. LEAVITT. The total of 188 awards under the scholars program includes 121 awards for the international research fellowships.

Mr. EARLY. How many of those 188 are Americans?

Dr. LEAVITT. Fifty-three will be made to Americans to go abroad so that we have a kind of exchange program.

Mr. EARLY. What is the participation from the other countries? Are there scholarships from the other countries offered to Americans?

Dr. LEAVITT. Yes, the Swedish Government has made three fellowships available each year to Americans and the Swiss Government has recently instituted a fellowship program which provides three fellowships for Americans to study in Switzerland.

Mr. EARLY. So you are saying it is not just an outgoing expenditure?

Dr. LEAVITT. No, sir. In addition, the Government of Japan awards fellowships to Americans to conduct research in Japan and the WHO provides short-term foreign travel awards to U.S. health personnel.

Mr. EARLY. Thank you.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. CONTE

INTERNATIONAL CONFERENCES

Mr. CONTE. What were the topics for the conferences which you sponsored over the past year? Can you provide some examples of important results of those conferences? What topics are proposed for the coming year?

ANSWER. Since the earliest days of the Fogarty International Center, conferences on advanced topics in biomedical research and related issues have been a major activity of the Center. During fiscal year 1976, 11 conferences and workshops were held as shown by the following list:

Academic Mission of Departments of Family Medicine;
The Atmosphere, Endangered and Endangering, Chairperson: Dr. Margaret Mead;
Consumer Health Education;
Cellular Regulation of Transport and Uptake of Nutrients;
Idiopathic Urinary Bladder Stone;
The Doctor-Patient Relationship in the Changing Health Scene;
The Ocular and Cerebrospinal Fluids;
Biochemistry of Cell Surfaces;
Changing National-Subnational Relations in Health;
Measures to Contain Health Care Costs and Expenditures; and
Egg Yolk Phosphoprotein Synthesis.

A number of these meetings were devoted to contemporary issues in the organization of health care. Several of these have been published including that on consumer health education, considered by many to be an extremely important aspect in provision of satisfactory health services.

The conference on Idiopathic Urinary Bladder Stone was of considerable importance to the research programs of NIAMDD. Beginning with a series of papers on the theoretical aspects of urinary stone formation, the conference considered the epidemiology of the disease including a survey of the incidence and etiological factors in many underdeveloped countries. Experimental evidence regarding the mechanisms of stone formation was discussed as well as the treatment and prevention of the disease. The formation of urinary stones is a major problem in the management of kidney disease. The prevention of bladder

stone disease by control of the basic defects, be they hormonal, as in the case of regulation of calcium metabolism due to excess of parathyroid hormone, or genetic as in the case of cystinuria, a full understanding of the fundamental biochemistry and physiology of the defect is essential. This conference on bladder stone formation represents a step forward in correlating valuable information about this painful and dangerous affliction.

As a result of a Fogarty international scholarship awarded to Dr. Herman M. Kalckar, a symposium on "Cellular Regulation of Transport and Uptake of Nutrients" was convened, the proceedings of which were published late in 1976. One hundred scientists from the United States and abroad gathered in Bethesda for 2 days with research presentations and intense discussions of this fundamental subject. The uptake of nutrients by cells and the elucidation of the regulatory mechanisms lies at the base of many metabolic defects. This conference considered the biochemistry of cell surfaces and enabled leading investigators to exchange information and to evaluate the relative importance of contemporary work in different laboratories. The report has been read with interest not only by fundamental investigators, but by clinical researchers interested in the application of research results with pure cell lines in tissue culture to improvement of research techniques for higher animals.

Topics which will be considered during fiscal year 1977 includes the following:

International Histological Classification of Tumors;
Anglo-American Conference on Priorities for the Use of Resources in Medicine;
Biliary Atresia;
Workshops in Somatomedins and Related Growth Factors;
Anglo-American Symposium on Tropical Medicine; and
Fulminant Hepatic Failure.

In addition to these subjects, the Fogarty International Center, in cooperation with one or more of the Institutes, is providing financial support to a number of conferences such as:

International Conference on Preservation of Kidneys for Clinical Transplantation;
Third International Conference on Comparative Virology; and
Twenty-seventh International Congress of Physiological Sciences.

FOGARTY SCHOLARS-IN-RESIDENCE

Mr. CONTE. Can you provide some examples of the work being done by your scholars-in-residence?

ANSWER. Dr. Elvin Kabat, Columbia University, spent a year, 1974–1975, at the Fogarty International Center as a scholar-in-residence. During that period, he not only rewrote his textbook Structural Concepts in Immunology and Immunochemistry, but began a new program in collaboration with NCI and other institutes on the immunology of cancer. In November 1976 Dr. Kabat, in collaboration with Dr. T. T. Wu of Columbia University and Dr. H. Bilosky of Northwestern University, produced a major publication called Variable Regions of Immunoglobulin Chains. Such a publication of hundreds of detailed structures in code form is important for biomedical and public health research. This has practical and theoretical aspects: immunoglobulins are special proteins circulating in the blood which can neutralize infectious agents such as bacteria and viruses. Vaccines, in general, are nothing more than substances which stimulate the production of immunoglobulins, or antibodies, having the ability to neutralize particular infectious agents.

Dr. D. W. van Bekkum from the Netherlands was a scholar during 1975 and will return in 1977–78. In his own country he is heavily involved in cancer research where he is director of the Radiobiological Institute in Rijswijk. Dr. van Bekkum studied the progress in organization of the Comprehensive Cancer Centers (CCC) supported by NCI. The Dutch Government plans to organize three such centers in Holland at Rotterdam, Amsterdam, and Groningen.

Dr. Harry Harris, the University of London, spent a year gathering material for an integrated treatment of heritable enzyme variants and deficiencies in man; he also spent a great deal of time studying how to estimate the upper limits of mutation rates in human populations. During his stay Professor Harris collaborated with Dr. J. V. Neel at the University of Michigan in calculations

of these limits from data collected by many geneticists. This work, now being published in professional journals, is relevant to genetic defects in human beings.

During his scholarship in 1973 Dr. Derek Denny-Brown, from Harvard University, interacted with many groups in the clinical branches of the NINCDS and other institutes. Dr. Denny-Brown used his period as a Scholar to develop and publish data accumulated during several years work at the New England Primate Research Center on the sensory pathways in monkeys. This work is fundamental to understanding of birth injuries to the human nervous system and to other neurological disorders as well.

GORGAS MEMORIAL INSTITUTE

Mr. CONTE. What major activities will the Gorgas Laboratory be concentrating on in the coming year?

ANSWER. Research studies are undertaken in the principal areas of virology, parasitology, bacteriology, disease ecology, zoonoses, and vector biology. In addition, the Laboratory serves as one of the few facilities for advanced training in tropical disease available to students, technicians, young postdoctorals, and established scientists of the United States and other countries.

Particular emphasis is being given to epidemiological surveillance of explosive viral diseases such as influenza, yellow fever, dengue and Venezuelan equine encephalitis. Such activity serves as an early warning system of dangerous epidemics for the Central American isthmus and the United States. Other important work relates to the changes in tropical disease transmission and the biology of disease vectors caused by economic development projects, especially, at this time, hydroelectric dam construction, and resulting water impoundment (for example Bayano Project). Another area of note is the development of animal models for the study of human malaria and their use in the testing of antimalarial drugs. Biological materials of this program have afforded a unique opportunity for cooperative projects and benefit to investigators from Panama, the United States and some 15 laboratories abroad.

INTERNATIONAL EXCHANGE PROGRAM

Mr. CONTE. Are there any other international exchange programs in biomedical science being supported by other parts of HEW? Where, and in what amounts?

ANSWER. To the best of my knowledge there are no other international exchange programs in biomedical science being supported by other parts of HEW.

GORGAS MEMORIAL LABORATORY

Mr. CONTE. What were the major financial problems of the Gorgas Laboratory in 1976, and how have they been resolved?

ANSWER. Financial support of the GML by the U.S. Federal Government was first provided in 1929 with an authorization and subsequent appropriation of $50,000. Authorizations and appropriations were increased periodically until in 1971 it reached a level of $500,000 in core support.

In 1962, the National Institute of Allergy and Infectious Diseases (NIAID) established the Middle America Research Unit (MARU) in the Panama Canal Zone to conduct research in tropical and infectious diseases, which reached a maximum annual funding level of nearly $800,000.

These two organizations existed in harmony and cooperated on mutual problems until 1972 when the NIAID was forced by personnel restrictions to eliminate its direct support of personnel working within its unit. Reluctant to discard this work in tropical and infectious diseases, many of which were potentially dangerous to the health of the people of the United States, NIAID entered into a contract with GML to continue its work. Thus the two laboratories were merged, and the GML immediately tripled its core support.

A serious financial situation arose in 1974 when funds from the NIAID were reduced and it was determined that financial support to the Laboratory was in jeopardy. Efforts were then initiated by the GML to increase the congressional authorization for the support of the Laboratory sufficient to fund the combined operations. In 1974, the House Committee for Inter-American Affairs authorized an increase in the permanent annual appropriation to $2 million. Fiscally, this new authorization was almost too late, since $500,000 had already been appro-

priated, and that amount was far too small to support the combined operations. However, the Laboratory took immediate action to restrict and reduce its research studies except in the most urgent of matters, and at the same time limited additional support was provided by NIAID.

This situation prevailed until late in fiscal 1976, when the Congress increased its appropriated level to $860,000 and recommended additional support from the NIAID. For fiscal 1977, the appropriation for the GML was increased to $1,400,000, a sum which is considered sufficient at this time for the core support of the Laboratory.

Mr. CONTE. What success has been achieved in obtaining support for the Gorgas Lab from other countries and international organizations?

ANSWER. In addition to the provision of buildings and land for the Laboratory, the Panamanian Government through its Institute of Hydroelectric Resources and Electrification has contracted with the Laboratory at a cost of $134,000 for an environmental assessment of the Fortuna area prior to the initiation of a hydroelectric project.

The Pan American Health Organization has stationed two senior scientists, a parasitologist and a malariologist, to the Laboratory, for which the Laboratory also receives $35,000 for their support services.

No other countries or international organizations are providing support at this time.

DISSEMINATION OF RESEARCH RESULTS

Mr. CONTE. How can the Center increase its effectiveness in providing rapid dissemination of research results on a world-wide basis?

ANSWER. The Fogarty International Center has, from its inception, sponsored conferences, workshops, and symposiums which reflect the most recent advances on the contemporary biomedical research scene and are organized to cope with expanding numbers of scientists and to foster an interdisciplinary approach to human health problems whenever appropriate. Because scientific knowledge is expanding so rapidly, the prompt dissemination of new findings and research results generated by our conference activity and advanced study program is afforded high priority within the Fogarty Center. While a major portion of these proceedings are published in their entirety by the Government Printing Office and are available to the lay and scientific communities at modest cost, the Center is increasingly publishing, by established medical and scientific journals, summary reports of Fogarty-sponsored conferences and symposiums to insure early and widespread distribution of new and important information to the biomedical readership. This rapid dissemination of research information is particularly critical in research fields that are moving rapidly and where data may become obsolete.

The vast majority of Fogarty conferences and workshops include foreign bioscientists. These meetings provide unique channels for formal and informal oral communication and direct exchange of information between American scientists and their counterparts from foreign countries. This exchange of research results is further strengthened and expanded through cooperative arrangements between the Center and international organizations such as the World Health Organization, Pan American Health Organization, International Agency for Research on Cancer, et cetera, which provide additional distribution of Fogarty publications to scientific colleagues and institutions overseas. On occasion the Center utilizes the services of Scientific Attachés stationed at U.S. Embassies abroad to insure that important biomedical research material is made immediately available to appropriate foreign scientists, science administrators, and Ministries of Health, for example, the release of guidelines on recombinant DNA research to over 100 foreign governments and investigators in June 1976.

In addition to the Fogarty Center's role in coordinating multiinstitute interests and sponsorship of scientific meetings, recent efforts have been undertaken to provide a mechanism for rapid and informal communication between investigators here and abroad while research is in progress. Through the preparation and dissemination of "Scientific Memoranda," issued on a regular periodic basis, these photo-offset documents provide up-to-date information concerning progress on research in selected areas, for example, leprosy, hepatitis, interferon, nucleic acid research, cancer, et cetera. Scientists in approximately 48 countries are now participating in this program.

Regular distribution of all Center publications and other documents is made—upon delivery from the GPO—to all depository and medical libraries in the United States, including the National Library of Medicine, to selected foreign medical libraries, international organizations and to Ministries of Health in both developed and developing countries abroad.

The Fogarty International Center recognizes the vital importance of the orderly and prompt dissemination of research results and transfer of technology to scientific colleagues in the United States and in foreign countries. A continuous effort is being made to improve the distribution of Center publications, including utilization of mechanical, electronic, and automatic devices for the improvement of biomedical communication.

MR. MICHEL

RUSSIAN INVOLVEMENT IN CONFERENCES

Mr. MICHEL. Are the Russians involved in the conferences conducted under the advanced study program? If so, are they forthcoming in discussing their research activities?

ANSWER. Soviet scientists have attended some of the scientific meetings. They made presentations and participated in scientific discussions based on their own research investigations and in so doing revealed, in general, up-to-date scientific knowledge. While the world scientific literature is available to them the Soviet scientists could not have performed at the meetings as well as they did without having actually conducted the research they described and discussed.

RECOMBINANT DNA RESEARCH

Mr. MICHEL. Your statement mentions a conference on recombinant DNA experimentation (genetic research). That subject has been in the news quite a bit lately. What is this conference likely to cover in this regard and when will it take place?

ANSWER. The conference on DNA recombinant research currently being planned will be conducted in June 1977 or as soon as planning for a high quality meeting can be completed. This meeting will be devoted to developing experimental studies to assess some of the risks in conducting DNA recombinant research. Many segments of the NIH guidelines call for safety procedures against hypothetical risks. The experiments to be planned at the conference will assess in a factual way the degree of some of these risks.

SCIENTIFIC MEMORANDA

Mr. MICHEL. You mention a new communications technique involving an exchange of informal scientific memoranda which is designed to speed up the availability of research data. Who will this information be exchanged among?

ANSWER. This information will be exchanged by nearly all research scientists throughout the world actually conducting research studies in the scientific field of each particular scientific memoranda; to date 47 different countries have been involved. For example, scientists conducting studies on hepatitis contribute progress reports and short informal summaries of completed experiments, as well as other informal exchanges, to the hepatitis scientific memoranda. This makes the new information available to the research scientists 12 to 18 months before the formal manuscripts on that research will appear in the scientific literature. Because research investigators throughout the world participate in these scientific memoranda, American scientists become aware of studies conducted in other countries that will be reported in foreign scientific journals.

Mr. MICHEL. Is there likely to be a reluctance on the part of scientists to make information on their research available prior to its completion?

ANSWER. Most scientists will not reveal research results, that is, new data, until they can be sure of credit for producing the new information. This assurance is, generally, in the form of a communication opportunity involving author identity, for example, presentation of a paper at a scientific meeting, publication of a manuscript in a scientific journal, the appearance of a communication in a scientific memoranda, or in a letter to a colleague. Such author protection is even more important when a patent might issue.

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SATELLITE COMMUNICATION

Mr. MICHEL. You mention two-way radios transmitting through satellites. How will this work, and who will be using it?

ANSWER. Communications between research scientists, conducting similar studies, while the investigations are being conducted are highly important to the successful outcome and to the efficient expenditure of research time, money and opportunities. The feasibility study being conducted by the Fogarty Center is to determine if the new communication satellites have any special value to research investigators. So far, very positive results have been obtained in two categories: (1) Scientists conducting field studies in isolated areas without normal communication facilities can, through the use of one of these small special radios communicate with their base laboratories or with scientific colleagues anywhere, as is necessary to conduct their field studies successfully; (2) Scientists at widely scattered sites but doing similar research can confer frequently. Scientists located in New Zealand, Australia and the United States including Hawaii and Alaska have conferred on current experiments on a person-to-person basis and have also held joint scientific conferences. The latter brings the conference to the scientists with significant savings in travel time and expense.

This communication system is open to any biomedical research scientist, with an appropriate radio, located anywhere in the coverage area of the satellites being used, that is, Western Hemisphere and all of the Pacific Ocean area.

U.S. BIOMEDICAL RESEARCH

Mr. MICHEL. Our scientists did quite well as far as Nobel Prize awards were concerned this year. Where do we rank as a nation in terms of biomedical research? Are we at the top?

ANSWER. At the present time no criteria exist which will permit a reliable qualitative or quantitative assessment of biomedical research support on an international scale. Excellent research is performed in other countries as evidenced by the award of Nobel Prizes to foreign physicians and scientists. However, the United States remains the leader among nations in the pace, character, direction, and financial support of a national medical research effort.

Nobel Prizes have been awarded to increasing numbers of Americans in recent years. Among these Nobel laureates in physiology and medicine are four NIH scientists: Marshall Nirenberg, Julius Axelrod, Christian Anfinsen, and Carleton Gajdusek. This excellent record reflects the commitment which the United States has made to the scientific attack upon health problems in this Nation through the broad support of biomedical research, the training of specialized manpower to enhance this capability, and the construction of research facilities to permit the further development of U.S. health-related research and training resources.

FOREIGN EXCHANGE PROGRAMS

Mr. MICHEL. Who benefits most by your various foreign exchange programs? Is it the United States or the other nations?

ANSWER. Our foreign exchange programs have as their ultimate purpose benefit to the health of the American people. Whether it is the young foreign scientist we may bring here under a fellowship or the senior scientist we send abroad, each is judged on the basis of scientific merit; but there is a contribution of expertise as well as a gain going both ways. There must be more or less benefit to both us and other nations for these exchanges to work and, if it could be measured, it is no doubt in about equal measure. Science and health are largely world commodities that we must share if we are to benefit.

GORGAS MEMORIAL INSTITUTE

Mr. MICHEL. What is the general composition of the staff of the Gorgas Memorial Institute in terms of nationality? Does it involve mostly United States citizens, or are Panamanians and other Latins in a predominance?

ANSWER. The regular professional scientific staff of the Gorgas Memorial Institute and its research arm, the Gorgas Memorial Laboratory, normally is about 18, with approximately two-thirds United States and one-third Panamanian. This may vary slightly from time to time with staff turnover. There will usually be five or six visiting scientists, most of whom are American, but occasionally other nationalities.

Mr. MICHEL. Is Panama fully cooperating with the Institute?

ANSWER. Panama cooperates fully with the Gorgas Memorial Institute and Laboratory. Beyond the original contribution of land and buildings, this cooperation includes such diverse elements as the provision of access to field study sites and materials, support for environmental impact studies, tax exemption for the laboratory and its foreign scientists, and exemption from certain labor code requirements.

Mr. MICHEL. To what extent would you say the Institute's research and training efforts benefit Panama?

ANSWER. Panama benefits greatly from the efforts of the Gorgas Memorial Institute and Laboratory. Most importantly are the long-term benefits derived from the research on tropical diseases which are prevalent in Panama as well as elsewhere in Latin America. Other benefits include the advisory services on health matters provided to Panamanian authorities, referral and consultation services on tropical disease, an excellent library accessible to local scientists and students, and experience and training given to Panamanian technical staff.

HEALTH SYSTEMS OF OTHER COUNTRIES

Mr. MICHEL. Have any of your studies on the health systems of other countries been completed as yet, and if so, what generally do they show?

ANSWER. We have completed and published a number of studies on the health care systems of other countries. These are published with the thought in mind that information concerning successful and unsuccessful efforts in other countries will provide U.S. health planners with data which is based upon actual experience with a variety of health systems. This information can be used in the development of new or improved systems for the provision of health care to the people of the United States.

Studies which we have published are:

(1) Health Care in Yugoslavia;
(2) Medicine in Chinese Cultures: Comparative Studies of Health Care in Chinese and Other Societies;
(3) Public Health Planning in the U.S.S.R.;
(4) The British National Health Service;
(5) Complaint Procedures of the British National Health Service;
(6) Community Medicine in England and Scotland;
(7) Health Care in Scandinavia; and
(8) The Danish National Health Service.

We believe that the facts, comparisons, and analyses contained in the above listed publications will provide guidance to U.S. health planners in their efforts to develop and improve U.S. health systems. For example, from "Health Care in Scandinavia," a chapter prepared by Drs. Erik Holst and Marsden Wagner, co-directors of the Joint Center for Health programs at the University of Copenhagen, states "There are at least three important reasons why the United States should take a close look at the Scandinavian experience with primary health care. First, the Scandinavian countries have had by far the longest experience in the world with collective funding of primary health care. Second, the Scandinavian countries are Western, industrialized countries with capitalistic economies and democratic forms of government. Their systems of primary health care, therefore, have relevance to what can or will develop in the United States. Third, the Scandinavian countries, happily but coincidentally, have developed contrasting primary health care systems. This will alllow Americans to observe the advantages and disadvantages of the different systems. We will look first at the scope of primary health care, then at the systems of primary health care in Scandinavia, and finally discuss the lessons Americans can learn from them."

EXCHANGE AGREEMENT WITH SOVIET UNION

Mr. MICHEL. We have an exchange agreement currently in existence with the Soviet Union. Would you describe for us the mechanics of how this agreement and cooperation is carried out?

ANSWER. The Department of Health, Education, and Welfare has been carrying out medical scientist exchange programs with the Soviet Union since 1958 under a series of Biannual U.S.-U.S.S.R. Cultural and Scientific Exchange Agreements. On May 23, 1972, an intergovernmental agreement was concluded

between the United States and the Soviet Union for cooperation in the fields of medical science and public health. Under this agreement a Joint Committee on Health Cooperation was established and issued a joint memorandum of understanding which designated specific collaborative areas: Cardiovascular diseases, including artificial heart research and development; malignant neoplasia; environmental hygiene; and arthritides and acute respiratory diseases. Joint experimental and clinical studies are carried out in these areas through a continuous intensive exchange of delegations, scientists, techniques, biological materials, publications, information, and equipment. In addition to those areas specifically covered in the memorandum of understanding the terms of the U.S.-U.S.S.R. agreement provide for the exchange of individual health professionals in a wide variety of specialties in medicine and public health. A yearly quota of 80 man-months of exchanges from each side is permitted and the entire program of cooperation is funded mutually by the DHEW and the Soviet Ministry of Health.

The Joint Committee on Health Cooperation meets each year to review progress of ongoing cooperative areas and to discuss the addition of new areas. An updated memorandum of understanding is used subsequent to these meetings.

JUSTIFICATION OF THE BUDGET ESTIMATES

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[1/]

	1977 Appropriation	1978 Estimate
Appropriation	$7,992,000	$8,369,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977-$200,000; 1978-$200,000.

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Budget Mechanism

	1977 Number	1977 Amount	1978 Number	1978 Amount
Grants				
Special				
Gorgas Memorial Institute.....	1	$1,400,000	1	$1,400,000
Total Grants.....	1	1,400,000	1	1,400,000
Direct Operations				
Scholars.....	209	3,300,000	188	3,400,000
International Center.....	---	3,044,000	---	3,307,000
Program Management.....	---	248,000	---	262,000
Total	---	7,992,000	---	8,369,000

DHEW - National Institutes of Health

CROSSWALK - 1977 Column of 1978 Justification

INSTITUTE: John E. Fogarty International Center for Advanced Study in the Health Sciences
(in thousands of dollars)

Program \ Mechanism	Research Grants Specials Other	Direct Operations	Total
1. Gorgas Memorial Institute.....	$1,400	--	$1,400
2. Direct Operations.....		$6,344	6,344
3. Program Management.....		248	248
Total obligations.....	1,400	6,592	7,992

DHEW - National Institutes of Health

CROSSWALK - 1978 Column of 1978 Justification

INSTITUTE: John E. Fogarty International Center for Advanced Study in the Health Sciences
(in thousands of dollars)

Program \ Mechanism	Research Grants Specials Other	Direct Operations	Total
1. Gorgas Memorial Institute.....	$1,400	--	$1,400
2. Direct Operations.....		$6,707	6,707
3. Program Management.....		262	262
Total obligations.....	1,400	6,969	8,369

Summary of Changes

1977 Estimated obligations	$7,992,000
1978 Estimated obligations	8,369,000
Net change	+377,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in				
1. Within-grade pay increases	---	$14,000	---	+$14,000
2. Federal Employee Compensation Fund	---	1,000	---	+2,000
3. Federal Telecommunications System rate increases	---	24,000	---	+1,000
4. Service and supply rate increases	---	90,000	---	+20,000
5. Payment for centrally funded services	---	297,000	---	+54,000
(Standard Level User Charges)	---	(32,000)	---	(+9,000)
Subtotal	---	---	---	91,000
B. Program				
1. Scholars - to support increased stipend levels		3,300,000	---	+100,000
2. International Center to support additional advanced studies, and the US USSR Individual Specialist Exchange Program	51	3,044,000	---	+190,000
Subtotal (program)	---	---	---	+290,000
Subtotal increases	---	---	---	+381,000
Decreases:				
Built-in				
One less day of pay	---	1,201,000	---	-4,000
Subtotal decreases	---	---	---	-4,000
Total, net change	---	---	---	+377,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
223	Gorgas Memorial Institute.....	---	$1,400,000	---	$1,400,000	---	---
224	Direct Operations.....	43	6,344,000	43	6,707,000	---	$363,000
	Standard Level User Charge....	---	(32,000)	---	(41,000)	---	(9,000)
227	Program Management.....	8	248,000	8	262,000	---	14,000
	Total obligations.....	51	7,992,000	51	8,369,000	---	377,000

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions..	51	51	---
Full-time equivalent of all other positions.....	9	9	---
Average number of all employees.....	58	58	---
Personnel compensation:			
Permanent positions.....	$1,058,000	$1,077,000	+19,000
Positions other than permanent.....	125,000	128,000	+3,000
Other personnel compensation.....	18,000	18,000	---
Subtotal, personnel compensation.	1,201,000	1,223,000	+22,000
Personnel benefits.....	143,000	147,000	+4,000
Travel & transportation of persons...	50,000	60,000	+10,000
Transportation of things.....	6,000	6,000	---
Rent, communications & utilities.....	123,000	136,000	+13,000
Printing and reproduction.....	315,000	332,000	+17,000
Other services:			
Payment for centrally funded services.....	297,000	351,000	+54,000
Other.....	1,047,000	1,182,000	+135,000
Supplies and materials.....	80,000	92,000	+12,000
Equipment.....	30,000	40,000	+10,000
Grants, subsidies, and contributions.	4,700,000	4,800,000	+100,000
Total obligations by object.....	7,992,000	8,369,000	+377,000

Authorizing Legislation

	1978	
	Authorization	Appropriation Requested
Legislation		
Public Health Service Act		
Title III Part A - Research and Investigation in General (Section 301)	Indefinite	$6,969,000 1/
International Cooperation (Section 307)	Indefinite	
"An act to authorize a permanent annual appropriation for the maintenance and operation of the Gorgas Memorial Institute" Public Law 70-350	$2,000,000	$1,400,000

1/ Funding estimate only.

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Comparable

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	3,460,000	2,954,000	2,954,000	2,774,600
1971	2,664,000	3,582,000	3,582,000	3,582,000
1972	3,369,000	3,813,000	4,338,000	4,338,000
1973	3,926,000	4,666,000	6,000,000	4,666,000 1/
1974	3,576,000	4,757,000	4,757,000	4,757,000
1975	4,587,000	4,187,000	5,803,000	5,392,000
1976	4,529,000	5,334,000	6,234,000	5,694,000
1977	7,492,000	7,992,000	7,992,000	7,992,000
1978	8,369,000			

1/ This appropriation was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate in the first vetoed bill.

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Actual

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	3,460,000	2,954,000	2,954,000	2,774,600
1971	2,664,000	3,582,000	3,582,000	3,582,000
1972	3,319,000	3,763,000	4,288,000	4,307,000
1973	4,545,000	4,666,000	6,000,000	4,666,000 1/
1974	3,586,000	4,767,000	4,767,000	4,767,000
1975	4,784,000	5,384,000	6,000,000	5,589,000
1976	4,540,000	5,345,000	6,245,000	5,705,000
1977	7,492,000	7,992,000	7,992,000	7,992,000
1978	8,369,000			

1/ This appropriation was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate in the first vetoed bill.

Justification

John E. Fogarty International Center
for Advanced Study in the Health Sciences

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Gorgas Memorial Institute..	---	$1,400,000	---	$1,400,000	---	---
Direct Operations.....	43	6,344,000	43	6,707,000	---	$363,000
International Center.....	(43)	(3,044,000)	(43)	(3,307,000)	(---)	(263,000
Scholars.....	(---)	(3,300,000)	(---)	(3,400,000)	(---)	(100,000)
Program Management.....	8	248,000	8	262,000	---	14,000
Total.....	51	7,992,000	51	8,369,000	---	377,000

General Statement

The Fogarty International Center was organized as a living memorial to Congressman John E. Fogarty to carry out his concept of a center to represent "... the visible and tangible embodiment of the nation's devotion to the use of science for peaceful purposes and the good of mankind." Accordingly, the Center's programs are designed to promote this concept through advanced study in the biomedical and related sciences and to develop practical methods to utilize the knowledge thus gained to improve the health and well-being of our society. Its programs encourage interaction, study, cooperation, and collaboration within the international biomedical community and provide opportunities for discussion of significant research, public health, medical, and biomedically related social and economic issues.

In 1976, a study of the Center's activities, its mission, and its relationship to the missions of the NIH Institutes by the Director, NIH, developed a more definitive role for the Center which encompasses four broad areas, i.e.

1. As a focal point for NIH international activities, providing advice and staff support to the Institutes and Divisions and to the Office of the Director, NIH, on such activities,

2. As a center for advanced international studies on aspects of biomedical research and the use of biomedical research in health services,

3. To augment Institute awareness of activities and opportunites in biomedical research and the applications of science to health problems in other countries, and

4. To oversee the general aspects of Institute relations with the Department of State, with representatives of countries with whom NIH has bilateral arrangements and with multilateral organizations.

The projects within the general areas delineated above and other projects that have developed within the Center over the past 8 years constitute a substantial spectrum of research and administrative support activities.

The Fogarty International Center is requesting $8,369,000 in 1978.

Gorgas Memorial Institute

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Gorgas Memorial Institute...	---	$1,400,000	---	$1,400,000	---	---

Introduction

The Gorgas Memorial Laboratory founded in 1921 and rendered functional in 1929 with direct support from the Congress of the United States, has the mission of conducting, assisting and encouraging "investigations in the sciences and arts of hygiene, medicine and surgery and allied subjects, in the nature and causes of disease and the methods of its prevention and treatment, and to make knowledge relating to these various subjects available for the protection of the health of the public and the improved treatment of disease and injury particularly as applied to tropical and preventive medicine." During the past forty-six years of scientific endeavor, the Gorgas Memorial Laboratory has placed major emphasis on the study of tropical infectious disease. Knowledge relating to the cause, natural history and control of malaria, Chagas' disease, leishmaniasis and vector-borne virus diseases has been greatly enhanced by the efforts of this research center. Incorporation of the Middle America Research Unit into the Gorgas Memorial Laboratory has increased the capability of this new educational and research complex and permits expansion of the scientific program to respond to a broader spectrum of health research needs of North and Latin America.

Program plans for 1978

Funds for the Gorgas Memorial Laboratory are requested through the budget of the Fogarty International Center which has been active in the affairs of the Laboratory including review of scientific programs and promotion of Laboratory interests in the scientific community. As a result of hearings on a proposal to increase the authorization for this Laboratory, the Committee on Foreign Affairs urged a more formal relationship between the Gorgas Memorial Institute and the Center to insure that the proposed expanded research and education program will be carefully coordinated with the overall Federal health research program. Early in fiscal 1977, the Center supported the site visit of a team to review the scientific and managerial operations of the Laboratory and suggest methods by which its operations might more fully be coordinated with the program planning processes of the Federal government. The current resources, both tangible and intangible, of the Laboratory, give it potential as a regional center for studies of major health problems of mutual interest to the United States and Latin America. These problems include diseases strongly influenced by environment, genetic and social factors and the ecologic derangements associated with industrial development. Of especial interest in this regard are the cause and effect relationships between these environmental factors and the major human health problems of atherosclerosis, hypertensive respiratory disease, cancer and certain nutritional derangements. In addition there are unique opportunities to pursue research in the delivery of preventive and therapeutic methods including large-scale clinical trials as well as the role of ancillary health personnel in health care delivery in community-oriented disease control programs.

Direct Operations

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Direct Operations.....	43	$6,344,000	43	$6,707,000	---	$363,000
(International Center)	(43)	(3,044,000)	(43)	(3,307,000)	(---)	(263,000)
(Scholars)	(---)	(3,300,000)	(---)	(3,400,000)	(---)	(100,000)

International Center

This activity supports the scientific, administrative and clerical staffs responsible for the management and operation of the International Exchange Program, the Advanced Study Program, the administrative support function and the staff support and advice in connection with international activities to the Institutes and Divisions. In addition it also supports the Advanced Study Program projects.

Program Plans for 1978

The search for improved knowledge on the cause and nature of disease through laboratory and clinical investigations is directed toward advances in the prevention, diagnosis, and treatment of disease. Research and its resultant acquisition of new knowledge are essential for advances in medicine that will ease disease suffering, reduce the economic burden of health care, and improve the quality of life. Consolidation, evaluation, and distribution of new knowledge are essential parts of the research process. It is in these areas that the Fogarty International Center makes a major contribution to the mission of the National Institutes of Health.

Among the areas which have been considered and will be further developed during the succeeding years are studies of health systems and health activities of other countries, the conduct of scientific conferences with new initiatives such as recombinant DNA research, clinical trials and trans-NIH areas of diabetes, nutrition, genetics and epidemiology.

The Fogarty International Center has the coordinating and policy formulation function and operating responsibility for the NIH Special Foreign Currency Program. The Program is now undergoing extensive evolutionary changes as a result of economic and political factors. The diminution of foreign currency available for U.S. uses has made it necessary to take measures to alleviate the impact of the loss of these funds upon the biomedical research community in those countries. One measure has been the development of bilateral agreements providing for collaborative funding by the countries involved. These agreements establish "institution-to-institution" collaboration between U.S. and foreign institutions. These new bilateral agreements with excess currency countries will be directed toward maintaining existing biomedical science collaborations and developing new projects.

The International Visitors Center provides an opportunity to visitors for discussion of international biomedical problems with professional staff and for the arrangement of appropriate contacts between such visitors and the Fogarty International Center and NIH staff members.

The International Education Program is responsible for arranging of professional programs for, providing supervision and consultation to, and maintaining on-going evaluation of the training experiences of World Health Organization supported medical and allied health professionals studying in the United States.

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The US-USSR Individual Health Exchange Program administered by the Center at NIH provides for a limited number of American medical scientists to engage in collaborative research in their professional fields in the Soviet Union.

Scholars

Fogarty Scholars-in-Residence

The Fogarty Scholars-in-Residence Program provides outstanding scientists and other scholars the opportunity to focus their attention on broad aspects of important issues in biomedical research. While in residence at the Center, the scholars individually and collectively engage in collaborative research with NIH and university scientists.

The unique environment at NIH offers an unusual opportunity for scholars to interact with large numbers of intramural staff scientists, initiate all types of meetings from formal international conferences to workships and seminars. The involvement of these scholars provides an impetus to the progress of biomedical research and will, hopefully, hasten the solution to many of the disease problems confronting the world.

Senior International Fellowships

The Senior International Fellowships Program is designed to provide opportunities to outstanding faculty members at mid-career from U.S. schools of medicine, osteopathy, dentistry, and public health with demonstrated productive scholarship and recognized stature in their profession to go abroad to study and share their expertise. It is intended that this award be a career enhancing educational experience with mutual benefits to all involved. These research and public health scholarships are intended to:

1. increase the interchange of ideas of mutual interest between U.S. scholars in academic medicine and those of other nations of the world,

2. permit the exchange of the latest advances in a particular area of medicine, both basic and clinical,

3. permit participation in the contribution to on-going research in the medical sciences or in science areas related to medicine, and

4. improve the academic, research and/or clinical biomedical potential of the U.S. medical institution.

International Research Fellowships

The International Research Fellowships Program offers a unique opportunity for the sharing of scientific information on an international basis by providing an opportunity to 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 and those in different environmental settings.

Program Plans for 1978

The Fogarty International Center will continue to seek outstanding individuals for invitation and participation in the Scholars Program. The response to the initiation of the Senior International Health Program reflects an evident

need within the U.S. biomedical academic community for this type of support. In 1977, 59 awards will be made and in 1978 funds requested will provide for 53 awards. Announcements concerning this Program have resulted in the submission of a large number of applications from highly qualified scientists. Nominations from national committees of other countries for the International Research Fellowship Program are always in excess of the opportunity for awards and we will continue to select only the very highest quality applicants. In 1977, 141 awards were made and in 1978, although the funds requested are increased, because of increased costs of awards, the funds will support 127.

Direct Operations

Increases	
A. Built-in (International Center)	
1. Within-grade pay increases	+$9,000
2. Federal Employees Compensation Fund	+ 2,000
3. Federal Telecommunications System	+ 1,000
4. Service and Supply rate increases	+11,000
5. Payment for centrally funded services	+45,000
6. Payment for SLUC	+ 9,000
Subtotal	+77,000
B. Program	
1. Scholars - to support stipend increases for scholars	+100,000
2. International Center - to support additional advanced studies, and the US-USSR Individual Specialist Exchange Program	+190,000
Subtotal	+290,000
Decreases	
Built-in (International Center)	
One less day of pay	-4,000
Total net change	363,000

Program Management

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management	8	$248,000	8	$262,000	---	$14,000

Purpose: The purpose of this activity is to provide overall program direction and management services to the functions and responsibilities of the Center.

Program Plans for 1978

To provide leadership and direction to the programs and activities seeking effective and efficient new methods of operations.

Increases

Built-in	
1. Within-grade pay increases	+$5,000
2. Service and supply rate increases	+ 9,000
Total net change	+14,000

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Research Grants (Public Law 70-350)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$1,400,000	$2,000,000	---	$1,400,000

Purpose: This grant provides the legislatively authorized U.S. support for the operation and maintenance of the Gorgas Memorial Laboratory now comprising the merged facilities of the former Middle America Research Unit and the Gorgas Memorial Laboratory. The purpose of this institution is to conduct research on tropical diseases of public health importance to the United States and Latin America, to provide guidance for the application of research findings to preventive and therapeutic ends and to provide educational opportunities for students of tropical medicine.

Accomplishments in 1977: During fiscal year 1977, the Gorgas Memorial Laboratory expanded its ecology research, especially in the Bayano River area. In response to requests from the Panamanian government environmental impact statements were developed for the Bayano and Fortuna projects reflecting upon the effects of large-scale disruption of the environment, particularly in complex tropical areas. Virological studies associated with the Bayano project have revealed the infiltration and potential spread of three viral agents, YF, SLE, and VEE viruses. These three viruses continue to pose a major epidemic threat over extensive areas of the Americas. Recent advances include the development of a greatly improved method of rearing the mosquito, Toxorhynchites, on an artificial diet rather than on live mosquito larvae. These species facilitate the study of viruses through serving as safe experimental hosts.

Objectives in 1978: Financial problems which plagued the Gorgas Memorial Laboratory in 1976 have been eased. Research will continue on the Bayano and Fortuna projects. The Gorgas Memorial Laboratory experience in these areas should increase requests of the Government of Panama, World Bank, PAHO and other agencies for assistance in ecological studies, including development of environmental impact studies. The improved financial situation will also have a direct effect upon the research initiated within the Departments of Ecology, Zoonoses, Experimental Biology, Parasitic Diseases and Bacteriology.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Direct Operations (Public Health Service Act Title III Part A)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
43	$6,344,000	Indefinite	43	$6,707,000

Purpose: 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 a number of International programs such as International Fellowships, Scholars-in-Residence, Advanced Study, International Visitors Center, Special Foreign Currency, and programming of health professionals of other nations.

Accomplishments in 1977: This activity provides personnel support to all the center activities and the Advanced Study, the International Exchange and Scholars-in-Residence Programs. During 1977, in cooperation with NIH Institutes, international organizations and foreign institutions, as well as independently, the Center supported international conferences and workshops on a number of subjects, including such timely efforts as recombinant DNA research, issues in clinical research, growth factors and organ transplantation. Results of conferences supported by the Center are published and distributed to libraries, universities and institutions in the United States and abroad.

The Center also awarded fellowships for research and study to 209 individuals from 35 foreign countries and the United States.

Objectives in 1978: Continued activity in the Advanced Study Program, through individual studies, workshops, seminars and conferences, will permit further analysis and comparative studies of medicine and public health and the transfer and exchange of scientific and biomedical knowledge.

It is proposed to award fellowships for research and study to 188 individuals from 40 foreign countries and the United States.

NATIONAL INSTITUTES OF HEALTH

John E. Fogarty International Center
for Advanced Study in the Health Sciences

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act Title III Part A)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
8	$248,000	Indefinite	8	$262,000

Purpose: The purpose of this activity is to provide overall program direction and management services to the functions and responsibilities of the Center.

Accomplishments in 1977: Provided leadership and direction to the programs and activities of the Center and supported the initiatives of Equal Employment Opportunity and Manpower utilization.

Objectives for 1978: To provide leadership and direction to the programs and activities seeking effective and efficient new methods of operations and maintaining an awareness of and with dedication to the programs, plans and desires of the Department.

MONDAY, MARCH 14, 1977.

NATIONAL LIBRARY OF MEDICINE

WITNESSES

DR. MARTIN M. CUMMINGS, DIRECTOR, NATIONAL LIBRARY OF MEDICINE
DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
MELVIN S. DAY, DEPUTY DIRECTOR, NATIONAL LIBRARY OF MEDICINE
KENT A. SMITH, ASSISTANT DIRECTOR FOR ADMINISTRATION, NATIONAL LIBRARY OF MEDICINE
FRANK B. POH, FINANCIAL MANAGEMENT OFFICER, NATIONAL LIBRARY OF MEDICINE
LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
NORMAN MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
ELLEN F. WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now we have the National Library of Medicine.

The presentation will be made by Dr. Martin M. Cummings, Director of the National Library of Medicine.

We have your biographical sketch, Dr. Cummings, which we will place in the record at this point as well as your statement.

[The biographical sketch and statement follow:]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH—BIOGRAPHICAL SKETCH

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, 1944.

Experience

Present: Director, National Library of Medicine.
1963–64: Associate Director for Research Grants, National Institutes of Health.
1961–63: Chief, Office of International Research, National Institutes of Health.
1959–61: Professor of microbiology and chairman, Department of Microbiology, University of Oklahoma School of Medicine.
1953–59: Director, Research Services, Veteran's Administration Central Office.
1953–59: Special lecturer in microbiology, George Washington University School of Medicine.
1953: Associate professor of bacteriology, Emory University.
1949–53: Chief, Tuberculosis Research Laboratory, Veteran's Administration Hospital of Atlanta.
1948–53: Instructor through associate professor of medicine., Emory University.
1947–49: Director, Tuberculosis Evaluation Laboratory, Communicable Disease Center, U.S. Public Public Health Service.
1945–47: Assistant resident, Boston Marine Hospital.
1944–45: Intern, Boston Marine Hospital.
1942–44: U.S. Army, Pfc.

Association memberships: American Association for the Advancement of Science, Board of Directors; American Academy of Microbiology, Inc.; American Board of Microbiology; American Federation for Clinical Research (Emeritus); American Society for Clinical Investigation (Emeritus); Association for American Medical Colleges; Medical Library Association; Society of Sigma XI; American Clinical and Climatological Association; Washington Society for the History of Medicine; Gorgas Memorial Foundation, Board of Director; Association of Research Libraries; Society of Medical Administrators; and Institute of Medicine, National Academy of Sciences.

Specal awards, citations, or publications: Veterans Administration Exceptional Service Medal; DHEW Superior Service Award; DHEW Distinguished Service Award; Honorary Doctor of Science, Bucknell University, 1969; Distinguished Alumnus Award, Duke University; Honorary Doctor of Science, University of Nebraska, 1971; Honorary Doctor of Science, Emory University, 1971; Honorary Doctor of Humane Letters, Georgetown University, 1971; Honorary Member, Alpha Omega Alpha; Honorary Doctor of Medicine, Karolinska Institute, Stockholm, Sweden, 1972; Honorary Fellowship, College of Physicians, Philadelphia, 1973; Rockefeller Public Service Award, 1973; Modern Medicine Distinguished Achievement Award, 1976; and 100 Scientific and Historical Publications.

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

Statement by the Director, National Library of Medicine

on

"National Library of Medicine"

Mr. Chairman and Members of the Committee:

When the forerunner of the National Library of Medicine was established in 1836 as the Library of the Army Surgeon General's Office, its basic role was to serve the needs of military medical officers by providing them with access to medical information which they needed as practicing physicians. As the mission and services of the Library expanded all civilian practicing health professionals were given access to the Library's holdings, and increasing emphasis was placed on serving the needs of health researchers and health educators as well. Notwithstanding the success which the Library has had in disseminating relevant medical information to all segments of the health community, it is our view that the information transfer process which serves the scientist so well does not respond as effectively to the clinically oriented needs of the health practitioners. Accordingly the Library will devote increasing resources toward the development of information services and the conduct of information activities which assist and enhance health care delivery.

Since the passage of the National Library of Medicine Act in 1956 the Library has become a major information resource for the nation's health community. The Library fulfills its responsibilities by collecting, organizing and disseminating the most extensive collection of health science literature and other informational materials in the world. Today the Library's collection is organized in a most efficient manner consistent with facilitating the timely and effective dissemination of medical information. This has been made possible because the Library has continued to pioneer in the application

of new technologies to library functions. Such revolutionary library technology as photoduplication for interlibrary loans and computerized information storage and retrieval systems were developed and applied successfully by the NLM.

The impact which these new technologies have had on the ability of the Library to disperse medical information is reflected in the continued growth in utilization of these tools by the health community. For example, the number of computer-based on-line searches performed has grown from approximately 250,000 in FY 1974 to 566,000 searches generated in FY 1976. In FY 1978 the number of searches will exceed 650,000. Similarly the number of interlibrary loans performed by the Library exceeded 200,000 in FY 1976, and the number of such loans performed by the NLM established Regional Medical Network reached over 1,000,000 in FY 1976. Other more traditional Library services continue to experience high growth rates. For instance, the number of reference inquiries which totaled 32,000 in FY 1976 is expected to reach 50,000 in FY 1978. Similar increases for reader services which totaled 96,000 in FY 1976 are expected to reach 125,000 by FY 1978.

NLM which is responsible for operation of a nationwide on-line computerized bibliographic retrieval service including MEDLINE (MEDLARS on-line), will encourage the use of these services in direct patient care facilities. This is in contrast to the earlier years of the MEDLINE network's development when the development of MEDLINE Centers was concentrated in medical school libraries and their affiliated health care facilities. Currently of the existing 445 MEDLINE Centers, approximately one-third are located in direct patient care facilities. Nearly 50 percent of the new Centers established (37 of 75) in 1976 were in hospitals. This trend to expand the network to include smaller hospitals and community based health oriented training programs, will be accelerated in FY 1977 and FY 1978. In addition to

providing services to physicians, dentists, nurses and allied health personnel, the Library has improved access to health care administrators, planners, economists, legislators and others who are playing an expanding role in our nation's health care delivery system.

This extension of services to health practitioners is being developed along several lines. A complete restructuring of the Library's "Scope and Coverage" policy is underway to expand our holdings in the field of health care delivery and related areas. This extension plan will be implemented this year. The Library has undertaken a careful review of significant health care periodicals from various sources such as the American Hospital Association, American Medical Association, Association of American Medical Colleges, and other organizations to develop a consolidated list of periodicals to consider for inclusion in our published Index Medicus or in the MEDLINE data base. Indexing of such material was begun early in 1977 and will be fully implemented by 1978. Concurrently the Library has been expanding the controlled vocabulary used in indexing the biomedical literature to make it more responsive to the information needs of the health care community. Combined with the capabilities of the MEDLINE system to search titles and abstracts on any term, the expanded vocabulary will enable more explicit and effective searching of the health care literature.

The NLM has been investigating the difficult task of rapidly translating research results into clinical practice, an assignment which it shares with the other Institutes within NIH. Whereas the Institutes assume responsibility for the content accuracy of the information to be disseminated, the Library is responsible for providing suitable communication channels through which the information reaches the practitioners and others who have a need for this information. As a part of this effort to fulfill our responsibility the Library has undertaken a technology transfer study in conjunction with

with several Institutes and leading academic and specialty societies. It is hoped that the outcome of this project will lead to a new mechanism which is capable of providing medical information in style and format more immediately useful to the health practitioner. Such an undertaking could impact on the health practitioner in several important ways. These include: 1) enhancing efforts in continuing education; 2) providing information about specific clinical problems; and 3) making medical literature and information less remote from the realities of medical practice. Our goal is to develop new mechanisms and products to identify, organize, and distribute information relevant to clinical problems and to improve the quality of health care delivery.

In addition to participating in this innovative effort, the Lister Hill National Center for Biomedical Communications continues to develop and coordinate experimental communication networks and systems for the entire biomedical community. Utilizing the Communications Technology Satellite the NLM, in conjunction with other U.S. health agencies has begun a national experiment to provide information for health education and the delivery of health services to remote areas. Six broadcast and receive stations will be installed this year in sparsely populated areas of the country. NLM's own broadcast studio has been completed. Such stations will facilitate teleconferencing among health agencies and provide professional consultation between academic health centers and professionals in remote settings.

The NLM administers a program of grants and contracts to assist medical libraries in developing improved health information services. This program is authorized by the Medical Library Assistance Act of 1965 and its extensions. Based on funds available through this program the Library provides resources to support the maintenance and operation of ten Regional Medical Libraries which serve as focal points for region-wide planning and

information services. In the past the emphasis of the Regional Medical Libraries was primarily on document delivery services (Interlibrary Loans); however, the NLM and the participating libraries recognize the need to move beyond document delivery activities by having the Regional Medical Libraries act as demonstration and information dissemination centers. Through these efforts more health care practitioners will have local access to the advanced health science information systems available to them.

The National Medical Audiovisual Center continues to encourage the use of effective learning materials and innovative educational techniques in support of health science education at the undergraduate and graduate levels. In FY 1978 the Center's major thrust will be to extend its program efforts to all levels of health science education with more emphasis being placed on improving the continuing education of health professionals. In this way the knowledge and skills of the health practitioner can more easily keep abreast of the new medical advances. The Center continued to make audiovisual learning and teaching packages available to the health community through its distribution and sales programs. The 53,000 loans in FY 1976 accounted for an estimated 5,000,000 viewing experiences, and over 4,000 packages were sold through the General Services Administration.

The Toxicology Information Program is responsible for collecting and organizing toxicology data from a variety of sources and making it more readily available to its user communities in industry, universities, health care facilities and government agencies. It obtains information from published scientific literature, files of governmental,industrial and academic organizations in many formats; organizes and enters this information into standardized computerized storage and retrieval systems for easy access. In FY 1978 the Toxicology Information Program will concentrate its efforts on improving the utility of its various services to its user communities through enrichments and expansion of its data bases. For example, TOXLINE, an on-line

toxicology data base, will be enhanced with special files on drug interference and drug interactions which are of special interest to the health practitioner. During FY 1976 over 30,000 on-line searches of the TOXLINE data base were completed. This represents over a 30 percent increase over FY 1975 levels.

We are proud of the accomplishments of the Library in serving the information needs of the health professional community. We believe the initiatives which have been presented today provide the potential for enabling the Library to continue to fulfill its Congressional mandate to assist the advancement of medical and related sciences by fostering the dissemination and exchange of information which is important to the progress of medicine and the public health.

In summary, Mr. Chairman, our request for FY 1978 is $36,746,000, an increase of $1,512,000 over the amount available for obligation in FY 1977. The net increase reflects $537,000 for mandatory requirements and $975,000 for additional program related costs. I shall be pleased to answer any questions and supply additional information desired for the record.

Mr. FLOOD. Do you have some people with you that you want us to meet?

Dr. CUMMINGS. I have with me Mr. Melvin Day, Deputy Director, and Mr. Kent Smith, our Executive Officer.

Mr. FLOOD. Dr. Cummings, you have been before us before many times. How long have you been Director at the Library?

Dr. CUMMINGS. Since January 1964—13 years.

BUDGET INCREASES

Mr. FLOOD. Now the reason I asked that is that your request today is about four times the size of the budget that you testified for before I became chairman, sometime ago. Let me ask you for a minute before we go into any specifics about your budget, what do you think are the most important accomplishments of the Library to justify all this expense over that period of time?

Dr. CUMMINGS. I believe there are several basic and most important accomplishments.

First: The provision of information service to health professionals throughout the country.

Second: The support of medical education through the provision of educational materials. Now, I believe, Mr. Chairman, we are entering the era when we may provide similar support to those who are concerned with health planning and with the health care delivery apparatus in all of its dimensions. I suppose if I had to identify the most significant technical achievement, it would, of course, be our application of new computer and communications technology on behalf of the medical programs of our country.

Mr. FLOOD. Hardware?

Dr. CUMMINGS. And software and peopleware.

Mr. FLOOD. Last year's increase was over 20 percent?

Dr. CUMMINGS. Yes, sir.

Mr. FLOOD. This year you are very moderate about it. Do you feel the budget is kind of leveling off now for a couple of years or a few years maybe?

Dr. CUMMINGS. This year's budget allows us to keep pace with the rise in inflationary costs. As this committee well appreciates, just the acquisition of materials, books, and journals and other materials have gone up enormously. So I would have to say that I would not project for the future the same modest increases if we are to serve the Nation properly.

MEDICAL LIBRARY ASSISTANCE

Mr. FLOOD. Now, I believe your authorization expires this year. Are you going to ask for any major changes in the law or is it going to be an extension of the existing program?

Dr. CUMMINGS. Yes; it is my understanding that the administration is requesting a 1-year extension of all the health legislation. With respect to requesting changes, we are pleased with the language of the law as written by the Congress in 1965 and we are not asking for any technical amendments. It is a broadly based, well-conceived act in my view.

Mr. FLOOD. About $8 million of this request is for medical library assistance?

Dr. CUMMINGS. That is correct, sir.

Mr. FLOOD. Other than the funds for the regional libraries that we know about, how many grants will be made?

Dr. CUMMINGS. In fiscal year 1978 we intend to make about 120 new and competing awards and about 50 noncompeting awards, for a total of about 170 grants.

Mr. FLOOD. What will be the average size of such a grant?

Dr. CUMMINGS. The average size of such a grant is about $30,000.

Mr. FLOOD. How many applications do you receive that you are not able to fund?

Dr. CUMMINGS. About one-third of the approved grants are funded. So I would expect that we will receive in the neighborhood of 500 applications which will be reviewed and approved from which one-third will be funded.

Mr. FLOOD. Is that a lot?

Dr. CUMMINGS. It is better than our past experience, Mr. Chairman. I believe in previous years I have reported to this committee that we were only able to fund about 20 percent of the approved grants.

Mr. FLOOD. Are the libraries that are going to receive the support required to pay a minimum percentage of the operating costs in order to qualify for this Federal grant?

Dr. CUMMINGS. Yes, sir, in our improvement grant program the institution is required to show evidence that our funds do not replace institutional support and in fact a retrospective analysis of this program shows that institutional support has increased over the years and has not been declining as a result of our grants.

Mr. FLOOD. Is there a maximum number of years that an institution can receive this support?

Dr. CUMMINGS. Yes; I believe that the improvement grants are made on a 2-year basis.

Mr. FLOOD. You provide funds here for training, you say, of library personnel, under this particular appropriation. How does that system work?

Dr. CUMMINGS. We have 11 training grants in health professional schools, not necessarily geared to train librarians but rather to train personnel who can use computer technology in pursuit of medical care and medical research activities. These grants are designed to integrate computer science and medical science.

We previously gave awards for the training of medical librarians and information specialists, but that was stopped about 3 or 4 years ago.

LISTER HILL CENTER

Mr. FLOOD. We looked at this a long time ago. How far along are you with the construction of that new facility at the Lister Hill Center? Remember when that started?

Dr. CUMMINGS. Yes; I do. That has been a long saga, Mr. Chairman. Bids were received by GSA from some 17 contractors about 6 weeks ago. We had anticipated the low bidder would be beginning his work

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about this time, but we have learned that because of a technicality in the way the contractors submitted their bids, not listing correctly their subcontractors, that we are going to have to go through this process again.

So this project will be delayed another 2 or 3 months.

Mr. FLOOD. Well, all right.

Now we were always interested in this you will remember: What about the audiovisual center down there? When the center is completed is that going to go with the center or stay in Atlanta?

Dr. CUMMINGS. The National Medical Audiovisual Center will be transferred to the Lister Hill facility and integrated into their program.

Mr. FLOOD. You tell us the Center will be moving away from using contractors so you can establish a stronger in-house research program. What is the reason for that change all of a sudden?

Dr. CUMMINGS. We believe that to be leaders in the field of information handling we must have our own competence. Even the monitoring of contracts, as I am sure you well appreciate, requires technical skills so that we know that the research and development are being done properly.

In the broadest sense we view the Lister Hill Center as a counterpart to the intramural research program at NIH.

PERSONNEL REQUIREMENTS

Mr. FLOOD. Now that being so, your justification there states, "The key to the success of the in-house research program is staffing." But no request here for new positions. How can you put that together?

Dr. CUMMINGS. Well, we originally submitted a request for increased personnel to man the Lister Hill Center and in fact to strengthen the library operations.

In the competition for limited personnel ceilings available to NIH, it was not apparently possible to receive any increase. In my view it is more important to the future of our institution, to acquire personnel than additional funding.

BIOMEDICAL COMMUNICATION NETWORK

Mr. FLOOD. That is quite a statement. I thought you would say that.

Can you explain for us what you mean by the biomedical communications network.

Dr. CUMMINGS. Yes, sir.

Over the course of the last 5 or 6 years we have brought together some 500 institutions in this country, connected them to their National Library of Medicine through available commercial communications channels. This permits them to do a number of things more economically and more efficiently than ever before. It permits them to search our data bases in our computers by on-line access. Also it permits them to make quick and ready exchanges of documents which heretofore depended upon the Postal Service.

We have in fact brought together the major health institutions of this country through this network.

COMMUNICATION SATELLITES

Mr. FLOOD. What is the total cost associated now with the satellite which you are using in the network?

Dr. CUMMINGS. Over the course of the past 2 years we have expended $2.9 million in the development of the satellite system.

Mr. FLOOD. Now also in your statement there you indicate that you are going to be building six new broadcast facilities for this whole network. What area of the country will these serve?

Dr. CUMMINGS. The six ground-based, two-way transmitting receiving stations will be located in Lexington, Ky.; Bozeman, Mont.; Denver, Colo.; Seattle, Wash.; Fairbanks, Alaska; and Bethesda, Md. Through these ground terminals links will be made to other remote and rural settings for transmission of the programs.

INFORMATION SERVICES

Mr. FLOOD. Now here is something you also talked about in your statement and in answer to one of my earlier questions: In your justifications as usual, you indicate there is a very large increase in the amount of services being provided by the library. You make quite a point out of that. I am sure you know there is a lot of concern about how broadly these services are used outside of the academic community.

Now, could you estimate what percentage of practicing physicians actually make regular use of your program?

Dr. CUMMINGS. I can't give you a precise number, but I can tell you that in the course of the last 4 years the percent of practitioner use of our services has doubled, that is to say it has gone from about 15 percent of all requests which we receive to about 30 percent. We are making a deliberate effort to reach the health practitioner.

I would hope that I can come back and say that half of all our services are now going to the practitioner.

In terms of our computer capacity and the on-line network, nearly half of all new terminals were located in community hospitals, the workplace of the practitioner. We think this is the strategy we should pursue.

Mr. FLOOD. You are trying to make your data more usable to the practitioner?

Dr. CUMMINGS. Yes; in behalf of patient care.

HEALTH EDUCATION COORDINATION

Mr. FLOOD. How closely have you been working with the health education programs in the whole department? It seems to me you could avoid a lot of mistakes as the program expands under this new law if you had that close cooperation.

What about that?

Dr. CUMMINGS. I believe that to be true. We are working closely with the Health Resources Administration in their efforts to implement comprehensive health planning and health care delivery pro-

grams. Also we work with the Health Services Administration, the Alcohol, Drug Abuse, and Mental Health Administration, the Food and Drug Administration and other Federal agencies.

So I believe we have a reasonably good degree of collaboration.

EXPANDED SCOPE AND COVERAGE

Mr. FLOOD. How far are you along with the effort to expand the bibliography to all the health care delivery areas?

Dr. CUMMINGS. Largely because of the interest of Congress through the new legislation that has been passed we are working very rapidly to increase the scope and coverage of our collection to include within our data base information that deals with administrative matters, social medicine, medical economics, fields that we did not cover comprehensively in the past.

I think we are making rapid progress in that direction.

Mr. FLOOD. In many of your appearances here you have talked about your CHEMLINE and TOXLINE programs in great detail. Are there any new developments we should be aware of in either or both?

Dr. CUMMINGS. I am not aware of any new data bases I can report to the committee since our last meeting. I can simply tell you that the services we are providing are being well received and the use is increasing in all of these areas.

TOXICOLOGY INFORMATION COORDINATION

Mr. FLOOD. On the TOXLINE alone, what kind of lines or communications between your TOXLINE people and those of others is involved? For example, EPA, and some of the others.

Dr. CUMMINGS. There is a coordinating committee established by the Assistant Secretary for Health which looks over the interrelationships among the various agencies interested in toxicology information. The role we perform is to collect and organize information derived from different sources, as well as the literature. We do not deal with proprietary or secret information. Our data base in TOXLINE is then shared with various agencies. They have terminals in their institutions. When they have need for information they merely search our files. I don't believe there is a redundant system in the agencies. We serve all the agencies. In fact, 11 are subscribers to this service.

USER CHARGES

Mr. FLOOD. As always, we discuss with you several times the possibility of putting more of your programs under a user fee system. Obviously, it would make it more self-supporting. Have you paid any more attention to that possibility?

Dr. CUMMINGS. We have, as you know, introduced user charges for access to all our computer-based services. The fee has been established at a level which we believe dissuades frivolous use of the system but is not sufficiently high to keep an honest inquirer from having access to the information he or she may require. This is balanced out roughly as follows: The user pays about $2 for each search performed and

the library pays $2. The user pays all communication costs to access the system. I believe, Mr. Chairman, this is a reasonable arrangement through which we have good management control not to allow the system to be overloaded and crash and, on the other hand, to allow us to extend our services broadly. We don't charge Americans for loans from our collection. However, foreign users pay $2 for each article they request us to provide them and $10 for the loan of audiovisual material.

So we do have a user fee which I think is reasonable. Last year we returned about $200,000 to the Treasury resulting from the imprecise calculation of user fees and we estimate that we may return about $300,000 to the Treasury in fiscal year 1978.

Mr. FLOOD. You have all these programs, you have MEDLINE, MEDLARS, CHEMLINE, et cetera. You certainly have them. That could be very confusing.

Is there a good, simple guide available to all the health community which would explain what each program does and how to get access to it?

Dr. CUMMINGS. Yes, sir, we have fact sheets which have been compiled and a pamphlet which is widely disseminated through the medical community. I believe it is fair to say that most people who would want to have access to these systems know how to go about it.

Mr. FLOOD. Thank you.

Mr. O'Brien.

USERS DEFINED

Mr. O'BRIEN. When you talk about a user you mean a practicing physician anywhere in the country or hospital or what?

Dr. CUMMINGS. Any health professional or health professional student, physician, dentist, nurse, osteopath, and any health professional administrator. They may be in industry, universities, or other Federal agencies.

Mr. O'BRIEN. I notice that you mention, I think in your statement, more emphasis was placed on improving the continuing education of health professionals.

Some of the health professionals you would describe would be the ordinary physician and then others would be scholars and the like. Do you make any distinction in the user fee by virtue of the person requesting?

Dr. CUMMINGS. No; it is as standardized as your telephone charge. We don't attempt to have different fees for different levels of use. It is based on the length of time they access the system and the number of requests they propose to the system.

REGIONAL MEDICAL LIBRARIES

Mr. O'BRIEN. When you speak of a regional medical library is that, in a sense, a branch of your library or of, say, Northwestern University?

Dr. CUMMINGS. I might say it could be Northwestern, but in your region it is the Countway Library of Medicine of the Harvard Medical School. They are institutions which have agreed to share their resources with larger geographic regions.

Mr. O'BRIEN. You mentioned the loans as to video experience. Please explain.

Dr. CUMMINGS. On the average, if we loaned a tape or film, 100 persons view this educational film.

Mr. O'BRIEN. Thank you, Doctor.

Mr. EARLY. Where did you say his medical regional library was?

Dr. CUMMINGS. Forgive me. It is the John Crerar Library in Chicago. The Harvard Library is is your region, Mr. Early.

Mr. EARLY. Here is an area where we could cut the budget a third and provide at least the same amount of services. In my area, several years ago they built the Massachusetts Medical School Hospital, a $100 million project. Several professionals came to me and said they don't need a big library. They are getting away from the documentary-type delivery, but they built a multimillion dollar library.

Dr. CUMMINGS. What has happened in your region and other regions, essentially, is that large institutions have agreed to share their resources with smaller institutions. The New England area is particularly interesting in that they have a library consortium, 10 or 12 community hospitals joined to serve their community. Instead of buying the same books and journals, some will concentrate on nursing, dentistry, others in clinical medicine. They have arranged a network to share the resources.

The University of Massachusetts wouldn't rebuild a library to equal those at Tufts or Harvard. They serve as an intermediary resource between Harvard and the community hospitals. In my view this is the only economical way to provide this service to the country.

Mr. EARLY. I agree with that theory and the consortium approach. But I suggest to you it is not in Massachusetts. They all have their own empire. The theory you mentioned is the way it is supposed to do. Here is a medical school costing $130 million, been in operation 4 or 5 years, has 400 beds and 85 patients. We have a State that won't give them any money. I don't know if they have a library.

Dr. CUMMINGS. That is a dilemma the librarian couldn't resolve. I believe they had a modest library complex and a good librarian. I believe they wouldn't be accredited as a medical school if they didn't have that.

Mr. EARLY. As I get with NIH and everyone, you know what happens when you don't get enough money, you hear, oh, oh, there goes another accreditation. It seems every time there goes a spending thing, up go the taxes, there has to be an end to it. Your theory is what I would like to see implemented, but it is not there. You say we have the Harvard Regional Center; that's fine. And I would like to think that's working, but it is not.

Dr. CUMMINGS. This may take more time than I anticipate to achieve the results.

Mr. EARLY. With regard to your comments on page 4 as to the MEDLINE, the small hospitals in Massachusetts, they have some involvement in the local planning. They are supported to, in this network, but I don't think they do. Or if they do, they all want an empire.

Dr. CUMMINGS. I would prefer not putting this in the record, but I shall.

Mr. EARLY. We need bold things in the record, nothing is changing for the better. We are spending more money for less service, we have to do something different.

Dr. CUMMINGS. When I entered this field of library and information science, I had the same lament. Everybody wanted to create a library equal to the National Library of Medicine. It is insane. The Nation can't afford it. That is when we decentralized. I believe in the course of the 10 years I have watched the program evolve, there has been better rationalization of resources and, in fact, in recent years they have been forced to be more reasonable in their budget. There are, in fact, many institutions unable to buy medical literature. As a result of that economic fact they are willing to cooperate and borrow from the next library in the network. That will drive the system in the direction we are talking about.

Mr. EARLY. I have not seen it happen, I have heard them all say they can't afford it. I don't think we have the group cooperation we are talking about.

I understood health library organizations that down through the years the cost would diminish, if information would be on microfilm, they could get it at the Harvard University and everything. Your statement is everything I would like to see work but it is just a theory.

Dr. CUMMINGS. I would like to persuade you it is working. For example, when the library network was created half a million interlibrary loans were made to all the libraries. Now, the figure has increased to 1½ million loans. It means people are borrowing more and buying less.

Mr. EARLY. The thing that would convince me was if your request would go down. It had not, it is increasing. Maybe your costs are getting broader but it is increasing at the local levels.

Dr. CUMMINGS. In fact, the cost is about the same. We are just fighting the inflationary trends. I would have to agree the costs are not going down in the aggregate, but the unit cost in giving service has gone down.

Mr. EARLY. The more I listen to NIH and everybody else I am convinced we can get the same service if we cut your budget a third. It is discouraging but the theory here is not the reality.

Mr. FLOOD. Thank you.

Mr. Schwartz, we will get back to you in a moment.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

Mr. MICHEL. What is the present size of the Library in terms of the number of volumes or any other measuring device you normally use, and how does this compare with, say, 5 years ago?

ANSWER. The present size of the National Library of Medicine's collection is 1,396,924 bound volumes as compared to 1,218,101 in 1972. This increase of 178,823 bound volumes during the last 5 years yields an approximate annual growth rate of 36,000 bound volumes. In addition, the Library's collection now contains 848,949 nonbook materials consisting mainly of manuscripts, audiovisuals, microforms, and pictures.

ON-LINE SEARCHING

Mr. MICHEL. Your statement mentions computer-based on-line searches for medical information. What types of information are normally requested, and in what form is it generally made available to the person requesting it?

ANSWER. Searches done in response to questions from users retrieve information in the form of bibliographic citations and abstracts of journal articles and monographs on a wide variety of health related topics. For instance a recent sampling of search titles included the following topics: Kidney tumors in rats, education in emergency medicine, comparative analysis of health status and trends, Vietnam amputees, etiology of anxiety neuroses, and professional standards review organizations. Printouts of citations retrieved in response to an information request normally include the author, title, source, publication date, and an abstract of the article, if available, and requested by the user. The printouts can be obtained almost immediately on-line at the requestor's terminal. If time is not a critical factor or if the size of the printout is large the requestor can have the response generated off-line at night on the Library's computer and mailed to him the next day. Printouts generated off-line cost less and are normally in the hands of the requestor within 4 days.

INTERLIBRARY LOAN PROGRAM

Mr. MICHEL. Regarding the interlibrary loans, what types of libraries normally request the loans?

ANSWER. The NLM serves as a local area medical library, the regional medical library for the Mid-Atlantic States, the national backstop to the entire regional medical library network, and as a resource for libraries abroad. Therefore it receives requests for loans from libraries covering the broadest spectrum of health professionals who have need of material from the Library's collections. Typical requestors of interlibrary loans include: hospitals, medical schools, clinics, medical societies, research organizations, public libraries, other Federal Government agencies, international organizations, and the Congress through its committees and the Library of Congress.

Mr. MICHEL. How quickly is the material requested for loan normally made available to the library making the request?

ANSWER. For the current fiscal year, 88 percent of requests were filled in 4 days or less after receipt. The remainder were completed and mailed within 10 days. Approximately 10 percent of requests are for monographs, the remainder are for journal articles.

Mr. MICHEL. Have you been asked to participate in the White House Conference on Libraries, and will you be doing so? I would think that your Library could contribute quite a bit to the Conference in view of your extensive efforts in setting up various networks and other informational systems.

ANSWER. We have not been asked to participate in the White House Conference on Libraries, however, we will be pleased to share our experience and systems development with the conferees. The record of the regional medical library network and our nationwide MEDLINE network should be of interest to the broad community of libraries.

TECHNOLOGY TRANSFER PROJECT

Mr. MICHEL. When do you expect the technology transfer project you are undertaking in conjunction with several institutes and other groups will be completed?

ANSWER. Exploratory development has already been started on what will be one of the Library's highest priority programs—expanding the Library's information services to meet the needs of those concerned with the delivery of health care. The Library hopes to develop and test new mechanisms capable of providing information in a language, format, and time frame more immediately useful to the health practitioner. This will involve experimental development of one or more processes by which information relevant to clinical problems can be identified, organized, and distributed—information which will improve disease outcomes in meaningful and measurable ways. The Lister Hill Center staff, with the help of consultants, has begun to develop and test a model of one such process for one disease entity, viral hepatitis.

In collaboration with a panel of subject matter experts, a synthesis of known information relevant to practitioners will be established and validated as an operational "baseline" or "textbook" on the subject of viral hepatitis, and a mechanism created and tested for its periodic updating. Thus, the computerized data base will be frequently augmented and changed as new research findings on hepatitis are published which are relevant to the practitioner. The total synthesized

body of information will be organized so as to readily provide answers to questions of practitioners. Present planning calls for completion of the hepatitis data bank model within the next 6 months.

During fiscal year 1978 a limited pilot study of the model will be undertaken, and refinements made as necessary. If it appears promising, a broader effort requiring a significant addition of resources will be undertaken in fiscal year 1979. This will permit a full scale field test and validation of the model. Results will facilitate decisions to extrapolate use of this method to other disease areas. A series of practitioner-acceptable data bank products will also be designed, tested, and evaluated at this time.

To accomplish these activities in a systematic fashion, a close collaboration between Federal agencies and professional societies will be necessary. The prime responsibility for content validity, organization, and assessment of learning products will remain with individual professionals and their professional societies.

REGIONAL MEDICAL LIBRARIES

Mr. MICHEL. Where are the ten regional medical libraries currently located?

ANSWER. The Francis A. Countway Library of Medicine, in Boston, Mass. serves the New England region; the New York Academy of Medicine, in New York City, serves New York and northern New Jersey; the Library of the College of Physicians in Philadelphia serves the Mid-Eastern region; the Shiffman Medical Library in Detroit serves Ohio, Kentucky, and Michigan; the A. W. Calhoun Medical Library in Atlanta serves the Southeastern region, the John Crerar Library in Chicago serves the Midwest region; the University of Nebraska Medical Center Library in Omaha serves the midcontinental region; the University of Texas Health Science Center at Dallas serves the South Central area; the University of Washington's Health Sciences Library in Seattle serves the Pacific Northwest; and, the U.C.L.A. Biomedical Library in Los Angeles serves the Pacific Southwest. The National Library of Medicine serves as the regional medical library for the Mid-Atlantic region.

LISTER HILL CENTER

Mr. MICHEL. What is the projected move-in date?

ANSWER. Provided construction begins this summer we will begin the first phase of occupancy immediately after completion of the facility in late 1979. The second phase, the move of the National Medical Audiovisual Center from Atlanta to Bethesda, will take place in the spring of 1980.

INFORMATION TRANSFER SYSTEM

Mr. CONTE. Would you explain why the information transfer system which serves scientists well does not respond as effectively to the needs of clinical and health practitioners?

ANSWER. To respond effectively to the needs of health practitioners an information system must, at a minimum, do the following: first, the information provided must be clearly responsive to the practitioners immediate needs; second, the information must be directly available on demand; third, the information must be formated in readily understandable language directly relevant to the question asked.

Most existing systems were not designed to meet these specifications. Instead of supplying a direct answer to a question, most existing systems provide citation to articles containing information about the subject. If these articles were obtained, read, analyzed and synthesized, the appropriate answers to specific questions can be derived.

The National Library of Medicine is working on developing a process model for information handling that could meet these specifications for a large percentage of practitioners' questions.

Mr. CONTE. What will be the value of such stations?

ANSWER. Previous experiments using similar technology were regional in nature. These stations, coupled with others which will be available to the Public Health Service, will permit extension of the regional network concept to a larger network which is widely dispersed geographically. This in turn will permit experimentation with two-way video as in information exchange mechanism

among more institutions and individuals, separated by up to five time zones. By involving more institutions, a broader range of health education and practice programs can be explored.

Mr. CONTE. Is this the entire program, or a demonstration of technology which might be made more widely available?

ANSWER. The latter. This is part of an ongoing program of the Lister Hill Center to demonstrate and explore all modes of communications potentially applicable to providing more effective and efficient services to the health professional community. The satellite has the potential for providing broadband communications—two-way interactive television, high-speed data—to remote areas, at prices which are independent of distance. Commercial satellite communications offerings are not presently cost-effective for all public service applications. By demonstrating technology, user acceptance can be determined, and technology alternatives evaluated. This will in turn provide a base for design of an operational network which would be more widely available, and affordable.

SERVICE CHARGES

Mr. CONTE. Is there a service charge for the use of your facilities or the TOXLINE or MEDLINE service?

ANSWER. Except for certain specialized services the library does not charge patrons who seek access to our collection. The most notable exceptions to this policy are interlibrary loan or audiovisual loan requests from foreign sources who pay $2 for each filled interlibrary loss, or $10 for each filled audiovisual loan either directly or through an agreement with the Agency for International Development. We do charge for specialized or unusual requests such as those requiring special photographic services. The library deposits the receipts from these specialized and foreign services in the U.S. Treasury as miscellaneous receipts.

The library has had a service or user charge in effect for TOXLINE services since it began in September 1972. User charges for MEDLINE services were instituted in August 1973 with the advice and consent of the library's Board of Regents after it became apparent that some form of management control over the growth of the on-line systems was necessary. Charges were established at levels which discourage frivolous use, but do not impede legitimate need. The current charge for all on-line services is $15 per connect hour between 10 a.m. and 5 p.m. eastern time and $8 per connect hour at all other times. The library also charges 10 cents for each page of citations which is printed off-line and sent to the requestor. In fiscal year 1976 the library returned $200,000 to the U.S. Treasury resulting from these on-line services user charges.

Beginning in April 1977 we plan to institute user charges for walk-in library patrons who utilize the terminals in our reading room to access our on-line computer services. The charges will be $4 per search processed between 10 a.m. and 5 p.m. and $3 at all other times. As with the other service charges receipts will be returned to the U.S. Treasury.

INSTRUCTIONAL MATERIALS

Mr. CONTE. Can you tell me more about your field testing program for instructional materials as conducted by the audiovisual center?

ANSWER. NMAC began a field testing project for two reasons: (1) Some faculty members are reluctant to use instructional materials that have not been established as effective for different student enrollments, geographical regions or curriculum; (2) instructional materials have not been evaluated nationally for their effectiveness in teaching in the classroom; faculty opinion often is used instead of effective measurement of student performance.

Since routine testing of instructional materials designed for medicine and allied health sciences on a nationwide total student basis is too expensive and would take too much time and administrative effort, a research project to determine ways of estimating a national response was begun. Some 24 schools have been selected to obtain a representative national sample. Using the materials from the NMAC learning materials collection, student test data will be obtained and analyzed. It should then be possible to identify a sample of schools that can be used as a testing ground to measure the teaching effectiveness for current and future instructional packages. Findings in the current project will estab-

lish methods and procedures for implementing low cost testing systems. The results of these studies will eventually lead to regular testing and sharing of data on most instructional materials enabling faculty to select materials for their curriculum with demonstrated ability to teach health science information and skills.

SECURITY AND FIRE PROTECTION

Mr. CONTE. What additional costs, if any, will be necessitated by the implementation of security and fire protection survey recommendations?

ANSWER. Implementation of the recommendations of the fire protection survey will cost approximately $300,000. Within the $26 million appropriated for the Lister Hill Center Building, there are funds set aside for renovation of the existing NLM Building. Part of the renovation funds will be utilized to upgrade our fire protection system.

JUSTIFICATION OF THE BUDGET ESTIMATES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Amounts Available for Obligation 1/

	1977	1978
Appropriation	$35,234,000	$36,746,000

1/ Excludes the following amounts for reimbursable activities carried out by this account: 1977 - $3,500,000; 1978 - $4,000,000.

Summary of Changes

1977 Estimated Obligations	$35,234,000
1978 Estimated Obligations	36,746,000
Net Change	+ 1,512,000

	1977 Base Pos.	1977 Base Amount	Change from Base Pos.	Change from Base Amount
Increases:				
A. Built-in:				
1. Within-grade pay increases	---	200,000	---	+210,000
2. FTS rate increases	---	180,000	---	+1,000
3. Increased cost of service and supply	---	140,000	---	+20,000
4. Payment for centrally furnished services	---	2,284,000	---	+285,000
(Standard Level User Charge)	---	(235,000)	---	(+148,000)
5. Federal Employees Compensation Fund (FECF)	---	160,000	---	+21,000
Subtotal	---	---	---	+537,000
B. Program:				
1. MLAA - to provide costs for non-competing MLAA awards	---	8,000,000	---	+586,000
2. Library Operations				
- Annualization of restored 1977 positions	---	650,000	---	+100,000
- Literature acquisitions	---	875,000	---	+150,000
- Computer rental increase	---	2,080,000	---	+132,000
3. Program Management - Postage cost increase	---	382,000	---	+100,000
Subtotal	---	---	---	+1,068,000
Total increases	---	---	---	+1,605,000
Decreases:				
A. Built-in:				
1. Employment savings - effect of one day less pay in FY 1978	472	12,023,000	---	-55,000
Subtotal	---	---	---	-55,000
B. Program:				
1. Program management	79	2,091,000	-2	-38,000
Subtotal	---	---	-2	-38,000
Total decreases	---	---	-2	-93,000
Net change	---	---	-2	+1,512,000

Obligations by Activity

Page Ref.		1977 Appropriation Pos.	1977 Appropriation Amount	1978 Estimate Pos.	1978 Estimate Amount	Increase or Decrease Pos.	Increase or Decrease Amount
243	Medical Library Assistance						
	Total	---	8,000,000	---	7,987,000	---	-13,000
	Direct Operations:						
245	Lister Hill Nat'l Ctr. for Biomedical Communications	24	4,730,000	24	4,775,000	---	+45,000
247	National Medical Audiovisual Center	88	3,401,000	88	3,561,000	---	+160,000
249	Library Operations	264	11,143,000	264	11,865,000	---	+722,000
251	Toxicology Information	17	2,166,000	17	2,206,000	---	+40,000
253	Program Management	79	5,794,000	77	6,352,000	-2	+558,000
	(Standard Level User Charge)		(235,000)		(383,000)		(+148,000)
	Subtotal	472	27,234,000	470	28,759,000	-2	1,525,000
	Total Obligations	472	35,234,000	470	36,746,000	-2	+1,512,000
	(Standard Level User Charge)		(235,000)		(383,000)		(+148,000)

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
Total number of permanent positions.....	472	470	-2
Full-time equivalent of all other positions.....	44	44	---
Average number of all employees.....	538	536	-2
Personnel compensation:			
Permanent positions.....	9,257,000	9,914,000	+657,000
Positions other than permanent.....	814,000	854,000	+40,000
Other personnel compensation.....	116,000	116,000	---
Subtotal, personnel compensation.....	10,187,000	10,884,000	+697,000
Personnel benefits.....	1,031,000	1,101,000	+70,000
Travel and transportation of persons.....	177,000	185,000	+8,000
Transportation of things.....	37,000	29,000	-8,000
Rent, communications and utilities.....	2,749,000	2,981,000	+232,000
Printing and reproduction.....	496,000	496,000	---
Other services:			
Project contracts.....	6,240,000	6,240,000	---
Payment for centrally furnished services.....	2,284,000	2,569,000	+285,000
Other.....	2,464,000	2,555,000	+91,000
Supplies and Materials.....	399,000	399,000	---
Equipment.....	295,000	295,000	---
Literature.....	875,000	1,025,000	+150,000
Grants, subsidies and contributions.....	8,000,000	7,987,000	-13,000
Total obligations by object.....	35,234,000	36,746,000	+1,512,000

Authorizing Legislation

Legislation	1978 Authorized	1978 Appropriation Requested
Public Health Service Act		
Section 381 - Purpose and Establishment of Library.....	Indefinite	$28,759,000
Health Services Research, Health Statistics, and Medical Libraries Act of 1975		
Section 393 through 397.....	1/	7,987,000 2/
Total....		$36,746,000

1/ Amount to be determined in extending legislation.

2/ Authorization expires September 30, 1977; extension legislation is pending.

National Library of Medicine

Comparable

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	21,162,000	18,662,000	21,162,000	19,912,000
1969	19,172,000	16,997,000	19,020,000	18,008,500
1970	22,882,000	19,682,000	19,682,000	19,682,000
1971	19,769,000	19,843,000	22,307,000	20,843,000
1972	21,981,000	22,781,000	25,086,000	24,086,000
1973	24,994,000	28,488,000	28,988,000	28,488,000 1/
1974	24,994,000	25,796,000	25,796,000	25,426,000 2/
1975	27,738,000	28,048,000	29,348,000	28,848,000
1976	28,815,000	28,994,000	29,744,000	29,244,000
1977	35,234,000	35,234,000	35,234,000	35,234,000
1978	36,746,000			

1/ Note: This appropriation authority was the continuing resolution. The appropriations amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

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National Library of Medicine

Actual

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	21,162,000	18,662,000	21,162,000	19,912,000
1969	19,172,000	17,149,000	19,172,000	18,160,000
1970	22,882,000	19,682,000	19,682,000	19,682,000
1971	19,769,000	19,769,000	22,233,000	21,440,000
1972	21,981,000	22,781,000	25,086,000	24,127,000
1973	28,568,000	28,568,000	29,068,000	28,568,000 1/
1974	24,994,000	25,871,000	25,871,000	25,871,000 2/
1975	27,738,000	21,768,000 3/	29,350,000	28,850,000
1976	28,815,000	28,815,000	29,565,000	29,065,000
1977	35,234,000	35,234,000	35,234,000	35,234,000
1978	36,746,000			

1/ This appropriation authority was the continuing resolution. The appropriations amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

2/ Appropriation after reduction as authorized by P.L. 93-192.

3/ Excludes Medical Library Assistance Grants not considered by House due to lack of legislative authorization.

Justification

National Library of Medicine

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Medical Library Assistance	---	8,000,000	---	7,987,000	---	-13,000
Direct Operations:						
Lister Hill National Center for Biomedical Communications	24	4,730,000	24	4,775,000	---	+45,000
National Medical Audio-visual Center	88	3,311,000	88	3,471,000	---	+160,000
Library Operations	264	11,233,000	264	11,955,000	---	+722,000
Toxicology Information	17	2,166,000	17	2,206,000	---	+40,000
Program Management	79	5,794,000	77	6,352,000	-2	+558,000
Subtotal	472	27,234,000	470	28,759,000	-2	1,525,000
Total Obligations	472	35,234,000	470	36,746,000	-2	+1,512,000

General Statement

The National Library of Medicine Act established the National Library of Medicine (NLM) on August 3, 1956. This legislation assigned to the NLM the mission of assisting the advancement of medical and related sciences by fostering the dissemination and exchange of medical, scientific and other related information which is important to the progress of medicine and to the public health. To accomplish its mission the Library undertakes program initiatives which can be categorized into three major areas of emphasis - library and information services, research and development in biomedical communications, and support to individuals and institutions through the Medical Library Assistance Program. To aid in the management of the Library's resources and to enable each of the various program components to effectively contribute to the accomplishment of the NLM's mission, the concept of a National Biomedical Communications Network (BCN) has been developed with Congressional encouragement. The BCN now links the Library with the major health care facilities, medical education centers, research institutions and private industries which have a need for biomedical and health related information. The continuously increasing growth in demand for those services which are offered through the BCN is a testimony to the success of the concept. Notwithstanding the recognized success of the Network, it is the Library's goal to modify the direction of the BCN in a manner which will place greater emphasis on the dissemination of relevant information to the health care community and indeed to the individual health practitioner and clinician in an effort to more effectively translate knowledge derived from research into the health care delivery system. The narrative which follows is a description of how each of three major areas of emphasis will contribute to that goal in FY 1978.

Medical Library Assistance

The Library's programs of Medical Library Assistance (MLA) are designed to improve health information services by providing grants to train and upgrade professional health personnel in the transfer of health information, to strengthen medical library resources especially at local levels, and to support and maintain a Regional Medical Libraries Network (RML) in support of health professionals through smaller medical libraries in the United States. Two MLA programs will move into new phases of evolution as they strive to better meet the needs of the health care delivery community. Currently underway is the first phase of a new initiative directed at establishing cooperative, resource sharing library consortia among the nation's community health care institutions. The operational phase will begin in FY 1978 with two initiatives: 1) to establish in medical libraries entry points to the RML Network; 2) to establish outlets for local access to advanced health science information systems.

The Regional Medical Library Program (RML) will continue to develop effective information service modalities in FY 1978. Until now, emphasis had been on document delivery activities, however, there is a need to move beyond document delivery activities to new areas of regional information transfer. This program expansion will result in an augmented role for the RML's. They will change emphasis from serving as document delivery coordinators to support the consortia program described above and will act as demonstration and information dissemination centers. Expansion of the role of RML's in conjunction with further development of the consortia will improve information access for health care practitioners by increasing markedly the number of health professionals with immediate access to the network.

Research and Development

The research and development component of the NLM, the Lister Hill National Center for Biomedical Communications, was established to explore the application of advances in computer and communications technology to the improvement of biomedical information transfer. The Center addresses this biomedical information transfer process in support of health science education and research, and in the delivery of health services.

The transfer of research results to clinical application can be more beneficial if the information being disseminated is organized in a way that permits its identification and retrieval in response to specific clinical problems. This improves the quality of health care delivery as practitioners have more rapid access to current information directly relevant to their patient's problems. In FY 1978 the Center, in collaboration with clinical societies and other health entities, will develop experimental systems models to improve this aspect of the transfer of biomedical information.

The Center will continue its emphasis on improving the application of computer technology to information handling. The power of minicomputers and microprocessors can be employed effectively and extensively in information transfer. Their application to library management and medical education will be explored.

The Center will also explore the use of high speed data transmission via satellite and other communications channels for interconnecting computer data banks. These capabilities will enhance the delivery of health services by permitting small, remote facilities to have access to resources such as large information banks which can only be supported at large control facilities.

The Lister Hill Center is moving from almost exclusive use of contractors for research and development to sophisticated in-house capability in biomedical computer and communications research. With the scheduled completion of the

new Lister Hill Center Building in late 1979, additional manpower resources with new expertise are needed to fully utilize the new communications technology laboratories to be contained in this facility. Staffing is the key to progress in biomedical communication experimentation.

Library and Information Services

Those NLM components which are responsible for the service operations acquire relevant information in the form of printed literature, audiovisuals, and medical data. The information is organized into computerized data bases, bibliographies, and catalogs and disseminated through the Biomedical Communications Network. These components also provide traditional library services such as reference and research assistance.

During FY 1978 emphasis will be placed on expanding the coverage of the collection to include information which is directly related to health care delivery; on development of additional automated/computerized procedures to improve the timeliness of information included in the collection and the various on-line services' data bases; and, on placing terminals for our on-line services in health care facilities. Specifically, the collection will be enhanced to include more material which has direct clinical applicability. Coverage of newly emerging areas of interest such as the social, ethical and legal aspects of medicine will be increased. The implementation of automated computerized techniques will be targeted at improving the efficiency of library processing functions. The new technology which is developed for this purpose will be made available to major health care institutions for application to their own literature and data handling problems.

Use of the NLM on-line services has continued to grow rapidly. The number of searches performed on the on-line systems slightly exceeded 250,000 in FY 1974. In FY 1978 the number of searches will surpass 650,000. The Library's greatest impact on health care delivery can best be realized by expanding in FY 1978 the use of its on-line services into hospitals and other health care facilities. Presently of 534 user organizations, 159 are in hospitals and other health care facilities. It is anticipated that on-line services will be available in additional such organizations by the end of FY 1978.

The Toxicology Information Program (TIP) is responsible for collecting and organizing toxicology data from a variety of sources and making it more readily available to its user communities in industry, universities, health care facilities and government agencies. TIP obtains information from published scientific literature, files of governmental, industrial and academic organizations in many formats; organizes and enters this information into computerized storage and retrieval systems. TIP also plays a key role in coordinating toxicology information activities within DHEW.

TIP's user communities utilize this toxicology data for many purposes which impact on the health of Americans. Specifically, the data is utilized by health professionals in the prevention of injury due to exposure to toxic chemicals in the workplace or the home; in writing regulations and tracking compliance efforts in the field of drugs, pesticides and hazardous household products; in identifying and monitoring the environmental effects of chemicals; and in wide ranging research on the biological effects of chemicals. During FY 1978 TIP will concentrate its efforts on improving the utility of its various services to its user communities through enrichments and expansion of its data bases. For example, TOXLINE, an on-line toxicology data base, will be enhanced with special files on drug interference, teratogenesis and drug interactions that are of special interest to the health practitioner. CHEMLINE, which is an on-line chemical dictionary, will be expanded to include 300,000 chemical records.

The National Medical Audiovisual Center (NMAC) provides educational technology assistance to health related institutions by developing, distributing, and encouraging the use of effective learning materials and innovative instructional techniques in support of health sciences education. In the recent past NMAC placed primary emphasis on preparations for teaching basic science in undergraduate health science curricula. A major thrust will be made to extend NMAC's program efforts in educational technology to all levels of health education with greater emphasis being given to improving the continuing education of health professionals since the knowledge and skills of the medical practitioner can rapidly become outdated by new technological advances. In cooperation with other organizations involved in continuing education programs, NMAC will implement a variety of projects to help provide appropriate multi-media educational materials to update health care practitioners.

The NLM FY 1978 budget request represents an increase of $1,512,000 over the FY 1977 level. This increase will be utilized to fund necessary mandatory cost increases and reflects a two position reduction in FY 1978.

MEDICAL LIBRARY ASSISTANCE PROGRAM

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Medical Library Assistance Program.....	---	8,000,000	---	7,987,000	---	-13,000
No. of Awards.....		168		165		-3

The NLM administers a program of grants to assist medical libraries in developing better health information services, particularly services that relate to the development of the Biomedical Communications Network. Types of support for medical libraries include: (1) Resource Improvement Grants, (2) Resource Project Grants, (3) Training Grants, (4) Research and Demonstration Grants, (5) Special Scientific Projects, and (6) Publication Grants. In addition, the NLM provides contract support for the maintenance and operation of ten Regional Medical Libraries (RML) which serve as focal points for region-wide planning and regional health information services. Excluding the RML's and the Resource Improvement Grants a brief description of the remaining types of support grants and their particular areas of emphasis for FY 1978 follows. Because the RML's and Resource Improvement Grants will undergo significant modification in FY 1978, a more detailed program description will be presented.

Resource Project Grants are available to assist health science libraries to initiate, expand, or improve services to educators, students, researchers and practitioners. The funds are intended to serve a "seeding" purpose where assurance is given that support beyond the grant will be assumed by the requesting organization. The grants are not intended to subsidize a library's normal operating costs or to provide for the development of book and journal collections. Resource Project Grants are closely related to the programs of the Regional Medical Libraries and are viewed as complementary activities in the development of the Regional Medical Library Network.

The goal of the Training Grant Program is to promote the integration of computer technology into all phases of clinical medicine--teaching, practice, and research. Priority will be given to projects designed for teachers or potential faculty members in the health sciences. As a result of their training the participants should be able to utilize computer technology as an aid in the solution of health problems. The grantee schools are expected to have well-established computer facilities, a strong research and education program, experienced staff and faculty, and fundamental courses available in related areas such as educational technology, communication science, and information science.

Research and Demonstration Grants for basic and applied research projects support investigations into more effective methods for processing and disseminating health information. These grants support innovative pilot projects to translate experimental results into actual operation. The general areas of support include biomedical librarianship and information science, application of new technologies, biomedical communications, and information activities relating to continuing education.

Special Scientific Project Grants support scientists, scholars, and practitioners in the health professions to write scholarly treatises on major health issues, disciplines, or medical problem areas. The objective of such scholarships is to assemble, analyze, synthesize and publish current authoritative knowledge. Priority will be given in FY 1978 to problem areas which are of particular concern to the health practitioner.

Publication Grants provide limited support for scientific publications of particular significance to the national health effort. Support is not provided for the preparation or publication of textbooks or other monographs which are commercially viable. Grants are available for preparing and publishing: (1) critical reviews and monographs on the present state of biomedical research or health care; (2) publications in medical librarianship, health information sciences, and biomedical communications; (3) secondary information tools such as handbooks, directories, manuals, bibliographies, and atlases; (4) proceedings of conference symposia related to important U.S. health needs.

Funding in FY 1978 for the five grant programs described in the preceding paragraphs will be at levels slightly below FY 1977 levels, and there will be a corresponding drop in the number of awards made.

The Regional Medical Library (RML) Program will receive increased attention and new direction in FY 1978. From a historical perspective the RML program established a network structure among the nation's medical schools and other health related institutions to facilitate the exchange and provision of health information. The RML program, supported initially through grants and now by contracts, has contributed to the provision of information services mostly in the form of document delivery (interlibrary loans). Increasing user demands on the network has resulted in an approximate 15% growth rate in document delivery activities per year. This growth rate has been funded through a cost sharing arrangement with an increasing amount of the cost being assumed by the participating institutions and their constituents. At the same time, the RML's, in recognition of the need for supporting other information services, are beginning a reallocation of NLM support beyond document delivery activities to expand capabilities for regional information transfer.

Increased emphasis will be directed at establishing cooperative, resource sharing library consortia among the nation's community health care institutions. A consortium will be composed of hospitals, mental health centers, health care delivery clinics, and other institutions which provide information services for health personnel. This program will enable the health professional to have access to more biomedical information at the institutional level not only close to his work but one that is also most familiar with his needs. The consortia will expand services to unaffiliated health professionals such as pharmacists and dentists.

LISTER HILL NATIONAL CENTER
FOR
BIOMEDICAL COMMUNICATIONS

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Lister Hill Nat'l Ctr. for Biomedical Communications.....	24	4,730,000	24	4,775,000	---	+45,000

The Lister Hill Center component of the Library is responsible for exploring more effective uses of computer and communications technology in support of health services education, research and delivery. The Center is currently investigating several methods of information organization, storage, retrieval and dissemination to more efficiently integrate newly developed biomedical information into the health care delivery system. The targeted audience for most of the Center's activities is the practicing health professional. The undertakings of the Lister Hill Center can be categorized under three broad headings - computer technology, communications technology, and translation activities (validated information in terms understood by the practitioner). The first two headings represent on-going efforts within the Center. The translation activity is a major new initiative which if successful can contribute to improved health care delivery.

Computer Technology

Libraries and other institutions involved in the dissemination of biomedical information have not, in general, been quick to employ computer technology. The reasons include initial cost, lack of technically oriented staff, and an absence of cost-effective models to emulate. In addressing this problem the Center is developing and demonstrating in its Learning Resource Laboratory models of computer technology that can be applied to library functions. The Laboratory is also engaged in developing solutions to information processing problems that affect the health community broadly. While current prototypes and experimental models place emphasis on library applications, the technology itself is potentially of value in primary health care and continuing education. It is these applications which will receive increased attention in FY 1978.

Another activity of the Laboratory is the development of computer based educational materials (CBEM). Several CBEM systems which have been developed by health science education institutions are available for demonstration in the Laboratory. Each of the systems is unique and their availability in the Laboratory provides a centralized facility where they may all be examined and compared in an objective forum. CBEM are written in many diverse computer languages. One of the goals of the Center is to improve the interinstitutional transportability of CBEM by encouraging language standardization within the field.

Communications Technology

The Lister Hill Center has for several years successfully engaged in a series of demonstration projects which apply satellite communications technology to the solution of recognized problems in health education and the delivery of health services. Based on this experience and expanding to a national experiment, the Center is working with other U.S. health agencies and the Canadian Government in utilizing the Communications Technology Satellite (CTS) to solve some of these problems using this unique communications system. During FY 1977 a number of stationary "broadcast-and-receive" ground stations are being installed in the less populated areas of the country. Additionally,

a broadcast studio within the Library is being completed. Actual broadcasts will begin soon thereafter from all sites. The possible applications of this technology to health care are many. For example, they include public and professional education, communication of research results, teleconferencing, and remote professional consultation. In all cases uses of the satellite will be experimental. Evaluation of the effectiveness and efficiency of this project compared to alternative systems will be an important objective of the Center throughout FY 1978.

Translation Project

Beginning in FY 1977 and continuing for several years the Library, as part of its long-range effort to develop a coherent medical information system to serve the needs of health practitioners, is undertaking, in cooperation with professional and clinical organizations, a "translation project." Whatever the information product, there is a need for a regularly updated summation of clinically relevant information in each major disease area. To accomplish this the information must be examined for its scientific accuracy (analysis); it must be selected and condensed from the total biomedical data base or pool (synthesis); and it must be validated for its clinical applicability and presented in a language which is understood by the practitioner (translation). The processes of analysis and synthesis are the responsibility of subject matter experts. In the past the translation function has been performed variously by different organizations and accomplished with uneven effectiveness. It is necessary to explore new ways and to develop system models to improve the organization and distribution of analyzed and synthesized biomedical information. Working with professional groups NLM will develop translation models that emphasize new knowledge which has applicability to the problems faced by the practitioner. The first basic requirement is that the information provided must be clearly responsive to the practitioner's immediate needs. Moreover, it must be available essentially on demand. Experience justifies the assumption that the physician is more likely to act on and learn from information supplied in response to an inquiry regarding an immediate clinical problem. Finally, the information must be transmitted in terms which are readily understood. . The goal of the NLM is to develop, in cooperation with professional medical groups, a new process by which medical information can be identified, organized and distributed in response to specific clinical questions.

NATIONAL MEDICAL AUDIOVISUAL CENTER

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
National Medical Audiovisual Center.....	88	3,401,000	88	3,561,000	---	+160,000

The National Medical Audiovisual Center (NMAC) administers an active program to foster the development and promote the use of effective learning materials and innovative instructional techniques ("Educational Technology") in support of health science education.

Learning Resources Program

To meet the increasingly complex demands which have been placed on health science educators, NMAC has strengthened its capabilities in the application of education technology. In 1975 a collaborative program was established between NMAC and the Bureau of Health Manpower of the Health Resources Administration. This effort, known as the Learning Resources Program, develops valid methods for assisting health educators in such areas as: (1) integrating scientific knowledge with clinical skills in health care delivery; (2) teaching such knowledge and skills to audiences possessing different knowledge levels and learning abilities; and (3) maintaining the quality of educational systems through use of validation and feedback mechanisms.

The Learning Resources Program is improving educational efficiency in the health sciences by developing methods for and training educators in: (1) job and performance analysis techniques which increase the relevance of the curricula for the learner and provides for better utilization of limited educational resources; (2) relating health care tasks to specific groups, thereby enabling better utilization of health professionals, building career ladders, and promoting development of interdiciplinary curricula and associate programs; (3) developing prototype instructional systems to increase learning effectiveness and reduce learning time.

One of the most important efforts in FY 1977 has been the development of a comprehensive curriculum for health science educators which contains all significant content/performance elements related to the application of educational technology to health science education. Projects supporting this effort included experimental research (e.g., studies of procedures and multidisciplinary approaches to continuing education); descriptive institutional research (e.g., documenting the value of videotape technology in training health professionals); and validation research (e.g., establishing a field-test program to validate the usefulness of instructional materials).

Media Development

The media development and production capabilities of NMAC have been utilized in support of the Center's research and development program. The materials NMAC develops for its training and distribution program serve as models for health science institutions to employ in their own design and development activities. In addition, NMAC works with national health professional organizations and schools of the health professions in developing shareable materials which incorporate effective educational design and production techniques. Assessment of these materials has been carried out to ensure the validity of these techniques. Presently, 100 health related schools have faculty or staff involved in cooperative instructional development projects with NMAC. These efforts have

provided a significant portion of the audiovisual learning and teaching packages in the NMAC distribution program; a service which processed 65,000 loans and accounted for an estimated six million viewing experiences in FY 1977 by health professional students and practitioners.

Educational Technology Training

The NMAC training program serves as a mechanism for transferring new educational technology knowledge and techniques through the traditional practice of conducting in-house workshops and through workshops at regional training centers. Such centers not only provide a local character to training programs but have a multiplier effect in the biomedical community. In FY 1978 approximately 800 health science faculty will be trained.

Objectives for FY 1978

In FY 1978 increased emphasis will be placed on projects which address directly the problems of improving the quality and cost-effectiveness of health education. Projects to be carried out include: testing cooperative materials development involving participation of health professional teams from related disciplines and from similar departments in different schools; identifying learner needs in continuing education, especially needs which are related to recertification and relicensure; identifying sets of knowledge and procedures to enable development of cost-effective learning systems which teach more students in less time; establishing procedures to maintain currency of knowledge in education programs; and, designing a national field-testing program to measure the effectiveness of instructional materials in terms of student learning.

For FY 1978 a vigorous new program is being planned for increasing the efficiency of health professional education. The need for this program is strongly suggested by the recently enacted Health Manpower Legislation (PL 94-484) which calls for increased enrollment in the primary care specialities. If practitioners are to be effectively trained without a proportional increase in health science faculty, new methods must be found to increase the efficiency of both faculty and media-based instructional resources.

LIBRARY OPERATIONS

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Library Operations.....	264	11,143,000	264	11,865,000	---	+722,000

Library Operations (LO) is responsible for providing what is considered the more traditional library services, although because of the volume of information which must be handled and the number of services which are provided, innovative methods have been adopted to fulfill its responsibilities. Some of the more advanced methods of service delivery include on-line computerized access to biomedical literature through a nationwide communications network (MEDLINE); authoritative bibliographic information through printed products compiled by advanced computer and photocomposition techniques (Index Medicus); and, the delivery of more than 200,000 articles from leading medical journals to health professionals through a network of libraries (Interlibrary Loan Program). The three major emphases within Library Operations during FY 1977 and FY 1978 will be on expanding its information services to meet the demand of additional segments of the health community; expanding the coverage of the documentary and audiovisual collections, and data bases; and, continuing to introduce automated and computerized techniques into Library functions to improve the quality, quantity and speed of information services. The purpose of these efforts is to improve information services to health professionals, especially those involved directly in health care delivery.

Automation/Computerization of Library Functions

Library Operations, more so than any other NLM component, has been impacted by the success of the Biomedical Communications Network. During FY 1976 there were over 550,000 searches performed by users of the Library's computer system. This number will surpass 650,000 in FY 1978. These same users were also provided nearly 2,500,000 pages of bibliographic citations resulting from those on-line computerized searches. The Library also acquired nearly 170,000 copies of new journal and serial publications in FY 1976. This volume represents almost a 25 percent increase over FY 1975 levels. Similarly, the number of interlibrary loans filled increased by 18 percent over FY 1975 levels totaling over 200,000 for the first time. In addition, the number of reading room patrons is up 27 percent, reader service requests received are up 28 percent and reference inquiries made are up 10 percent.

This continually growing level of service demands has been difficult to sustain without additional manpower resources. In order to continue to satisfactorily meet the growing service demands, efforts are underway to improve productivity through the utilization of advanced automated techniques in operating technical processing activities in the Library. Major automation projects are underway which will improve the Library's ability to provide expanded collection coverage, to handle increased service loads, and to improve the speed of delivery of information to health science professionals. Specific projects include the enhancement of decentralized computerized processing systems to handle acquisitions, cataloging, serials control, and document delivery. The Library will also, where feasible, make these advanced processing techniques available to other libraries to assist in reducing manual processing requirements

at all levels help avoid costly duplicative activities among libraries, and release resources for other uses.

Expansion of On-Line Services

The present computerized on-line services of the NLM now provide the health community with the most advanced information services available to any professional group. The unit processing cost of computers and communications are dropping rapidly, and more and more information can be expected to be transferred via computer services. In order to provide the capacity necessary to meet the growing breadth and increasing use of the NLM services, NLM is working with the General Services Administration on the competitive replacement of its computer system. The replacement system will provide the capacity required to meet an anticipated growth rate of 20-25 percent per year until 1985. In addition, it will provide a more efficient system such that the cost of providing each hour of service will be much less than at present. This, in turn, will allow NLM to expand its service to reach a larger population of health professional users. The proposed new computer configuration will also provide improved support of the document delivery process as well as provide other improved information services.

Other efforts will be targeted at providing to the health care institution and health care practitioner greater access to the Library's service systems. Of the existing 534 user institutions which have access to the NLM's computerized on-line services, 159 are hospitals. Since the translation of biomedical research into improved health care is a major goal of NLM, additional effort will be directed toward expanding on-line services into other health care facilities. It is anticipated that on-line services will be available in 250 hospitals by the end of FY 1978.

The effort directed toward supporting the translation and transfer of research results into medical practice will focus on improved information support to the medical specialists who provide to their practitioner colleagues advice and assistance in complex medical situations. Simplified search techniques will be developed for them to more effectively utilize NLM computerized data banks. Terminals will be installed in locations convenient to practitioners to simplify the process of accessing the services.

Coverage of Collection

Coverage of the NLM's collection will include more information which has direct clinical applicability. Coverage of social, ethical and legal aspects of medicine will be expanded. In the coverage of health care planning and delivery, the Library collection and the vocabulary controlling access to the biomedical literature (MeSH - Medical Subject Headings) will be enriched to provide greater retrieval capability in this area.

Toxicology Information Program

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Toxicology Information Program	17	2,166,000	17	2,206,000	---	+40,000

The Toxicology Information Program (TIP) is responsible for collecting and organizing toxicology information and data from various sources and making this information more readily available to user communities in industry, universities and government agencies. These communities use the information for a variety of purposes including research on the biological effects of chemicals; prevention of injury from exposure to toxic chemicals; treatment of poisoning; prevention, monitoring and treatment of adverse drug effects; preparation of regulations and monitoring of compliance in the field of drugs, pesticides, hazardous household products; and identifying and monitoring environmental effects of chemicals. TIP obtains its information from the published scientific literature and files of governmental, industrial and academic institutions. This information is organized and entered into computerized storage and retrieval systems from which are derived a variety of information dissemination services.

On-Line Systems

The TIP continues to utilize the technology of computerized on-line, interactive retrieval systems to make toxicology information and data readily available. In FY 1977 TIP enhanced the contents of its bibliographic retrieval service, TOXLINE, with the addition of 80,000 records. Files were added to improve TOXLINE coverage in specialty areas of toxicology. These enhancements have made the TOXLINE data base a more useful resource to individuals responsible for delivery of health care services. TOXLINE users performed over 35,000 on-line searches and requested over 1,700,000 citations printed off-line in FY 1977. TOXLINE service has been a valuable aid to the health and environmental agencies of the government involved in regulating the use of pharmaceuticals and chemicals that may have an effect on health and the environment.

TIP operated and maintained as a service a computerized on-line, interactive chemical dictionary called CHEMLINE. The CHEMLINE file size was doubled to a content of over 200,000 compound records in FY 1977. This service has proven to be a useful adjunct to other NLM on-line bibliographic retrieval services. CHEMLINE has also been useful to other Federal agencies by making chemical registry numbers and chemical nomenclature information readily available to them. TIP's user community now consists of over 300 organizations from the commercial (50%), academic (35%) and government (12%) communities.

The Toxicology Data Bank (TDB) is being developed as a new computerized on-line, interactive data retrieval service. The file contains chemical, physical, biological, usage and distribution attributes on over 1,000 chemicals which are known to be hazardous and to which population groups are exposed. TDB provides detailed specific data in response to a query rather than only bibliographic references to articles which may contain the desired data. Uses of TDB include toxicological research, prevention and treatment of poisoning, preparation of toxic substances criteria documents, and in determining the impact manufactured chemicals may have on employee health.

In FY 1978 TIP will continue to maintain the TOXLINE system and will seek to increase its use within the health care delivery community. This will be accomplished through the enrichment of the file in special subject areas such as drug interactions, drug interference and teratology. The CHEMLINE files

will be maintained and expanded to include records for 100,000 additional chemicals. The Toxicology Data Bank will become operational and will be increased to 2,000 records.

Collaborative Activities With Other Organizations

TIP has been given the responsibility by the Assistant Secretary for Health, DHEW, to chair and maintain the Toxicology Information Subcommittee of the DHEW Committee to Coordinate Toxicology and Related Programs and to implement the projects initiated by this Subcommittee. This Subcommittee was established to help coordinate DHEW activities dealing with the collection, storage and dissemination of toxicological related information and to serve as the mechanism for undertaking special toxicological information projects of interest to a number of cooperating agencies. Projects are funded by the DHEW or by specific agencies and implemented by the TIP.

One of these Subcommittee projects, the Laboratory Animal Data Bank (LADB), is being tested as a new on-line data retrieval service by those industrial and governmental organizations that provided data for LADB. The data bank contains baseline response data on more than 50 selected species and strains of laboratory control animals (including rats, mice, dogs, hamsters, and primates). LADB is designed to be used by scientists conducting research and testing involving laboratory animals, for the selection of animal models, and for monitoring the testing of compounds for biological effects. Comparisons--including statistical manipulations--of the experimenter's data with data stored in LADB can be performed on-line at the experimenter's terminal. LADB should become operational in FY 1978.

Another Subcommittee-sponsored projected is a monthly current awareness bulletin on Toxicology Testing-in-Progress (TOX-TIPS). TOX-TIPS now reaches a user group of over 3,000 administrators and scientists in industry and government concerned with the long-term testing of toxic substances. The bulletin contains information on planned or on-going long-term biological testing of chemical compounds in the U.S. and abroad. This helps prevent the unknowing duplication of expensive, long-term biological testing of compounds.

Query Response

The TIP-supported Toxicology Information Response Center (TIRC) at the Oak Ridge National Laboratory continued to provide query response and literature search services in toxicology to several Federal agencies and more generally for health professionals and other members of the health community on a demand basis. In FY 1977, over 700 searches were completed.

PROGRAM MANAGEMENT

	1977 Appropriation		1978 Estimate		Increase or Decrease	
	Pos.	Amount	Pos.	Amount	Pos.	Amount
Program Management.....	79	5,794,000	77	6,352,000	-2	+558,000

Program Management provides the overall administration, coordination and direction of the various programs of the National Library of Medicine. The primary functions carried out by this activity include the preparation and processing of grant applications for review by the NLM's Board of Regents; management of the programs identified under Medical Library Assistance; financial and personnel management; public inquiries processing and management of the NLM's publications requirements; contracts processing and management; program analysis and legislative coordination activities; execution of basic administrative services such as supply, mail, travel, and security functions; and, coordination of the NLM's equal employment opportunity activities.

Since funds for the construction of the new Lister Hill Center Building were appropriated in FY 1976 a major undertaking of this activity has been to coordinate with the General Services Administration, responsible NIH personnel, and the NLM's program areas to assure that all clearances are obtained and that the overall program requirements of the Library are met in the design of this new facility. With the completion of the final specifications for bids for the new building attention will now be turned toward renovation of the existing Library. Particular emphasis will be placed on reclamation of areas which had originally been designed as stack spaces but which had temporarily been utilized as office space. Those library functions which will remain in the existing building will be thoroughly studied to assure that their new locations are conducive to good space management, facilitate suitable workflow patterns, and fulfill processing requirements with the least disruption.

With the completion of the Lister Hill Center Building all NLM organizational components will be housed in the same facility for the first time. To more effectively manage the integration of programs which will result, the planning activity of the NLM will be strengthened. This will be done to assure that the various components effectively contribute to the overall accomplishment of the NLM's mission and to assure that the NLM's resources are utilized most efficiently.

During the recent past the NLM has also devoted manpower and fiscal resources to security and fire prevention considerations within the Library. During FY 1977 and FY 1978 protection of the employees and the irreplaceable collection of the NLM from fire damage will be closely examined. A report on this matter has already been completed by experts in this field. Several of their recommendations will be implemented by the end of FY 1978. Specifically the recommendations for installation of automatic sprinkling systems, more sophisticated smoke detection devices, and completion of a Library fire salvage plan to minimize further damage to wet materials in the event of a fire will be pursued.

Two administrative positions have been removed in FY 1978 with the goal of minimizing potential duplication and layering in the Public Health Service.

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NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Medical Library Assistance Act: Title III, Part J, Sec. 393-397 (extended by Health Services Research, Health Statistics, and Medical Libraries Act of 1974)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
---	$8,000,000	$20,000,000	---	$7,987,000

Purpose: NLM's programs of Medical Library Assistance are designed to improve health information services by providing grants to train professional personnel, strengthen library resources, produce medical reviews, and conduct research in ways of improving information transfer. In addition, contracts provide a network of Regional Medical Libraries with the necessary resources and services to provide backup support for local medical libraries.

Explanation: Awards are made to individuals directly or to public or non-profit institutions. The grants awarded are project grants and do not require matching funds except for the Resources Improvement Grants.

Accomplishments in FY 1977: Expanded efforts directed at establishing cooperative, resource sharing library consortia among the nation's health care institutions. During FY 1977 support was provided for data gathering and planning operations for 50 consortia projects.

The Regional Medical Library Program (RML) continued to grow in terms of the number of services it provided. Document delivery services funded by the NLM exceeded 450,000 in FY 1977. The RML's in cooperation with the NLM began a reallocation of resources directed at expanding the RML's role in regional information transfer.

Objectives for FY 1978: The library consortia project will move to an operational phase in 1978 as it strives to provide better methods to meet the needs of health professionals for information services. This phase will consist of two initiatives: 1) establish in medical libraries entry points to the RML Network; 2) establish outlets for local access to advance health information systems.

In FY 1978 the RML's will change emphasis from serving as document delivery coordinators to support the consortia program described above and by acting as demonstration and information dissemination centers. Expansion of the role of RML's in conjunction with further development of the consortia will improve information access for health care practitioners by increasing markedly the number of health professionals with immediate access to the network.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Lister Hill National Center for Biomedical Communications
(Public Health Service Act, Title III, Part I, Sec. 381)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
24	$4,730,000	Indefinite	24	$4,775,000

Purpose: The Lister Hill Center facilitates, through the use of advanced computer and communications technology, the transfer of biomedical information and the interinstitutional sharing of resources to enhance the effectiveness of health manpower, of health and medical services, and the transfer of research results into practice norms.

Explanation: The Center works closely with the health and medical community to determine high priority needs and matches these needs with technological capabilities in order to develop experimental programs and evaluate their feasibility.

Accomplishments in FY 1977: The learning resources laboratory became operational. The laboratory initially developed experimental models which placed emphasis on the application of computer technology to library functions.

A number of stationary "broadcast-and-receive" ground stations were installed as part of the Library's cooperative efforts with other U.S. health agencies and the Canadian Government in utilizing the Communications Technology Satellite (CTS). Also broadcast studio in the Library for this project was completed.

Working with professional medical groups the NLM began a translation project to disseminate validated medical information (research results) to health practitioners in terms which they can understand.

Objectives for FY 1978: The learning resources laboratory will address applications of computer technology which are potentially of value in primary health care and continuing education.

The CTS will be operational in FY 1978. Evaluation of the effectiveness and efficiency of this project compared to alternative systems will be an important objective of the Center in FY 1978.

The translation project will receive major emphasis. Efforts will be directed at defining the roles of responsible organizations as the NLM, in conjunction with various professional medical groups, strives to transform medical information into products best suited for use by the health care practitioner.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: National Medical Audiovisual Center (Public Health Service Act, Title III, Part I, Sec. 381)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
88	$3,401,000	Indefinite	88	$3,561,000

Purpose: The National Medical Audiovisual Center (NMAC) located in Atlanta, Georgia applies audiovisual technology to the instructional needs of the biomedical community. Its primary mission is to stimulate the development and use of instructional media in schools of the health professions and in the continuing education of health professionals.

Explanation: NMAC functions as a clearinghouse for assembling, cataloging, and disseminating information on available instructional material. It evaluates, acquires and distributes materials appropriate for health professional education, and provides consultation and training in the use of instructional audiovisual technology. It also conducts research in instructional technology and systems and develops protorype instructional media programs.

Accomplishments in FY 1977: The Learning Resources Program, a collaborative program between NMAC and the Health Resources Administration, expanded into such areas as: (1) integrating scientific knowledge with clinical skills in health care delivery; (2) teaching such knowledge and skills to audiences possessing different knowledge levels and learning abilities; and (3) maintaining the quality of educational systems through use of validation and feedback mechanisms.

NMAC also developed a comprehensive curriculum for health science educators which contains all significant content/performance elements related to the application of educational technology to health science education.

NMAC maintained cooperative instructional development project with 100 health related schools. These efforts provided many of the teaching packages for NMAC distribution program which processed 65,000 loans and accounted for an estimated 6,000,000 viewing experiences.

Objectives for FY 1978: A vigorous program is being planned for increasing the efficiency of health professional education. NMAC, in conjunction with medical schools will: test cooperative training materials development involving participation of health professional teams from related disciplines in different schools; identify learner needs in continuing education; identify sets of knowledge and procedures to enable development of cost-effective learning systems; and establish procedures to maintain currency of knowledge in education programs; and will design a national field testing program to measure the effectiveness of instructional materials.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Library Operations (Public Health Service Act, Title III, Part I, Sec. 381)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
264	$11,143,000	Indefinite	264	$11,865,000

Purpose: Library Operations is responsible for selecting, acquiring, processing, indexing, cataloging, preserving, and disseminating the world's output of substantive biomedical literature. It also serves as the Regional Medical Library for the five-state Mid-Atlantic Region and provides back-up service for the National Regional Medical Library Network as a whole. In carrying out these responsibilities, Library Operations functions as the traditional service arm of the National Library of Medicine.

Explanation: Library Operations, through manual and machine methods prepares bibliographies and publishes indexes, catalogs, and other publications for use by the biomedical community; manages a national on-line information retrieval network, and conducts an extensive educational program for its network participants.

Accomplishments in FY 1977: Library Operations completed approximately 600,000 on-line searches of various library data bases in FY 1977. The number of user institutions which have access to these on-line services grew from 350 in FY 1975 to over 550 in FY 1977. Similarly demand for all major services provided by Library Operations increased between 10 and 25 percent in FY 1977. To meet these service demands without an increase in manpower resources the Library continued to pursue major undertakings designed to improve service capacity by automating and computerizing library functions where possible. Several phases of the acquisitions and cataloging functions were computerized in FY 1977. Work was begun on automating and computerizing the document delivery (interlibrary loan) program.

Because of increasing demands for computer processing capacity, work was completed by the computer services component of Library Operations, in conjunction with the General Services Administration, on a request for proposals for a replacement computer system which will meet the Library's projected workload requirements through FY 1985.

Objectives for FY 1978: As part of the Library's overall goal of translating biomedical research results into improved health care, additional effort will be directed toward expanding on-line services into health care facilities.

The document delivery program will become largely computerized in FY 1978. This will allow quicker delivery of interlibrary loans to health care practitioners.

The number of on-line searches is expected to reach 650,000 in FY 1978.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Toxicology Information (Public Health Service Act, Title III, Part I, Sec. 381)

1977 Appropriation		1978		
			Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
17	$2,166,000	Indefinite	17	$2,206,000

Purpose: The Toxicology Information Program (TIP) is responsible for collecting and organizing toxicology data from diverse sources and making it more readily accessible to the biomedical community.

Explanation: TIP obtains information from the published scientific literature and files of governmental, industrial, and academic organizations in whatever form it is available; organizes and enters this information into computerized storage and retrieval systems; and provides specialized services and products. TIP plays a key role in coordinating toxicology information activities within DHEW.

Accomplishments in FY 1977: The Toxicology Information Program (TIP) maintained its on-line bibliographic retrieval service (TOXLINE). The file was enhanced with additional records to increase its usefulness to those involved with the delivery of health care. During the year users performed over 35,000 on-line searches and requested over 1,700,000 citations printed off-line.

The size of the on-line chemical dictionary file (CHEMLINE) was doubled to contain over 200,000 compound records.

The Toxicology Data Bank (TDB) was developed. This data base is designated to be used by government, industry and academia for such tasks as identifying categories of compounds that exhibit certain toxic effects.

TIP continued to carry major responsibility for the management of the Toxicology Information Subcommittee (TIS) of the DHEW Committee to Coordinate Toxicology and Related Programs and for the implementation of its projects. A major TIS project, the Laboratory Animal Data Bank (LADB) underwent testing.

Objectives for FY 1978: TIP will continue to maintain the TOXLINE data base and enhance this file with special files in drug interference, teratogenesis and drug interactions that are of benefit to the health care delivery community. A study will be conducted to develop an on-line chemical structure display capability for the CHEMLINE service. The CHEMLINE file will be maintained and expanded to 300,000 records. Data for an additional 1,000 chemical substances and drug products will be added to the Toxicology Data Bank and where necessary, existing records will be enriched and updated.

NATIONAL INSTITUTES OF HEALTH

National Library of Medicine

Program Purpose and Accomplishments

Activity: Program Management (Public Health Service Act, Title III, Part I, Sec. 381)

1977 Appropriation		1978	1978 Budget Estimate	
Pos.	Amount	Authorization	Pos.	Amount
79	$5,794,000	Indefinite	77	$6,352,000

Purpose: This activity provides the funds for salaries and other related operating costs for the overall administration and direction of the National Library of Medicine programs.

Explanation: This program provides support for the Office of the Director, which has responsibility for overall administrative management and scientific direction of all NLM programs.

Accomplishments in FY 1977: The specifications for bids for the Lister Hill Center Building were completed in FY 1977. Invitations for bids were released on November 10, 1976. In FY 1977 attention turned toward renovation of the existing Library facility.

A security and fire prevention survey was completed and several recommendations were made to improve protection of the physical plant, the employees and the valuable collection of the Library.

NLM grants and contracts were awarded and administered under legislation authorized by the Medical Library Assistance Act and its extensions. Awards totaled nearly $8,000,000 in FY 1977.

Objectives for FY 1978: It is anticipated that several of the recommendations contained in the security and fire protection survey will be implemented. Specifically the recommendations for installation of automatic sprinkling systems, more sophisticated smoke detection devices, and completion of a Library fire salvage plan to minimize further damage to wet materials in the event of a fire will be pursued.

With the completion of the Lister Hill Center Building in FY 1979 all organizational components will be housed in the same facility for the first time. To more effectively manage the integration of programs which will result, the planning activity of the NLM will be strengthened. This will be done to assure that the various components effectively contribute to the overall accomplishment of the NLM's mission and to assure that the NLM's resources are utilized most efficiently.

OFFICE OF THE DIRECTOR AND BUILDINGS AND FACILITIES

MONDAY, MARCH 14, 1977.

WITNESSES

LEON M. SCHWARTZ, ASSOCIATE DIRECTOR FOR ADMINISTRATION, NATIONAL INSTITUTES OF HEALTH
DR. DONALD S. FREDRICKSON, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
ROSS HOLLIDAY, DIRECTOR, DIVISION OF ENGINEERING SERVICES, NATIONAL INSTITUTES OF HEALTH
NORMAN MANSFIELD, DIRECTOR, DIVISION OF FINANCIAL MANAGEMENT, NATIONAL INSTITUTES OF HEALTH
JACK GLASS, BUDGET OFFICER, OFFICE OF THE DIRECTOR, NATIONAL INSTITUTES OF HEALTH
ROBERT B. LAUDER, JR., BUDGET OFFICER, DIVISION OF ENGINEERING SERVICES, NATIONAL INSTITUTES OF HEALTH
ELLEN F. WORMSER, DIRECTOR, DIVISION OF HEALTH BUDGET ANALYSIS, OFFICE OF THE ASSISTANT SECRETARY, COMPTROLLER

Mr. FLOOD. Now, we will have the NIH, buildings and facilities and salaries and expenses for the Office of the Director. The presentation will be made by Leon M. Schwartz, the Associate Director for Administration, NIH. We have your biographical sketch, Mr. Schwartz, which we will place in the record at this point, and also your accompanying statement.

(The biographical sketch and statement follow:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service, National Institutes of Health

Biographical Sketch

NAME: Leon M. Schwartz

POSITION: Associate Director for Administration, NIH

BIRTHPLACE AND DATE: Baltimore, Maryland, April 26, 1928

EDUCATION: A.B., Economics, Johns Hopkins University, 1950

EXPERIENCE:
Associate Director for Administration, NIH, January 1972-present
Deputy Assistant Director for Program Management, Research Applications Directorate, National Science Foundation, 1971
Assistant Commissioner for Administration, Office of Education, DHEW, 1968-1971
Deputy Assistant Commissioner for Administration, Office of Education, DHEW, 1967-1968
Goddard Space Flight Center, National Aeronautics and Space Administration, 1960-1967
- Chief of Program Review and Resources Management, 1966-1967
- Director of Program Support Division, 1965-1966
- Business Manager, Meteorology Satellite Program, 1962-1965
- Financial Cost Analyst, 1960-1962

Assistant Treasurer and Chief Accountant, Carpel Incorporated, 1954-1960
Part-time Instructor, Accounting, Baltimore Institute, 1958-1963

ASSOCIATION MEMBERSHIPS:
Maryland Association of Certified Public Accountants
Federal Government Accountants Association
American Society for Public Administration

SPECIAL AWARDS, CITATIONS OR PUBLICATIONS:
Certified Public Accountant
HEW Superior Service Award, 1970
Consultant to National Science Foundation, Advisory Panel for the Research Management Improvement Program, 1973-1974

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Statement by Associate Director for Administration

National Institutes of Health

on

Office of the Director

Mr. Chairman and Members of the Committee:

The Office of the Director appropriation provides for the central executive direction and management of the National Institutes of Health, as well as the provision of some essential support services. Specifically, this appropriation covers:

(1) The Director and his immediate staff and the offices responsible for program planning and evaluation, public and scientific communication; and

(2) the following management support functions: budget and financial management, personnel, contracts and grants, and management analysis and review.

The functions and responsibilities of this appropriation are carried out through the offices of various associate directors and their supporting staff.

Program Management

The Director's immediate office includes his principal associates who assist him in policy development and coordination of the extensive extramural, intramural, and collaborative programs of the Institutes and Research Divisions, and the programs of the National Library of Medicine. Staff offices responsible for program planning and evaluation and for public and scientific communications support the Director in carrying out these responsibilities.

The management and program services financed by this appropriation support the overall management of the National Institutes of Health and provide a number of services to individual institutes and other operating components. It is expeditious and economical to provide management and program services on a consolidated basis since most of the National Institutes of Health is located within a single geographical area. The services financed through this appropriation include overall development of financial policies and procedures, and budget formulation, execution and analysis; position classification and salary administration, activities to assure equal employment opportunities, and a wide range of other personnel management services for over 11,000 employees; contracts and grants management services relating to approximately 24,000 projects; and management studies and reviews which promote economies and efficiency of operations and insure effective application of policy and procedural controls throughout all of the operating components of the National Institutes of Health.

The Office of the Director provides the overall leadership in implementation of Congressionally mandated programs, such as dissemination of research results, protection from research risks, fair information practices, as well as Executive Branch priorities in civil rights compliance, and equal employment opportunity programs.

Direct Operations

The direct operations activity of this appropriation provides for the direction, operation and administration of NIH accounting functions including financial reporting and analysis, payment and settlement, and accounting and voucher auditing for all of the National Institutes of Health. This activity also provides for payment to the NIH Management Fund.

Appropriation Request

Mr. Chairman, the appropriation request for the Office of the Director is $17,871,000 for 1978, a net increase of $937,000 over the 1977 level of $16,934,000.

The requested net increase of $937,000 provides for mandatory increases amounting to $975,000 and a decrease of $38,000 for the reduction of two administrative positions.

Buildings and Facilities

The Buildings and Facilities appropriation provides funds for design, construction, repair and improvement of facilities for the National Institutes of Health.

In total, we are requesting $65,650,000 in fiscal year 1978 for the following:

Ambulatory Care Research Facility	$57,400,000
Master Utilities Extension	4,000,000
Potable Water Systems, Building 10	250,000
Repairs and Improvements - Plant	1,250,000
Repairs and Improvements - Program	2,000,000
Solar Control, Building 31	750,000

I will discuss each of these briefly.

Ambulatory Care Research Facility

1978 Budget Request $57,400,000

These funds are requested to permit construction of this facility to continue. $21,700,000 was appropriated in 1977 for Stage I construction and the funds requested in 1978 will allow Stage IIA construction to be initiated. This facility is a major addition to the Clinical Center and is needed to support an increase in emphasis in translating basic research results to health care by enlarging outpatient clinical programs. In addition, the project will provide for modernization of outmoded clinical departments such as surgery, intensive

care, pathology and diagnostic radiology.

Design funds for the project in the amount of $3,580,000 were provided in FY 1973 and the construction contract for Stage I is scheduled for award in FY 1977. Additional funds for the completion of the facility and renovations to the Clinical Center will be requested in 1979 and 1980.

Master Utilities Extension

1978 Budget Request $4,000,000

These funds will provide for new electrical power distribution, an additional refrigeration machine and an additional boiler to serve the utility requirements of the Ambulatory Care Research Facility.

Potable Water Systems - Building 10

1978 Budget Request $250,000

These funds, together with the $200,000 provided in 1977, will provide for alterations and improvements to the domestic water distribution systems in the Clinical Center (Building 10) to properly isolate the laboratory water systems from the potable (drinkable) water systems and to correct deficiencies in water pressures on the upper floors of the 14-story structure.

Repairs and Improvements - Plant

1978 Budget Request $1,250,000

These funds are needed to continue the program of major repairs and improvements to the various electrical, mechanical and structural components of the physical plants at Bethesda, Maryland; Poolesville, Maryland; Hamilton, Montana; Baltimore, Maryland; and other field stations for which NIH is the real property holding agent. As you know, the plants are quite extensive and many of the buildings and facilities have been in service between 35 and 40 years. This

is a continuing need of providing for the care and upgrading of the physical plants.

Repairs and Improvements - Program

1978 Budget Request $2,000,000

These funds are also required to continue a source of funding, established in 1975, of financing miscellaneous alterations directly related to program needs which must be characterized as capital improvements. The work includes changes in physical facilities to accommodate revisions and new initiatives in research efforts.

Solar Control - Building 31

1978 Budget Request $750,000

These funds will provide for an initial effort to reduce the solar heat load on Building 31 and to improve the working environment within this facility. The existing building air conditioning system is inadequate to accommodate the high solar loads and a pilot project has been initiated to develop a feasible and practical solution to this problem.

Thank you, Mr. Chairman, I will be pleased to answer any questions you may have.

OFFICE OF THE DIRECTOR AND BUILDINGS AND FACILITIES

Mr. FLOOD. Now, do you have somebody with you that you want us to meet?

Mr. SCHWARTZ. Yes, sir, Mr. Ross Holliday, Director, Division of Engineering Services and Mr. Norman Mansfield, Director of Financial Management.

CONSTRUCTION OF FACILITIES

Mr. FLOOD. All right, Mr. Schwartz, before getting into this business of asking questions about requests made for the Office of Director, we may have a question or two about your construction program, itself. Can you tell us briefly where you stand on each of the major items on the facilities under construction?

Mr. SCHWARTZ. Yes, sir, I think you would be interested in the Lister Hill Center for Biomedical Communications. Dr. Cummings gave you a rundown previously on the Lister Hill Center. We would have hoped to have the awards made, however, that has been delayed because of a technicality in the bidding in February. We are still quite confident we will have an award by the middle of this calendar year.

AMBULATORY CARE RESEARCH FACILITY

The Ambulatory Care Research Facility is in a critical part of its development. We have given the go-ahead for acceptance of the guaranteed maximum price for stage 1, an expenditure of approximately $20 million in fiscal year 1977. We hope to have that under contract within 2 months. We are anticipating a groundbreaking ceremony during the month of April, so we feel very good about that. The other major projects is the Environmental Health facility in North Carolina. The design of the site development phase has proceeded quite well, it is 99-percent finished and we hope to make the award on the site development within a few months.

The design of the building phase is also moving along quite well and we expect to have that awarded this fiscal year.

Mr. FLOOD. Assuming you get the approval for the $66 million request, how much additional money would be required in fiscal 1979, and fiscal 1980, to complete the current projects you have just mentioned?

Mr. SCHWARTZ. We are presently budgeting the ambulatory research facility at $105 million. In fiscal 1977 and 1978 we will have approximately $79 million. So, this will mean essentially a $26 million cost to complete.

There has been one change in the scope of the project, Mr. Chairman. We are no longer planning to build the multi-level parking garages. These were scheduled for construction at the later stages of the project. They have been deleted.

Mr. FLOOD. What will you need for fiscal 1979 and 1980?

Mr. SCHWARTZ. The $26 million.

Mr. FLOOD. Of the facilities you have mentioned, how do the current cost estimates compare with the proposals made originally to the committee?

Mr. SCHWARTZ. The Lister Hill project still looks good at the $26 million ceiling which the Congress gave us. We see no problem at this point in the Environmental Health project. The original estimate on the Ambulatory Care Research project was $95 million. So there is an increase in that project. We won't be able to complete that construction in this fiscal year. Phase I construction, soon to be awarded, will include the excavation, foundation, and below-grade work. Phase II to be funded in fiscal years 1978 and 1979 will provide for the remaining pedestal and tower construction, but there will remain some additional costs for fiscal 1979.

ENVIRONMENTAL HEALTH SCIENCES CENTER

Mr. FLOOD. The cost of the construction, how is the cost of construction in North Carolina, how does it compare with the costs in the Washington area? Supply that for the record.

Mr. SCHWARTZ. Yes, sir.

[The information requested follows:]

An indication of the relative costs of building construction at Raleigh, N.C. compared to Washington, D.C. is provided by the Means Buildings Construction Cost Data Publication, published by Robert Snow Means Co., Inc., construction consultants and publishers, 100 Construction Plaza, Duxbury, Mass., Library of Congress Card No. 55–20084.

The 1977, 35th Annual Edition, provides index figures based on a 30 major city average cost of 100, and represents costs in each of the cities as of January 1, 1977. The Washington, D.C. index is 99.7 and the Raleigh, N.C., index is 84. That is, construction costing approximately $1 in Washington would, on the average, cost approximately 84 cents in Raleigh.

Mr. FLOOD. Are there any new projects you are anticipating within the next 2 years, major new projects?

Mr. SCHWARTZ. There are a number of new facilities.

Mr. FLOOD. New projects?

Mr. SCHWARTZ. Dr. Fredrickson mentioned the project at Fort Detrick. It is not in our current budget but we are looking forward to the provision of that facility. Over the next several years we will be going through a process of modernization of the Clinical Center. We expect to have plans substantially developed by fiscal year 1979.

In addition, five of our older laboratory buildings (Nos. 2, 3, 4, 5, and 8) constructed in the late thirties and early forties are in need of major interior renovation which will necessitate vacating the buildings during renovation. Additionally, two buildings (Nos. 7 and 9) have become obsolete and our studies indicate due to building configuration and deterioration, renovation cannot be justified. These two buildings are therefore programed to be razed.

To accomplish the renovations and razing of these buildings we will be asking for planning funds in fiscal year 1979 to construct a new laboratory building. Upon completion, we will vacate one of the older buildings by moving the programs into the new laboratory building. With one building vacated we will then through a series of efforts renovate and vacate another building until all five have been upgraded. We expect these programs to take about 8 to 10 years.

Mr. FLOOD. Does NIH have a long-range building, renovation and replacement plan or do you make these decisions on an ad hoc basis?

Mr. SCHWARTZ. We do have a long-range plan. Every year we go through the process of developing a 5-year plan. We have an approved plan which is required.

PATIENT SELECTION CRITERIA

Mr. FLOOD. With the completion of the new ambulatory care facility, you indicate your patient capacity will increase four times, 200,000 out-patient visits that would be; 200,000 visits a year is what you are talking about. When you get that increase, will you have to change substantially the criteria under which you select your patients?

Dr. FREDRICKSON. No; I think we will carry out an increasing amount of research with out-patients. We are not increasing the number of beds.

SOLAR CONTROL

Mr. FLOOD. What is that solar energy project you are talking about, also is the $750,000 the total amount needed?

Mr. SCHWARTZ. That is part of our total program at NIH. We have quite a few buildings with a lot of sun exposure. We are trying to minimize the solar heat gain for the purpose of reducing air conditioning requirements.

Mr. FLOOD. For obvious reasons, I would like for you to expand on that for the record.

[The information requested follows:]

The NIH is actively pursuing measures to economize on use of energy. The objective of the project for which these funds are requested is to correct deficiency in the coordination of the architecture, and the heating, ventilating, and air conditioning features of the original design and construction of Building 31, NIH, Bethesda.

This building is a major office building consisting of three connecting wings. Two of the wings (A and B) were occupied following completion of construction in 1962. The third wing (C) was completed and occupied in 1968. The building contains about 580,000 gross square feet of space and the wings A, B, and C are 11, 8, and 9 stories above grade respectively.

The long sides of both A and B wings face north and south and are of curtain wall construction employing generous amounts of glass. The solar heat resulting from the southern exposure of these wings causes overloading of the building air conditioning systems during the summer months, and need for air conditioning on sunny days during the months of December, January, and February.

It is expected that with the application of sun shades on insulating glass and spandrel panels, a major portion of the heat build-up in occupied spaces adjacent to the southern facades will be eliminated thus reducing air conditioning needs during the summer and eliminating air conditioning needs in the winter months. This development will reduce energy requirements and improve the environmental control of occupied spaces.

It is estimated that these funds will be adequate to support the cost of the needed changes to this building.

Mr. FLOOD. While it is not very much money, you have $250,000 for a new water system. Why is it so expensive?

Mr. HOLLIDAY. That is an improvement to the water distribution system in our building 10, our clinical center. I believe in the previous year we were given an appropriation of $200,000. This year it is $250,000.

Mr. FLOOD. $250,000, we have. We are not questioning the project, it is just why should it be so expensive. We have the impression that is pretty expensive.

Mr. HOLLIDAY. In the clinical center building we are separating the drinkable water from the laboratory water system and improving the

pressure. The pressure is currently inadequate on the upper floors of the 14-story building. Yes; it is a rather extensive project.

PROJECT COSTS

Mr. FLOOD. One more question. On page 269 and 270 of the justifications you list all the projects for 1977 and 1978. You can do that for the record. But you remember somebody might want the list and the amount of money requested for each of them. You can do that for the record.

[The information requested follows:]

Active projects,[1] 1977 and 1978	Funds appropriated		
	Prior to 1977	1977	1978 request
Ambulatory care research facility	$3,580,000	$21,700,000	$57,400,000
Electrical and air-conditioning improvements, Building 10	6,275,000		
Environmental Health Sciences Center	28,892,500	42,000,000	
Improvements to blue collar work areas	1,957,979		
Incinerator, Rocky Mountain Laboratory	383,500		
Lister Hill National Center	26,765,000		
Master utilities extension, phase II	6,160,000	500,000	4,000,000
Medical-pathological incinerator	500,000		
Modifications to NIH heating plant	240,000		
Modifications to NIH waste handling facilities	1,400,000		
Potable water systems, Building 10		200,000	250,000
Repairs and improvements	10,829,804	3,000,000	3,250,000
Solar control, Building 31			750,000

[1] An active project is one which is currently under design and/or construction.

OFFICE OF THE DIRECTOR

Mr. FLOOD. Now, as to the Office of Director, $17,871,000 is requested for the Office of the Director.

Mr. SCHWARTZ. Yes, sir.

Mr. FLOOD. Here you indicate the entire increase for 1978 is for what you call mandatory items, yet almost three-fourths of what you are looking at, of that increase, is for unspecified, you call them, payments for centrally furnished services. Those increases for those services are 30 percent over last year.

Mr. SCHWARTZ. Yes, sir, that is correct. The Office of the Director has a fair share of the allocation of the management fund. These are the central services which support all appropriations at NIH. As you might expect over the last few years, the overhead expenses, energy, the cost of personnel for guard services, housekeeping, security, have all increased. This is the fair share of the Office of the Director.

Also, in here is the cost of the Office of Director's share of the standard level user charge fund.

Mr. FLOOD. You furnish the security?

Mr. SCHWARTZ. Yes; we have approximately 100 guards there.

EMPLOYMENT

Mr. FLOOD. It appears there is an increasing nonpermanent employment. You increase that rather substantially. Six hundred thirty jobs. Why such a big increase and why nonpermanent?

Mr. SCHWARTZ. Our permanent ceiling has not changed. As a matter of fact, it has gone down. I think our other than permanent remains approximately the same as last year.

Mr. FLOOD. Aren't you increasing this substantially, from 2,084—I am looking at your records in 1977, 2,084 to 2,714, that is plus 630.

They are your figures.

Mr. SCHWARTZ. The overview statement is for NIH, the total institution, not just the Office of the Director. During the last few years, as you know, Mr. Chairman, our permanent ceiling has remained approximately the same. We have found that we can effectively use part-time——

Mr. FLOOD. Are you talking about NIH now?

Mr. SCHWARTZ. Yes, sir, this is a summary of all the institutes including the program budgets. We have found this is a very effective way to enhance the personnel and the staffing that we do have.

EXECUTIVE PAY

Mr. FLOOD. Now, here is something, we talked about this for several years, about the executive pay problem. At some length we talked about that for several years. I mean by that, its effect on your attempt to retain top scientists. With the substantial pay raise passed last month, do you feel that problem will pass?

Mr. SCHWARTZ. We think that will go a long way toward minimizing this problem. We still do have some problem in attracting from the outside. We are not competitive with many of the clinical laboratories at the university level.

Mr. FLOOD. But it will be a big help?

Mr. SCHWARTZ. Yes, sir.

PROGRAM EVALUATION

Mr. FLOOD. How much money are you setting aside in this budget for evaluation?

Mr. SCHWARTZ. As you know, the legislation allows that up to 1 percent be available for evaluation purposes. For the NIH, this could be as much as $25 million. However, our record for the past few years is an expenditure of approximately $8 million. I would say the program for fiscal year 1978 would be about that size.

Mr. FLOOD. How much of this evaluation is done by groups outside NIH?

Mr. SCHWARTZ. The way these funds are distributed, one-quarter is available to the Office of the Secretary for their expenditure. One-quarter available to the Public Health Service and the remaining one-half remains for NIH.

These funds are entirely spent for outside contracts. The cost of the civil servants to manage the program is not included in the 1-percent set-aside funds.

WOMEN AND MINORITIES

Mr. FLOOD. NIH, like all other areas of Government, has had increasing difficulty in increasing the number of women and minorities in its management structure.

Where do you stand with your affirmative action efforts?

Mr. SCHWARTZ. We are quite pleased with our performance. We think over the last few years when we look at the statistics we do find we have increased the number of minorities and women in our management structure. We have been very successful at the intern level to attract women and minorities. That really is the payoff for the future. We have a very active program going and we think we are achieving results.

Mr. FLOOD. Mr. O'Brien.

Mr. O'BRIEN. No questions.

EMPLOYMENT

Mr. EARLY. Would you repeat what you said about enhancing personnel by shifting from permanent employees to temporary.

Mr. SCHWARTZ. We have found we can successfully use other than permanent people for advisory purposes when you bring them in on an ad hoc basis.

Mr. EARLY. Is that the consulting type of employee?

Mr. SCHWARTZ. Yes, sir.

Mr. EARLY. I have never found that to be cost saving. It is always supposed to be but it never is. Everything I saw in ways and means in Massachusetts showed that consultants only brought on more confusion.

Where in your operation would it be better to go to consultants?

Mr. SCHWARTZ. Advisory council, peer review groups, where you are deliberately seeking the views of individuals who are not in the career civil service.

Mr. EARLY. Do you have career people doing the same thing?

Mr. SCHWARTZ. No; the career people make the final program judgments.

Mr. EARLY. Are they actually doing the same thing?

Mr. SCHWARTZ. They are making the management decisions, yes, sir.

Mr. FLOOD. Thank you very much.

[The following questions were submitted by members of the subcommittee with the request that they be answered for the record.]

MR. MICHEL

DISSEMINATION OF RESEARCH RESULTS

Mr. MICHEL. How is your program to increase dissemination of research results coming along? Is substantial headway being made?

ANSWER. We feel that we have made progress in our efforts to improve the dissemination of research results. Our initial projects have concentrated on communications of research-derived information to the practicing health professional, particularly the primary physician.

The report on dissemination activities initiated by NIH during 1976, which I filed with the committee at the opening of these hearings, describes 11 projects which we either have completed or are in process of carrying out. Some are substantial. A total of $1,692,000 has been budgeted for the special projects for dissemination improvement during fiscal year 1977. These activities are over and above the large information and demonstration programs carried out by the National Cancer Institute and the National Heart, Lung, and Blood Institute as mandated by Congress.

There is heightened awareness on the part of all components of NIH of the need to make sure that important new knowledge about the prevention, treatment, and cure of disease is made widely available.

In my office a substantial amount of staff time is being devoted to the whole question of "technology transfer" of which the dissemination improvement effort is a major component.

INDIRECT COST RATES

Mr. MICHEL. Last year you told us that your division of grants and contracts negotiates indirect cost rates with profitmaking institutions. What kind of criteria are used to determine these rates? I presume they are not the same as the criteria used for educational institutions?

ANSWER. Rates for both profitmakers and educational institutions are determined based on cost principles set forth in Federal Procurement Regulations chapter 1–15 (Contract Cost Principles and Procedures). Allowability of costs and acceptability of cost allocation methods for profitmakers are determined in accordance with subpart 2 of chapter 1–15; similar determinations for educational institutions are found in subpart 3 of chapter 1–15. It should be noted that subpart 3 of 1–15 and the much-discussed Federal Management Circular 73–8 are virtually identical.

Mr. MICHEL. I understand that the indirect cost rate for profitmaking institutions is generally higher than that for the nonprofitmakers. Is this true, and if so, why?

ANSWER. There are a myriad number of reasons why profitmaker's rates are high, comparatively speaking (i.e., combining profitmaker's overhead and general and administrative costs and comparing the total with total indirect costs of educational institutions). However, in answering this question, only the more significant reasons will be covered.

The first significant reason is the difference in treatment accorded costs by the two types of institutions. For example, profitmakers normally treat vacation, holiday, sick pay, and other fringe benefits (e.g., pension costs) related to direct personnel as an indirect cost. Educational institutions, on the other hand, treat the same costs as direct charges and usually include these costs in the base to which indirect costs are allocated. This difference in cost accounting treatment usually results in the profitmaker's rate being 20 to 30 percentage points higher than the educational institution's rate, assuming all other costs are comparable in amount and treated similarly by both institutions. Also, profitmakers usually treat administrative and clerical labor charges as an indirect charge, whereas educational institutions normally charge such costs direct.

Another factor accounting for differences in rates is the added indirect cost to the profitmaker for equipment depreciation and space occupancy. Profitmakers, because they are in business to do research or produce hardware, are expected to provide from corporate funds all the scientific equipment and buildings necessary to perform under Federal contracts, and to charge those contracts with their allocable share of the annual depreciation costs for the equipment and facilities through application of an indirect cost rate. Educational institutions, because their primary purpose is education and training rather than research, are not expected to provide scientific equipment out of institutional funds, and often the Federal sponsor is willing to underwrite the cost of constructing laboratories to accomplish the objectives of research and training projects. Since the aforementioned costs are therefore a direct charge to research or training agreements, the educational institution's annual indirect depreciation costs are significantly lower than the profitmakers, given comparable complements of scientific equipment and facilities. On this same subject, profitmakers, notwithstanding restrictions in subpart 2 of 1–15, normally rent the facilities in which the research is performed. Educational institutions, because they can construct buildings with donated or State-appropriated funds, tend to own rather than rent most of their research facilities. This results in lower space and occupancy costs to the educational institutions. Another factor that may contribute to a lower indirect cost rate for educational institutions, and particularly State-supported educational institutions, is that the institution's indirect costs may not include all the costs that the State incurs in supporting the operations

of the educational institution. This would be true even if the State had an approved State-wide cost allocation plan. The States maintain that these plans rarely recover the full cost of administering the activities of State-affiliated institutions engaged in health-related research and training.

Mr. MICHEL. What is average indirect cost rate for the profitmaking institutions?

ANSWER. In a recent study performed by the Division of Contracts and Grants, it was determined that indirect cost rates for profitmakers were in an average range of 105 to 120 percent of salaries and wages including vacation, holiday, sick pay, and all other fringe benefits. The individual indirect cost pools utilized in computing rates for this study included both overhead costs and general and administrative expenses of the profitmaker.

The latter point is made because overhead costs of profitmakers are normally allocated to contracts based on direct salary and wage costs and general and administrative costs are normally allocated on a total direct cost plus overhead base.

In addition, the purpose in combining these two types of indirect costs and allocating them on the basis of direct salaries and wages (including the fringe costs mentioned above) is to put the profitmaker on an allocation base comparable to that used by educational and other nonprofit institutions.

EMPLOYMENT OF MINORITIES AND WOMEN

Mr. MICHEL. According to your testimony last, NIH's affirmative action plan has established specific goals and timetables for increasing the employment of minorities and women. What exactly are these goals and timetables?

ANSWER. NIH had planned to establish goals and timetables, based on a formula called FAIR (Feasible Allocation to Improve Representation). After consideration, it was decided to further establish this formula on a trial basis and to review its usefulness, adequacy, and applicability for increasing minority and women employment before initiating it NIH-wide. The study is continuing.

Mr. MICHEL. Can you tell us what specific steps are being taken under affirmative action to increase the employment of minorities and women?

ANSWER. NIH is increasing its contacts with minority and women's institutions and individuals by visitation of workshop teams to discuss employment programs and research programs available at NIH. A minority and women's recruitment staff has been established to handle referrals and meet with high schools and colleges.

The following seven action items, which are related to increasing employment of minorities and women at NIH, are in the current affirmative action plan:

(*a*) Design and implement a systematic recruitment strategy in the NIH to reach minorities and women throughout the country.

(*b*) Commit resources and personnel through a special minority assistance program to assist qualified minorities in qualifying for vacancies at NIH.

(*c*) Evaluate the effectiveness of NIH recruitment teams in recruiting minority employees to NIH.

(*d*) Commit an increased percentage of positions at all levels, including scientific and administrative, for minority employment.

(*e*) Increase recruitment efforts and hiring of Hispanics, minority women, and Native Americans.

(*f*) Review and analyze accession and promotion rates by race, sex, occupational series, and grade.

(*g*) Establish commensurate goals and timetables based upon available data.

Mr. MICHEL. Is it wise policy to hire people on the basis of race or sex rather than strictly on the basis of merit?

ANSWER. Obviously, the question is strictly rhetorical. It presupposes a school of thought that race and sex should be used in lieu of merit as a basis for selection. Common sense dictates that we could not support such a position. Ideally, any effective hiring policy is one that addresses our needs in terms of selecting from among the highly qualified candidates, as well as our commitment under existing EEO laws to take affirmative action toward improving opportunities for minorities and women to compete on an equal basis.

AMBULATORY CARE RESEARCH FACILITY

Mr. MICHEL. How many patients will this new ambulatory research facility be capable of accommodating?

ANSWER. This new ambulatory research facility will be capable of accommodating up to 200,000 patient visits per year.

Mr. MICHEL. What is the criteria for determining who can receive care in this facility?

ANSWER. Patients will be selected upon referral from outside practicing physicians according to the needs of ongoing clinical investigations.

Mr. MICHEL. Last year we were told that the total cost of this facility would be $95 million. Is that still the estimate?

ANSWER. The $95 million estimate provided last year was derived by the construction management firm, based on conceptual plans. Estimating at early stages in the planning is essentially accomplished by using aggregate historical estimating guides, that is, comparing costs on a gross basis with construction costs of similar construction. We are now at a point where we have made adjustments in comparative cost estimates that were inherent in this project because of the unique characteristics of the construction. The latest estimates based on the same scope work, but derived from more complete working drawings by detailed take-off methods, resulted in an increased estimate. In view of the increase it has been decided to omit the multilevel parking structure estimated to cost $8 million, and to introduce possible alternatives in the bidding documents to reduce the costs to $105 million.

Mr. MICHEL. What is the present projected completion date?

ANSWER. It is estimated that, 3 years will be required to complete the building without the multilevel parking. Construction is expected to start in June 1977.

ENVIRONMENTAL HEALTH SCIENCES CENTER

Mr. MICHEL. What is the current status of that Environmental Health Sciences Center at Research Triangle Park, N.C.?

ANSWER. The design work for the project is essentially completed and we expect to make construction contract awards in the next few months. Some minor site preparation work has been started.

MANAGEMENT FUND

Mr. CONTE. You mentioned that your direct operations activity provides for payment to the NIH Management Fund. There has been some controversy over payments to the management fund, particularly regarding the manner in which the different institutes are tapped for such contributions. I wonder if you could tell me exactly how payments to the management fund are assessed.

ANSWER. Payments for centrally furnished services by the Institutes to the NIH Management Fund are derived by means of a pro rata formula. Depending on the nature of the services provided, the formula distributes the costs on the basis of the numbers of positions, intramural research dollars, clinical center bed assignments, and the amount of funds for research grants and individual training awards. We think this a simple but effective method of allocating central service costs.

AMBULATORY CARE RESEARCH FACILITY AND RENOVATIONS

Mr. CONTE. Can you tell me more about what will be included in the proposed ambulatory care research facility? Which institutes will be making the most use of the facility?

ANSWER. The new facility will provide clinical area and clinical laboratories from the 3d floor through the 13th floor. These spaces will connect with the existing Clinical Center Building on each floor. Space will be provided on the first and second floors for the clinical departments such as surgery, pathology, diagnostic radiation, nuclear medicine, and patient services. Parking will be provided below grade. The facility will be used by all Institutes since an ambulatory clinical program can be developed by all of them. As might be expected, the larger Institutes, NCI, NHLBI, and so forth, will be assigned the greater amount of space.

Mr. CONTE. What additional requests will you be making for 1979 and 1980 for the completion of the clinical center facility and renovations?

ANSWER. We have placed a $105 million ceiling on the construction costs of the new facility which will require an additional appropriation of $26 million in fiscal year 1979.

Major renovation of the existing clinical center will be required over the next 6 to 8 years. This will be necessary to realign programs to better accommodate to the new building and to upgrade obsolescence. We expect to ask for $6 million for each year for the fiscal years 1979 and 1980. As an order of magnitude estimate we expect this work to cost in total about $30 million; we expect to have the program better defined by next year.

SOLAR CONTROL

Mr. CONTE. Could you tell me what your pilot project to reduce the solar load in building 31 involves? Why is this suddenly become such a problem?

ANSWER. This building is a major office building consisting of 3 connecting wings rising 8, 9, and 11 stories above grade. Extensive glass construction on the southern facades results in a very high internal heat load from solar radiation. This is not only a problem in summer but requires air-conditioning during the winter months of December, January, and February. This project is recommended for the purpose of correcting this deficiency.

Our studies so far suggest that we can solve the problem with the use of sun shades or insulating glass or a combination of the two. This has been a problem since construction of the building in 1962. We believe this approach will produce a significant energy saving.

OFFICE OF THE DIRECTOR PROGRAM RESOURCES

Mr. CONTE. How do you propose to meet congressional mandates such as improved dissemination of research results, protection from research risks, civil rights compliance, and so forth, without additional program resources?

ANSWER. It will most likely have to be at the expense of other programs and offices in the Office of the Director. We will have to reexamine our programs and curtail those that we feel will be least detrimental to our operations.

Mr. CONTE. On page 280 of your justification, you show a $550,000 increase for the restoration of program level which had been reduced in 1977 to absorb statutory pay raise costs. Would you explain the background and need for that item?

ANSWER. We have provided Congress with a revised justification which reflects a proposed 1977 supplemental for statutory pay raise costs; therefore, the restoration increase is no longer required. The 1978 total OD budget request remains the same in both submissions.

Mr. CONTE. You are proposing a two-position reduction for next year. Will that give you adequate people to perform the many necessary tasks assigned to your office with adequate levels of efficiency?

ANSWER. Even at the current staff level, it becomes exceedingly more and more difficult to perform the many necessary tasks assigned to the Office of the Director with adequate levels of efficiency. This is a result of the increased responsibilities for managing congressional, as well as executive, mandates without any increase in program resources for the past several years. Any reduction in manpower could certainly exacerbate the situation.

JUSTIFICATION OF THE BUDGET ESTIMATES

BUILDINGS AND FACILITIES

For construction of, and acquisition of sites and equipment for, facilities of or used by the National Institutes of Health, where not otherwise provided, [$67,400,000] *$65,650,000*, to remain available until expended.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

NATIONAL INSTITUTES OF HEALTH

Buildings and Facilities

Amounts Available for Obligation

	1977 Estimate	1978 Estimate
Appropriation	$ 67,400,000	$ 65,650,000
Unobligated balance, start of year	60,618,000	9,470,000
Unobligated balance, end of year	-9,470,000	-5,067,000
Total, obligations	$118,548,000	$ 70,053,000

Summary and Explanation of Changes

1977 Budget Authority	$67,400,000
1978 Budget Authority	65,650,000
Net Change	-$1,750,000

Increases:

A. Program

1. Ambulatory Care Research Facility	$57,400,000
2. Master Utilities Extension	+4,000,000
3. Potable Water Systems, Building 10	+250,000
4. Repairs and Improvements, Plant	+1,250,000
5. Repairs and Improvements, Program	+2,000,000
6. Solar Control, Building 31	+750,000
Total, increases	$65,650,000

Decreases:

B. Program

1. Ambulatory Care Research Facility	-21,700,000
2. Environmental Health Sciences Center	-42,000,000
3. Master Utilities Extension	-500,000
4. Potable Water Systems, Building 10	-200,000
5. Repairs and Improvements, Plant	-1,000,000
6. Repairs and Improvements, Program	-2,000,000
Total, decreases	-67,400,000
Total, net changes	-1,750,000

Obligations by Activity

Page Ref.		1977 Appropriation	1978 Estimate	Increase or Decrease
267	Research facilities	$108,522,000	$60,500,000	-$48,022,000
267	Service and administrative facilities	10,026,000	9,553,000	-473,000
	Total obligations	118,548,000	70,053,000	-48,495,000

Obligations by Object

	1977 Appropriation	1978 Estimate	Increase or Decrease
NATIONAL INSTITUTES OF HEALTH			
Printing and reproduction	$ 3,000	$ 2,000	$ -1,000
Other services	98,761,000	69,251,000	-29,510,000
Subtotal	98,764,000	69,253,000	-29,511,000
ALLOCATION TO GENERAL SERVICES ADMINISTRATION			
Other services	19,784,000	800,000	-18,984,000
Total obligations by object	118,548,000	70,053,000	-48,495,000

Actual

Buildings and Facilities

Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
1968	$10,715,000	$10,715,000	$15,075,000	$10,715,000
1969	12,495,000	---	5,310,000	---
1970[1/]	1,000,000	1,000,000	1,900,000	1,615,000
1971	---	---	---	---
1972	3,565,000	3,565,000	5,065,000	3,565,000
1973	8,500,000	8,500,000	33,480,000	8,500,000[2/]
1974	8,000,000	8,000,000	8,000,000	8,000,000
1975	3,000,000	3,000,000	3,000,000	3,000,000
1976	3,000,000	93,000,000	41,000,000	54,000,000
1977	25,400,000	67,400,000	67,400,000	67,400,000
1978	65,650,000			

1/ Prior to 1970, funds include all DHEW health activities. Separate NIH appropriation enacted in 1970.

2/ This appropriation authority was the continuing resolution. The appropriation amount was the House Allowance, which was the lower of the House or Senate amounts in the first vetoed bill.

Buildings and Facilities, NIH

New Obligational Authority	1977 Appropriation	1978 Estimate	Increase or Decrease
Research facilities	$63,700,000	$57,400,000	-$6,300,000
Service and administrative facilities	3,700,000	8,250,000	+4,550,000
Total	$67,400,000	$65,650,000	-$1,750,000

General Statement

This appropriation includes all proposed direct construction items of the National Institutes of Health and all continuing projects.

Research Facilities

Includes those facilities used directly by the research activities of the National Institutes of Health.

Service and Administrative Facilities

Those facilities which render administrative and service support to the research activities of the National Institutes of Health.

Ambulatory Care Research Facility

1978 appropriation estimate..... $57,400,000

The funds requested in 1978 for Stage II A, when added to the $21,700,000 appropriated in 1977, provide a total of $79,100,000, and will permit construction of this facility to continue. Additional funds for the completion of the facility and renovations to the Clinical Center will be requested in 1979 and 1980.

The Ambulatory Care Research Facility will be used to expedite the translation of basic research into health care services. The outpatient visits to NIH will be increased from 45,000 to 195,000 visits per year. The facility will also provide for the modernization of grossly outdated and inadequate departments including surgery, intensive care, pathology and diagnostic radiology. This facility will be a new major resource for all institutes engaged in clinical research.

The total project will provide for a building addition to the NIH Clinical Center, major renovations to the Clinical Center and multilevel parking facilities to accommodate the parking which will be displaced by the construction as well as additional parking required by the program for employees, patients, and visitors.

Master Utilities Extension

1978 appropriation estimate..... $4,000,000

The 1978 request will provide for new electrical power distribution, an additional refrigeration machine and an additional boiler to serve the utility requirements of the Ambulatory Care Research Facility.

Potable Water Systems - Building 10

1978 appropriation estimate..... $ 250,000

The 1978 request, together with the $200,000 appropriated in 1977, will provide for alterations and improvements to the domestic water distribution systems in the Clinical Center (Building 10) to properly isolate the laboratory water systems from the potable (drinkable) water systems and to correct deficiencies in water pressures on the upper floors of the 14-story structure.

Repairs and Improvements - Plant

1978 appropriation estimate..... $1,250,000

This project is for the continuance of the program of major repairs and improvements to the various electrical, mechanical and structural components of the physical plants at Bethesda, Maryland; Poolesville, Maryland; Hamilton, Montana; Baltimore, Maryland; and other field stations for which NIH is the real property holding agent. The physical plants are extensive and many of the buildings have been in service over 38 years.

Repairs and Improvements - Program

1978 appropriation estimate..... $2,000,000

In 1978, these funds will provide for the continuance of the program of financing major improvements to program-related space. These improvements are frequently required with limited lead time to adapt to changes in research procedures, installation of new equipment, or the initiation of new programs.

Solar Control - Building 31

1978 appropriation estimate..... $ 750,000

This project will provide for an initial effort to modify building fenestration to reduce the solar heat load on Building 31 and to improve the working environment within this facility. A pilot project has been initiated to develop a feasible and practical solution to the reduction of the solar load. The existing building air conditioning system is inadequate to accommodate the high solar loads.

NATIONAL INSTITUTES OF HEALTH

Building and Facilities

Program Purpose and Accomplishments

Activities: Research Facilities and Service and Administrative Facilities

1977 Amount	1978 Authorization	1978 Budget Estimate
$67,400,000	Indefinite	$65,650,000

Purpose: The NIH direct construction program provides for the construction, improvement and major repair of the buildings and supporting facilities essential to the conduct of the mission of the National Institutes of Health.

Explanation: Buildings and facilities funded under this appropriation include those required for both research programs and for supportive services at the main NIH reservation, Bethesda, Maryland; the NIH Animal Center, Poolesville, Maryland; the Research Triangle Park, North Carolina; the Rocky Mountain Laboratory, Hamilton, Montana; the Gerontology Research Facility, Baltimore, Maryland; and other NIH field stations.

Accomplishments in 1977:

Construction Completed

Installation of refrigeration machine #12, Building 34 (MUE)
Replacement of low-pressure gas mains (MUE)
Improvements to NIH Laundry, Building 13
Improvements to electrical service, Building 10
Modifications to NIH Heating Plant, Building 11
Medical-Pathological Incinerator #1, Building 11A
Incinerator - Rocky Mountain Laboratory, Hamilton, Montana

Construction Contracts in Process or Scheduled for Award

Ambulatory Care Research Facility - Phase I
Environmental Health Sciences Center, Research Triangle Park, North Carolina
Lister Hill National Center for Biomedical Communications
Addition to Refrigeration Plant, Building 34
Solid Waste Facility Improvements
Modifications to Waste Water Treatment Plant, NIH Animal Center
Improvements to Air Conditioning, Building 10

Design Contracts Completed

Environmental Health Sciences Center, Research Triangle Park, North Carolina
Lister Hill National Center for Biomedical Communications
Addition to Refrigeration Plant, Building 34
Modifications to Waste Water Treatment Plant, NIH Animal Center

Accomplishments in 1977 - Continued

Design Contracts in Process or Scheduled for Award

Potable Water Systems, Building 10 - Phase I
Master Utilities Extension (part)
Replacement of Nurses Call System, Building 10

Repairs and Improvements

Continuation of major repairs and improvements for both plant and program facilities.

Objectives in 1978:

Construction Completed

Improvements to Blue Collar Work Areas
Improvements to Air Conditioning, Building 10
Solid Waste Facility Improvements
Modifications to Waste Water Treatment Plant, NIH Animal Center

Construction Contracts in Process or Scheduled for Award

Ambulatory Care Research Facility
Environmental Health Sciences Center, Research Triangle Park, North Carolina
Lister Hill National Center for Biomedical Communications
Master Utilities Extension (part)
Potable Water Systems, Building 10 - Phase I
Replacement of Nurses Call System, Building 10

Design Contracts Completed

Potable Water Systems, Building 10 - Phase I
Master Utilities Extension (part)
Replacement of Nurses Call System - Building 10

Design Contracts in Process or Scheduled for Award

Master Utilities Extension (part)
Potable Water Systems, Building 10 - Phase II
Solar Control, Building 31

Repairs and Improvements

Continuation of major repairs and improvements for both plant and program facilities.

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