COOLEY'S ANEMIA SCREENING AND COUNSELING PROGRAM

HEARING

BEFORE THE

SUBCOMMITTEE ON PUBLIC HEALTH AND ENVIRONMENT

OF THE

COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE HOUSE OF REPRESENTATIVES

NINETY-SECOND CONGRESS

SECOND SESSION

ON

H.R. 14016 (and all identical bills)

BILLS TO AMEND THE PUBLIC HEALTH SERVICE ACT TO PROVIDE FOR THE PREVENTION OF COOLEY'S ANEMIA

MAY 23, 1972

Serial No. 92-68

Printed for the use of the
Committee on Interstate and Foreign Commerce

U.S. GOVERNMENT PRINTING OFFICE
79-753 O WASHINGTON : 1972

COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE

HARLEY O. STAGGERS, West Virginia, *Chairman*

TORBERT M. MACDONALD, Massachusetts
JOHN JARMAN, Oklahoma
JOHN E. MOSS, California
JOHN D. DINGELL, Michigan
PAUL G. ROGERS, Florida
LIONEL VAN DEERLIN, California
J. J. PICKLE, Texas
FRED B. ROONEY, Pennsylvania
JOHN M. MURPHY, New York
DAVID E. SATTERFIELD III, Virginia
BROCK ADAMS, Washington
RAY BLANTON, Tennessee
W. S. (BILL) STUCKEY, JR., Georgia
PETER N. KYROS, Maine
BOB ECKHARDT, Texas
ROBERT O. TIERNAN, Rhode Island
RICHARDSON PREYER, North Carolina
BERTRAM L. PODELL, New York
HENRY HELSTOSKI, New Jersey
JAMES W. SYMINGTON, Missouri
CHARLES J. CARNEY, Ohio
RALPH H. METCALFE, Illinois
GOODLOE E. BYRON, Maryland
WILLIAM R. ROY, Kansas

WILLIAM L. SPRINGER, Illinois
SAMUEL L. DEVINE, Ohio
ANCHER NELSEN, Minnesota
HASTINGS KEITH, Massachusetts
JAMES T. BROYHILL, North Carolina
JAMES HARVEY, Michigan
TIM LEE CARTER, Kentucky
CLARENCE J. BROWN, Ohio
DAN KUYKENDALL, Tennessee
JOE SKUBITZ, Kansas
FLETCHER THOMPSON, Georgia
JAMES F. HASTINGS, New York
JOHN G. SCHMITZ, California
JAMES M. COLLINS, Texas
LOUIS FREY, JR., Florida
JOHN WARE, Pennsylvania
JOHN Y. McCOLLISTER, Nebraska
RICHARD G. SHOUP, Montana

W. E. WILLIAMSON, *Clerk*
KENNETH J. PAINTER, *Assistant Clerk*

Professional Staff

JAMES M. MENGER, Jr.
WILLIAM J. DIXON
ROBERT F. GUTHRIE
KURT BORCHARDT

CHARLES B. CURTIS

SUBCOMMITTEE ON PUBLIC HEALTH AND ENVIRONMENT

PAUL G. ROGERS, Florida, *Chairman*

DAVID E. SATTERFIELD III, Virginia
PETER N. KYROS, Maine
RICHARDSON PREYER, North Carolina
JAMES W. SYMINGTON, Missouri
WILLIAM R. ROY, Kansas

ANCHER NELSEN, Minnesota
TIM LEE CARTER, Kentucky
JAMES F. HASTINGS, New York
JOHN G. SCHMITZ, California

CONTENTS

COOLEY'S ANEMIA SCREENING AND COUNSELING PROGRAM

TUESDAY, MAY 23, 1972

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON PUBLIC HEALTH AND ENVIRONMENT,
COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE,
Washington, D.C.

The subcommittee met at 10:45 a.m., pursuant to notice, in room 2218, Rayburn House Office Building, Hon. Paul G. Rogers, chairman, presiding.

Mr. ROGERS. The subcommittee will come to order, please.

The hearings today are on H.R. 14016 and similar bills which would provide for an expanded national attack on Cooley's anemia.

Cooley's anemia is caused by a genetic blockage of the synthesis of adult hemoglobin and is characterized by severe anemia, enlargement of the spleen, and characteristic changes in the skin and facial features.

Individuals who have the disease generally do not live beyond the first decade of life, although some persons can be kept alive for a longer period of time with the aid of transfusions.

Cooley's anemia is not primarily associated with a particular racial group, but instead appears in a number of populations, notably those whose ancestors lived near the Mediterranean, especially Italians and Greeks.

As you know, on March 22, 1972, the House passed a bill designed to mount an attack on sickle-cell anemia, another little understood genetically transmittable blood disease. Only last week, the President signed this legislation into law. The legislation we are considering today is patterned very closely upon the sickle cell legislation.

At this point in the record there will be inserted the text of the bills.

(The text of H.R. 14016 and all identical bills follow:)

[H.R. 14016, 92d Cong., 2d sess., introduced by Mr. Giaimo (for himself and Mrs. Grasso) on March 22, 1972;
H.R. 14109, 92d Cong., 2d sess., introduced by Mr. Monagan on March 27, 1972;
H.R. 14113, 92d Cong., 2d sess., introduced by Mr. Brasco, March 27, 1972;
H.R. 14233, 92d Cong., 2d sess., introduced by Mrs. Hicks of Massachusetts on March 29, 1972;
H.R. 14477, 92d Cong., 2d sess., introduced by Mr. Podell on April 19, 1972;
H.R. 14557, 92d Cong., 2d sess., introduced by Mr. Rodino on April 20, 1972;
H.R. 14586, 92d Cong., 2d sess., introduced by Mr. Delaney on April 25, 1972;
H.R. 14684, 92d Cong., 2d sess., introduced by Mr. Pike on April 27, 1972;
H.R. 14755, 92d Cong., 2d sess., introduced by Mr. Thompson of New Jersey on May 3, 1972;
H.R. 14833, 92d Cong., 2d sess., introduced by Mr. Roe on May 8, 1972;
H.R. 14861, 92d Cong., 2d sess., introduced by Mr. Rosenthal on May 9, 1972;
H.R. 14874, 92d Cong., 2d sess., introduced by Mr. Ruppe on May 9, 1972;
H.R. 14910, 92d Cong., 2d sess., introduced by Mr. Helstoski on May 10, 1972;
H.R. 14925, 92d Cong., 2d sess., introduced by Mr. Biester on May 11, 1972;
H.R. 14942, 92d Cong., 2d sess., introduced by Mr. Minish on May 11, 1972;
H.R. 15072, 92d Cong., 2d sess., introduced by Mr. Kuykendall on May 19, 1972;
H.R. 15128, 92d Cong., 2d sess., introduced by Mr. Kyros on May 23, 1972; and
H.R. 15133, 92d Cong., 2d sess., introduced by Mr. Biaggi on May 23, 1972,

are identical as follows:]

A BILL

To amend the Public Health Service Act to provide for the prevention of Cooley's anemia.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SHORT TITLE

SECTION 1. This Act may be cited as the "National Cooley's Anemia Control Act".

FINDINGS AND DECLARATION OF PURPOSE

SEC. 2. (a) The Congress finds and declares—

(1) that Cooley's anemia is a debilitating, inheritable disease that afflicts approximately two hundred thousand American citizens and has been largely neglected;

(2) that efforts to prevent Cooley's anemia must be directed toward increased research in the cause and treatment of the disease, and the education, screening, and counseling of carriers of the trait;

(3) that simple and inexpensive screening tests have been devised which will identify those who have the disease or carry the trait;

(4) that programs to prevent Cooley's anemia must be based entirely upon the voluntary cooperation of the individuals involved; and

(5) that the attainment of better methods of prevention, diagnosis, and treatment of Cooley's anemia deserves the highest priority.

(b) In order to preserve and protect the health and welfare of all citizens, it is the purpose of this Act to establish a national program for the diagnosis, prevention, and treatment of, and research in, Cooley's anemia.

AMENDMENTS TO PUBLIC HEALTH SERVICE ACT

SEC. 3. (a) Section 1 of the Public Health Service Act is amended by striking out "titles I to X" and inserting in lieu thereof "titles I to XI".

(b) The Act of July 1, 1944 (58 Stat. 682), as amended, is amended by renumbering title XI (as in effect prior to the enactment of this Act) as title XII, and by renumbering sections 1101 through 1114 (as in effect prior

to the enactment of this Act), and references thereto, as sections 1201 through 1214, respectively.

"TITLE XI—COOLEY'S ANEMIA PROGRAM

"PROGRAMS RELATING TO COOLEY'S ANEMIA

"SEC. 1101. (a) (1) The Secretary may make grants to public and nonprofit private entities, and may enter into contracts with public and private entities, for projects for the establishment and operation of Cooley's anemia screening, treatment, and counseling programs.

"(2) The Secretary may make grants to public and nonprofit private entities, and may enter into contracts with public and private entities and individuals, for projects for research in the diagnosis, treatment, and prevention of Cooley's anemia.

"(3) The Secretary may make grants to public and nonprofit private health profession schools for fellowships for training in the diagnosis, treatment, and prevention of Cooley's anemia. Fellowships provided under grants under this paragraph shall be limited to such amounts as the Secretary finds necessary to cover the cost of the training of, and stipends and allowances (including travel and subsistence expenses and dependency allowances) for, the fellows.

"(4) The Secretary shall carry out a program to develop information and educational materials relating to Cooley's anemia and to disseminate such information and

materials to persons providing health care and to the public generally. The Secretary may carry out such program through grants to public and nonprofit private entities or contracts with public and private entities and individuals.

"(b) (1) For the purpose of making payments pursuant to grants and contracts under subsection (a) (1), there are authorized to be appropriated $500,000 for the fiscal year ending June 30, 1973, and for each of the next two fiscal years.

"(2) For the purpose of making payments pursuant to grants and contracts under subsection (a) (2), there are authorized to be appropriated $1,700,000 for the fiscal year ending June 30, 1973, and for each of the next two fiscal years.

"(3) For the purpose of making grants under subsection (a) (3), there are authorized to be appropriated $150,000 for the fiscal year ending June 30, 1973, and for each of the next two fiscal years.

"(4) For the purpose of carrying out subsection (a) (4), there are authorized to be appropriated $25,000 for the fiscal year ending June 30, 1973, and for each of the next two fiscal years.

"VOLUNTARY PARTICIPATION

"SEC. 1102. The participation by any individual in any program or portion thereof under this title shall be wholly

voluntary and shall not be a prerequisite to eligibility for or receipt of any other service or assistance from, or to participation in, any other program.

"APPLICATIONS; ADMINISTRATION OF GRANT AND CONTRACT PROGRAMS

"SEC. 1103. (a) A grant under this title may be made upon application to the Secretary at such time, in such manner, containing and accompanied by such information, as the Secretary deems necessary. Each applicant shall—

"(1) provide that the programs and activities for which assistance under this title is sought will be administered by or under the supervision of the applicant;

"(2) describe with particularity the programs and activities for which assistance is sought;

"(3) provide for strict confidentiality of all test results, medical records, and other information regarding screening, counseling, or treatment of any person treated, except for (A) such information as the patient (or his guardian) consents to be released; or (B) statistical data compiled without reference to the identity of any such patient;

"(4) provide for appropriate community representation in the development and operation of any program funded by a grant under this title;

"(5) set forth such fiscal control and fund accounting procedures as may be necessary to assure proper disbursement of and accounting for Federal funds paid to the applicant under this title; and

"(6) provide for making such reports in such form and containing such information as the Secretary may reasonably require.

"(b) In making any grant or contract under this title, the Secretary shall (1) take into account the number of persons to be served by the program supported by such grant or contract and the extent to which rapid and effective use will be made of funds under the grant or contract; and (2) give priority to programs operating in areas which the Secretary determines have the greatest number of persons in need of the services provided under such programs.

"PUBLIC HEALTH SERVICE FACILITIES

"SEC. 1104. The Secretary shall establish a program within the Public Health Service to provide for voluntary Cooley's anemia screening, counseling, and treatment. Such program shall be made available through facilities of the Public Health Service to any person requesting screening, counseling, or treatment, and shall include appropriate publicity of the availability and voluntary nature of such programs.

"REPORTS

"SEC. 1105. (a) The Secretary shall prepare and submit to the President for transmittal to the Congress on or before April 1 of each year a comprehensive report on the administration of this title.

"(b) The report required by this section shall contain such recommendations for additional legislation as the Secretary deems necessary."

Mr. ROGERS. We are especially pleased to have two of our distinguished colleagues to testify. The major sponsor of the bill, a long time friend of this committee and one who has been very active in the health field, the Honorable Robert N. Giaimo and of course the Honorable Ella T. Grasso who also has taken a most active interest in this whole area.

The committee is particularly pleased to welcome you both to the committee and because of your determination and insistence I might say the committee is very pleased to hold these hearings today.

So we welcome you.

STATEMENT OF HON. ROBERT N. GIAIMO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mr. GIAIMO. Thank you very much, Mr. Chairman and members of the committee. It is a pleasure for Congresswoman Grasso and me, who cosponsored this legislation and introduced it together with 15 or more cosponsors to have this opportunity to testify before your committee in behalf of thalassemia or Cooley's anemia or Mediterranean anemia, as it is commonly called.

I have a prepared statement which for the sake of brevity I wish to insert in the record because I am most anxious to have the subcommittee receive the testimony of our medical experts.

Mr. ROGERS. Without objection your statement will be made part of the record immediately following your verbal statement.

Mrs. Grasso may also, if she desires, submit her statement.

Mr. GIAIMO. We are quite anxious to hear the testimony of our medical experts who are truly outstanding men, not only in the field of Cooley's anemia but also in sickle cell anemia with which this committee certainly is most familiar.

For example, from Yale University in my own city of New Haven we have Dr. Howard Pearson who has been one of the outstanding research men in Cooley's anemia and sickle cell anemia. He will be a recipient of the Martin Luther King Award in Philadelphia either at the end of this month or next month for his work in sickle cell anemia. Certainly he can tell you much more than I can about this disease.

Based upon what I have been able to find, and this is in keeping with some of the statements which the chairman made just prior to my testimony, apparently sickle cell anemia, and certainly Cooley's anemia, is found in a belt which radiates the world in a central area in which the Mediterranean would be a part. Apparently the belt is the area of the world where malaria existed and perhaps still exists, and in prehistoric times, this type of genetic blood disorder arose as a defense against malaria. Now, there is no need for that defense.

One of the byproducts of this gentic development is this Cooley's disease which is quite similar to sickle cell, equally devastating and fatal.

It happens then in our own country, because of the population makeups that we find most of the people in this belt come from the Mediterranean area, especially the large Italian and Greek population in the United States. It also would affect, for example, Chinese, Filipinos, and people in that part of the world.

As you know, we have people from that racial origin in the United States too.

Another point I would like to make, which is made more clearly in my prepared statement, is that from time to time we have heard the argument that we are already funding assistance for Cooley's anemia. In fact, I think testimony was heard at one time that almost $600,000 has been awarded in this area.

Well, a very careful search of the grants which have already been made indicates very clearly to us who have studied this matter that most, if not all, of that money was for basic research on hemoglobin problems almost all of which were unrelated to Cooley's. So, this was sort of a general statement that the agencies claim when they say they are already funding large sums in this area.

We have many distinguished people with us here today. I would like to make mention of them because of the tremendous interest in this area.

In addition to our witness, Dr. Pearson, we have Dr. James A. Wolf of Columbia Presbyterian Medical Center, Baby's Hospital; Dr. David Nathan, Children's Hospital; Dr. Edward Zaino, chairman, Medical Advisory Board, Cooley's Anemia Blood and Research Foundation for Children; Edward Paradiso, president of the Foundation also the parent of a child with Cooley's anemia; and Dr. Denis Miller of the Pediatric Hematology Clinic, New York Hospital, Cornell Medical Center.

We also have Miss Ann Freedman, executive director of the Cooley's Foundation; Anthony Larele; Mrs. Edward Paradiso, secretary of the national federation and mother of a child who has Cooley's anemia; and Mrs. Casseta, first vice president of the national board of directors.

I know this very sophisticated subcommittee does not have to be impressed with great numbers of people. Suffice it to say if that were the case we could have packed not only this room but the hall and the building.

As the gentleman from Florida knows, the great organization AHEPA has made this one of their priority concerns, the Sons of Italy Organization and many other organizations are also vitally interested. We told them there really would be no need to have any kind of massive demonstration of support because we are dependent seriously and totally on our medical witnesses.

I will now conclude my statement so that we may hear the testimony of the distinguished group of witnesses we have with us today.

(Mr. Giaimo's prepared statement follows:)

STATEMENT OF HON. ROBERT N. GIAIMO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Chairman Rogers and members of this subcommittee, let me at the outset express my deep and sincere appreciation for your willingness to devote your time to the subject of Cooley's anemia, also known as thalassemia.

I know that you have been spending many long days in consideration of important health and environment legislation, including the very important subject of health maintenance organizations, in addition to the many other vital concerns of the individual members of this subcommittee.

Foremost among the recent accomplishments of this subcommittee was the passage of legislation authorizing funds for screening, research and treatment programs to deal with sickle cell anemia, the genetic blood disorder primarily affecting black Americans.

Sickle cell, of course, is one of the two genetic blood disorders leading to anemia commonly found in the American population. The other, less commonly found but no less important to the parents and children affected by it, is Cooley's anemia, a genetic blood disorder primarily affecting children and young adults of Italian and Greek parentage. In addition, as you well know, in the American "melting pot" Cooley's anemia, like sickle cell, can be found in children and young adults of almost any parentage and any ethnic background.

Just as sickle cell anemia was relatively unknown in the general population five years ago, however, Cooley's anemia has been a "low profile" disease. I first learned of the problems faced by young people with this disease in January of this year when a representative of the Connecticut Chapter of the Cooley's Anemia Blood and Research Foundation for Children and a patient with Cooley's anemia came to my congressional office.

At that time I learned two important things about Cooley's Anemia: First, that although the major form of the disease has no known cure and invariably leads to an early death, the victims of the disease have the potential to live productive lives and want very much to help themselves. The young man I met who has the disease—to cite one example—is working toward his Ph. D. degree in chemistry, despite the multiple handicaps and medical setbacks in his life. Second, I learned that the Federal Government is doing very little indeed to search for a cure for this disease or to help those who currently have it.

I attempted after that meeting to add Cooley's Anemia to sickle cell anemia legislation as the second major genetic blood disorder leading to anemia which the Federal medical effort should be addressed to. I can understand, of course, why this subcommittee wished to see its bill passed unchanged, and why this is the more appropriate time to explore Cooley's Anemia.

There are three important questions which this subcommittee can address today, and I will outline them briefly before turning the witness chair over to the experts.

First, what is the true extent of the Federal commitment to deal with this disease? You may remember that during consideration of the sickle cell anemia bill it was claimed that currently Federal research in excess of $600,000 is devoted to Cooley's anemia. That is just not true. An examination of the titles of research projects supposedly devoted to Cooley's anemia reveals that they are only peripherally related to this disease. The truth is that little if any Federal money has gone into researching the cause or possible cure of Cooley's Anemia, and none at all into screening or treatment programs.

Second, how can this subcommittee obtain in-depth and accurate information about Cooley's anemia. I have been fortunate to meet Doctor Howard Pearson, professor of pediatrics at Yale Medical School and head of the pediatric hermatology division of the Yal-New Haven Hospital, and to obtain my information from him. This subcommittee will have the opportunity to discuss Cooley's anemia with Doctor Pearson and other medical authorities in the field, but I trust you will permit me to note an honor I am sure Doctor Pearson would be reluctant to bring up himself. At the end of this month, Doctor Pearson is slated to receive the Martin Luther King Award for his research into sickle cell anemia, a presentation which will be made by the President or his representative and Mrs. Coretta King in Philadelphia. He is therefore truly a resource in two areas of concern to this subcommittee.

In addition to the medical authorities present, representatives of the national Cooley's Anemia Foundation will be before you today. They can adequately and eloquently present the concerns of the victims of this disease and their parents.

Third, this subcommittee will be asking "what should the Federal Government be doing to attack Cooley's anemia"? The major form of this disease is estimated to affect as many as five thousand children and young adults in America; the minor form, or genetic trait, is estimated to affect more than 200,000 other people, many of them parents or potential parents who can pass the trait on to their offsprings. Just so, approximately ten percent of the population of black Americans have the genetic trait for sickle cell anemia, and a much smaller number have the actual major form of sickle cell disease itself. Federal goals in dealing with Cooley's anemia, therefore, should be both to help those who currently have the disease and to help prevent new cases.

The bill before you aims to provide the modest amount of $7.1 million for purposes of research, screening and treatment programs for Cooley's anemia. This estimate—submitted by the Cooley's anemia foundation—should be considered a minimum amount necessary for the stated purposes, a skeleton on which

this subcommittee's deliberations can build. I urge you to give the most serious consideration to the problems of Cooley's anemia, to answer your questions about this disease with the resources available today, and to complete the job of providing Federal assistance to the victims of genetic blood disorders leading to anemia.

Thank you again.

Mr. ROGERS. Thank you very much.

I might say that the order of AHEPA has sent a telegram in support of the legislation which will be made a part of the record.

(The telegram referred to follows:)

[Telegram]

ORDER OF AHEPA SUPREME LODGE HEADQUARTERS,
Washington, D.C., May 22, 1972.

Hon. PAUL G. ROGERS,
House of Representatives, Washington, D.C.

In behalf of our membership of more than 1,100 local chapters of the Order of Ahepa throughout the United States we respectfully urge approval of the bill on Cooley's anemia by Congressman Giaimo which is before your committee at this time. The Order of Ahepa, a national association of American citizens of Greek descent, appeals for governmental support to combat this hereditary disease which attacks American citizens of Italian, Greek, Spanish, and North African descent and ancestry and their future generations. Action now will safeguard future generations of our children against Cooley's anemia, also known as thalassemia. The Order of Ahepa is actively engaged in disseminating information about Cooley's anemia to all those who may be affected, but Federal funding is necessary we feel, and at this time, if the disease is to be effectively controlled. Your full support will be gratefully appreciated.

SAM NAKIS,
Supreme President.
Dr. MICHAEL N. SPIRTOS,
Supreme Vice President.

Mr. ROGERS. Mrs. Grasso, we welcome you to the committee with your great interest in this field along with Mr. Giaimo.

STATEMENT OF HON. ELLA T. GRASSO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mrs. GRASSO. Mr. Chairman, I want to take this opportunity to thank you and the subcommittee for making possible this meeting this morning and the testimony that will come from the expert witnesses.

Like Mr. Giaimo I feel I should yield to them so that they can explain to you the magnitude and the effect of this disease.

Certainly our presence here indicates our own concern.

It may be of interest to the members of the subcommittee that a film on Cooley's anemia has been prepared by Channel 3, WTIC, in Hartford. The station president, Mr. Leonard J. Patricelli has done yeoman work in the sickle cell field. The film will be made available to the members of the subcommittee on request and any Members of Congress during the week of June 6 to June 8.

In the testimony I have prepared and would like to submit to the subcommittee are letters from organizations such as the Justinian Society, Sons of Italy, Unico National, all attesting to their interest and concern and profound hope that this committee in its wisdom will be of assistance in finding a cure for this dread disease.

Mr. ROGERS. Certainly without objection. We are grateful to you. I might say I am an honorary member of the Sons of Italy, Ft. Lauderdale chapter.

Thank you for being here and for your great interest in this subject matter.

(Mrs. Grasso's statement and attachments referred to follow:)

STATEMENT OF HON. ELLA T. GRASSO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mr. Chairman, H.R. 14016—a bill to amend the Public Health Service Act to provide for the prevention of Cooley's anemia—must become law.

On behalf of the children and young adults who are ravaged by this disease, let me take this opportunity to commend the subcommittee for holding hearings today. Just as you reported legislation earlier this year to combat sickle cell anemia, so I am sure you will provide the vital authorization needed to launch a program to combat the other major genetic hemoglobin disease, Cooley's anemia.

This dread disease, known medically as thalassemia, is a genetically transmitted blood disorder which occurs in a major and minor form. Individuals with the single Cooley's trait live normal lives, but could pass the trait and disease on to their children. Individuals who develop the major form of Cooley's anemia, encounter defective hemoglobin synthesis which leads to eventual death. Most of the victims of Cooley's anemia are children of descendants from the Mediterranean littoral—primarily Italians and Greeks. However, because of widespread intermarriage, the Cooley's trait has been passed on to other nationalities as well. If both a man and women with the Cooley's trait have children, the Mendalian law of genetics holds that, statistically, 25 percent of their children may contract the major form of thalassemia, and another 50 percent may become carriers of the Cooley's trait.

For those children who are unfortunate enough to inherit the genetic "code" causing Cooley's anemia in the hemoglobin chains, symptoms known as thalassemia major usually appear after the first three months of life. Victims of Cooley's anemia also suffer from enlargement of the spleen, changes in skin and facial features, poor bone growth, as well as susceptability to other ailments and fatigue.

At this time only supportive therapy exists for victims of Cooley's anemia. The patient must undergo periodic blood transfusions, usually once a month, to help maintain a stable hemoglobin count. However, as the illness progresses, iron from the blood transfusions accumulates in all the tissues of the body and may affect the endocrine glands and muscles, including the heart.

Recent medical advances have lengthened the life expectancy of Cooley's anemia sufferers from a few years to over two decades. Nevertheless, the over 100,000 people with the major form of Cooley's anemia can only look forward to an agonizing life and a painful, early death.

Despite the admirable research and educational work being conducted by the Cooley's Anemia Blood and Research Foundation for Children, more assistance is desperately needed to help the victims of Cooley's anemia and to inform the carriers of the Cooley's trait about the disease. Moreover, without substantial continuous funding, the programs undertaken may never provide fruitful and hopeful results.

It is my belief that the legislation before you today will help meet the pressing need for continued research and educational projects. The provisions of H.R. 14016—which I introduced with my friend and colleague from Connecticut, Mr. Giaimo—would authorize $7,125,000 to be used over a three-year period in the field of medicine as well as for educational and informational services.

First, in the area of medicine, over $5.5 million would be authorized for fellowships to train specialists and for funds to enable the continuation of important ongoing research and new research projects aimed at finding methods for diagnosis, treatment and prevention of this dread disease. The research provides hope for present victims of the disease. It could mean the improvement of their condition and lengthening of their lives. And this research also holds out the prospect of healthy lives for thousands of children yet unborn who could be afflicted with Cooley's anemia.

The second major area of support provided by this bill includes over $1.5 million for educational and informational services, for screening, counseling, and treatment projects. It is tragic that over 100,000 children and young adults are ill with Cooley's anemia. Each deserves the best available treatment known to medical science. Also every one of the many hundreds of thousands of people who carry the Cooley's trait must have the benefits of voluntary screening programs and counseling.

79-753 O—72——3

At this time, except for the families and friends of those people afflicted with the disease, the general public knows little about Cooley's anemia. Fortunately, times are changing. People are being informed about this disease through the work of such dedicated individuals as Leonard J. Patricelli, president of Broadcast House, WTIC-Radio and TV in Hartford, Connecticut. Mr. Patricelli was in the forefront of the battle to make the public aware of Sickle Cell Anemia, and his activities contributed to the passage of the National Sickle Cell Anemia Prevention Act. Recently, he has been mobilizing support on behalf of efforts to educate the people of our nation about Cooley's anemia. On February 25, WTIC-TV ran a half-hour documentary program about the various aspects of Cooley's anemia. Informative and moving, this program received acclaim throughout the area. WTIC graciously made the video tape available to me. Members of the subcommittee and other of our colleagues will have the opportunity to view the program on June 6 and 8, at 11:00 a.m., in the House Recording Studio, Room B310 of the Rayburn Building.

This legislation has the support of many important organizations and individuals. These include UNICO National, a service organization of business and professional leaders of Italian descent; the American Justinian Society of Jurists, comprised of lawyers of Italian descent; Grand Lodge of Connecticut, Order Sons of Italy in America; the Department of Connecticut, Italian American War Veterans of the U.S., Inc.; the Bernardino-Badolato Post #2 and The Columbian Federation, both of New Britain, Connecticut. At their Connecticut state convention last Sunday, the Order Sons of Italy in America passed a resolution giving their full support to our Cooley's anemia bill. At this point I request permission to include as part of the permanent record letters of support from Dr. John X. R. Basile, Executive Vice President of UNICO National; Mr. John A. Vigilante, Grand Venerable, Grand Lodge of Connecticut, Order Sons of Italy in America; Mr. Joseph Cannata, Adjutant, Department of Connecticut, Italian American War Veterans of the U.S., Inc. and President of The Columbian Federation; and Mr. Paul J. Manafort, Commander, Bernardino-Badolato Post #2.

Mr. Chairman, we cannot put a price tag on human life, on the heartache and suffering of Cooley's anemia victims, or the mental anguish of their families and friends. But we can and we must help eliminate the agony of this disease for present and future generations by passage of H.R. 14016.

UNICO NATIONAL,
OFFICE OF EXECUTIVE VICE-PRESIDENT,
Hartford, Conn., May 19, 1972.

Representative ELLA T. GRASSO,
6th District, Connecticut, Cannon Office Building, House of Representatives, Washington, D.C.

DEAR REPRESENTATIVE ELLA T. GRASSO: I humbly submit a plea for help on behalf of the many children afflicted with Cooley's Anemia or Thalassemia. This is a plea that unfortunately cannot be made in person by these children and young adults who are so ravaged by this disease. These victims need constant medical attention and constant supervision by their immediate families, as well as their multitude of friends. For the over two hundred thousand victims of this disease, there are some two million people directly or indirectly affected. Their heartache and suffering cannot be measured in words, money, mental anguish or constant medical care. The number of people in this country and in the world that carry that trait reaches staggering numbers. Pilot screening studies have thus far shown that possibly seventeen percent of Greek Americans may have the Cooley's Anemia trait. A large number of Italian Americans are afflicted with the same problem. A significant number of cases have been reported among the descendants of Jewish, Syrian and Lebanese ancestors. A large number of people in Thailand and other Southeast Asian countries have been discovered to have the Cooley's Anemia trait or disease. Greece and Italy have more than significant numbers with this trait and this disease.

There are over twenty-five million Americans of Italian descent in this country. There are a significant number of Americans of Greek descent in this country.

United States has been eminent in the discovery of many diseases in the past twenty-five years. We have been pioneers and the driving force in medical research and have effectively nearly eradicated poliomyelitis, measles, mumps, whooping cough, diphtheria, small pox, rabies and tetanus. We are on the threshold of breakthroughs in the field of cancer. The medical centers in the

United States are leaders in transplant surgery, psychiatry, care of burned patients and cardiac disorders. United States has been the focal point for peoples from all over the world to do research in most of the medical disciplines.

Our organization, Unico National, is a national service organization throughout of this disease, Cooley's Anemia

This Bill, H.R. 14016, is extremely important if we are to maintain the posture of the number one country in the field of medical research.

Our organization, Unico National, is a national service organization throughout the United States. It is comprised of business and professional leaders in the 50 states. We are Americans of Italian descent. We are very active and prominent in encouraging work done in the mental health and mental retardation. Our scholarship program is second to none.

We are proud of the work done by our government. We strongly endorse the House of Representatives to take a step forward in the fight for the prevention of Cooley's Anemia.

Sincerely,

JOHN X. R. BASILE, M.D., F.A.C.S.,
Executive Vice-President.

GRAND LODGE OF CONNECTICUT,
ORDER SONS OF ITALY IN AMERICA AND CANADA,
Norwalk, Conn., April 20, 1972.

ELLA T. GRASSO,
Congress of the United States,
House of Representatives, Washington, D.C.

DEAR ELLA: Thank you for your recent correspondence concerning the above captioned matter. I have just returned from the Supreme Council meeting in Philadelphia, Pennsylvania wherein they have adopted my resolution concerning the Order's support for yours and Bob Giaimo's bill, HR14016.

Very truly yours,

JOHN A. VIGILANTE, Esq.,
Grand Venerable.

DEPARTMENT OF CONNECTICUT,
ITALIAN AMERICAN WAR VETERANS OF THE U.S., INC.,
New Britain, Conn., May 20, 1972.

U.S. Representative ELLA GRASSO,
Cannon Building,
Washington, D.C.

DEAR MRS. GRASSO: The Department of Connecticut, Italian American War Veterans goes on record as supporting your efforts for the passage of H.R. 14016 (Cooley's Anemia).

This bill is of great importance to us as Italians as this anemia is more prevalent among the Italians of our country.

We urge the passage of this bill so that grants can be given for the research in the diagnosis, treatment and prevention of this type of anemia.

We hope and pray that this bill will become a reality before many lives are taken through this dreaded disease.

Sincerely yours,

JOSEPH CANNATA,
Adjutant.

THE COLUMBIAN FEDERATION,
New Britain, Conn., May 20, 1972.

U.S. Representative ELLA GRASSO,
Cannon Building,
Washington, D.C.

DEAR MRS. GRASSO: The Columbian Federation fo New Britain hereby goes on record as supporting H.R. 14016 in reference to Cooley's Disease.

Little is known of this disease to date, even though it was discovered in 1925 by Cooley and Lee. I have taken the time to do some researching on this type of Anemia and it is a proven fact that this anemia is hereditary and there is no known effective treatment for this disease.

H.R. 14016 is another milestone in the betterment of health among our nations citizens. We urge that this bill be passed so that we can eradicate or at least try to get effective drug treatment for those now having this type of anemia.

I also wish to express our sincere thanks to you and your fellow congressmen who are supporting this bill and the many Italians of our community, state and nation are supporting your efforts for a healthier country.

Sincerely,

JOSEPH CANNATA,
President.

BERNARDINO-BADOLATO POST NO. 2,
ITALIAN-AMERICAN WAR VETERANS OF THE UNITED STATES,
New Britain, Conn., May 20, 1972.

U.S. Representative ELLA GRASSO,
Cannon Building,
Washington, D.C.

DEAR MRS. GRASSO: The members of our organization are in favor of the passage of H.R. 14016 which is in reference to the research of Cooley's disease or better known as Cooley's Anemia.

We urge the passage of this bill so that immediate steps can be taken to start research and to try to get an effective treatment for this type of anemia.

Your efforts on this bill are greatly appreciated.

Sincerely,

PAUL J. MANAFORT,
Commander.

Mr. ROGERS. The following Representatives have submitted statements for the record, and without objection the statements will be placed in the record at this point.

STATEMENT OF HON. FRANK THOMPSON, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. THOMPSON. Mr. Chairman, I would like to take this opportunity to thank the subcommittee for permitting me to testify in behalf of H.R. 14755.

Less well known than multiple sclerosis, but equally as deadly, is Thalassemia major, commonly called Cooley's anemia. I was prompted to introduce H.R. 14755 by a letter which I received from Mrs. Robert Auto of Camden, N.J., describing the agony of continual blood transfusions which her brother's 11-year-old grandson must go through in order to survive.

Cooley's anemia, an inheritable and debilitating disease primarily affecting children of Mediterranean descent, is incurable and usually fatal. In 1930, 5 years after Dr. Thomas B. Cooley of Detroit identified the disease, the life expectancy of an afflicted child was little more than a year. Today, it is more than 20 years. Simple and inexpensive screening tests have been devised which will identify those who have the disease or carry the trait yet public education, counseling, and screening of carriers of the trait has been largely neglected. Approximately 200,000 American citizens are afflicted with this disease.

H.R. 14755 would amend the Public Health Service Act to provide for the prevention of Cooley's anemia. It would empower the Secretary of Health, Education, and Welfare to make grants for research into causes and cures of the disease; carry out a program to develop information and educational materials relating to Cooley's anemia; to

disseminate such information to persons providing health care and to the public generally; and establish a voluntary program within the Public Health Service to provide for Cooley's anemia screening, counseling, and treatment. The Secretary would also be required to prepare and submit to the President for transmittal to the Congress a comprehensive report on the administration of these programs by April 1 of each year.

I wholeheartedly urge the subcommittee to act favorably on this legislation in the interests of those afflicted by Cooley's anemia, and in the interests of future generations.

Thank you.

STATEMENT OF HON. JOHN S. MONOGAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CONNECTICUT

Mr. MONOGAN. Mr. Chairman and members of the subcommittee, I appreciate having this opportunity to express my support for H.R. 14109, National Cooley's Anemia Control Act, which I introduced, and other similar bills to amend the Public Health Service Act to provide for the prevention of Cooley's anemia.

Cooley's anemia is a disorder of the hemoglobin of the blood and is transmitted genetically. There are approximately 200,000 Americans afflicted with this painful disease, and tragically the majority are children. The disease becomes manifest during the first year of life. The victims suffer a reduction in the formation and duration of red blood cells, loss of appetite, listlessness, enlargement of the spleen and liver, pallor, and a slight degree of jaundice. Those afflicted require frequent and costly blood transfusions to correct their anemia. These transfusions may be required weekly and in some instances as often as once a day. They also suffer malformed development leading to brittle, easily broken bones and alteration in facial appearance. In most instances, death occurs before the 20th year.

The existing programs in the research of the causes and possible cures for this disease are totally inadequate. In fact, at this time very little is known about Cooley's anemia even though it was described as a separate and specific type of blood disease about 1925 by Dr. Thomas B. Cooley. There is no known cure for the disease. Treatment consists solely of the frequent administration of blood transfusions to alleviate the constantly recurring anemia. These research programs must be given adequate monetary resources to carry their activities to positive effect.

We must not continue to neglect those individuals afflicted with Cooley's anemia. I have received numerous communications from Connecticut constituents and others throughout the country concerning the tragic experience of years of anguish and enormous medical expenses and the ultimate death of a brother, sister, son, daughter, nephew, niece, or grandchild. Decisive action must be taken by this Congress before additional children become the victims of this killing malady.

The National Cooley's Anemia Control Act would provide $7.1 million for research, treatment, and training programs to ease and eventually eliminate the agony of Cooley's anemia. I urge the members

of this subcommittee to take favorable action on H.R. 14109 and provide for the establishment of this national program for the elimination of this dread disease.

STATEMENT OF HON. SILVIO O. CONTE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MASSACHUSETTS

Mr. CONTE. Mr. Chairman, I would like at this time to express my wholehearted support for H.R. 14016, to amend the Public Health Service Act to provide for the prevention of Cooley's anemia.

I believe that passage of this measure is vitally necessary in order to give hope to the 200,000 Americans who are debilitated by this inheritable disease and to the many millions of Americans who live in fear lest their children be struck down by this lethal affliction.

Cooley's anemia, as you know, is—like sickle cell anemia—a genetic blood disorder. We in the Congress have already sworn to try to eradicate sickle cell anemia. Cooley's anemia, however, affects primarily people of Mediterranean descent—potentially 20 million Americans.

In other words, all Greek, Italian, and Spanish-Americans could conceivably carry the gene which causes Cooley's anemia. Their children could be stricken with this incurable disease—their only hope to be a short and painful life with continual blood transfusions.

Two hundred thousand Americans, as I said, presently suffer from this malady. We cannot delay action on the grounds that it is still a relatively minor problem. We should begin now to seek a cure for this killer.

The purpose of this legislation is to provide funds for research, screening, treatment, and training programs for Cooley's anemia. This is the approach we have already chosen to combat sickle cell anemia. I urge you, as I did when several of us attempted to broaden the scope of the sickle cell bill, not to delay action to combat this other equally deadly disorder. Do not let this tragic situation ever reach the catastrophic proportions of sickle cell anemia.

Already, Cooley's anemia has spread through intermarriage to persons of Jewish, Scandinavian, German and even oriental backgrounds. It spares no race or nationality.

The disease becomes manifest during an infant's first year of life. Along with the necessity for frequent transfusions, those afflicted suffer malformed development, brittle bones and distortion of facial features. In most cases, death strikes before the 20th year.

The picture I paint is tragic. The message, I believe, is obvious. The Congress must act to beef up inadequate research programs. We must commit ourselves to finding a cure for Cooley's anemia. And we must do it now.

Thank you, Mr. Chairman.

STATEMENT OF HON. JOSEPH G. MINISH, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. MINISH. Mr. Chairman and members of the subcommittee, I appreciate this opportunity to submit a statement in support of H.R. 14942, my bill to combat Cooley's anemia.

Thalassemia major, more commonly known as Cooley's anemia, is a little known, but deadly disease which now affects over 100,000 of

our fellow Americans. The disease occurs mostly in individuals whose ancestors were of Mediterranean stock such as Italians and Greeks. However, due to intermarriage, Cooley's anemia today is found among a great variety of ethnic groups.

Cooley's anemia is an hereditary blood disorder which usually manifests itself during the first year of life. The earliest signs may be pallor, listlessness, loss of appetite, and irratibility. Examination of the patient usually reveals an enlargement of the spleen and liver, pallor of the skin and mucuous membranes, and sometimes a slight degree of jaundice of the whites of the eyes. Blood examination will usually show changes in the shape and numbers of the red blood cells, and a variety of alterations from the normal in special properties of the blood cells, in addition to a severe enemia.

Children with the disease are greatly handicapped. Bone growth is poor—they are therefore usually small for their age. The bones are more fragile than normal, and fractures occuring almost spontaneously are common. Rarely does a victim of Cooley's anemia live beyond the age of 20, and from early life, victims are compelled to undergo frequent blood transfusions in order to survive.

Mr. Chairman, although great progress has been made by private individuals and groups in fighting Cooley's anemia, the Federal Government has largely neglected the disease. The legislation I am cosponsoring would provide more than $7 million for research, screening, treatment, and training programs to ease and eventually eliminate the agony of Cooley's anemia.

For too many years this disease has brought pain, suffering, and death to its victims and their families. I respectfully urge the subcommittee to take prompt and affirmative action on legislation to combat Cooley's anemia.

STATEMENT OF HON. FRANK ANNUNZIO, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

Mr. ANNUNZIO. Within the last year the Congress and the American people have had brought to their attention the existing threat of certain blood diseases which are selective in their victims and deadly to those who suffer the effects. One of these diseases is sickle cell anemia. Another is Cooley's anemia. Although a distinct disease, Cooley's anemia, like sickle cell anemia, is a disorder of the blood and is transmitted genetically.

Little is known about Cooley's anemia, even though it was described nearly 50 years ago by Dr. Thomas B. Cooley. One thing about Cooley's anemia is certain—those who have the disease rarely grow to maturity; it is a disease of adults and young children. It is estimated that there are over 100,000 Americans affected with this dreadful disease—and tragically, the majority are children. The victims of Cooley's anemia do not survive, but the carriers of a new generation of victims survive and reproduce. Like sickle cell anemia, this deadly disease is inherited when both parents carry the disease trait.

Initially Cooley's anemia was peculiar only to people of Mediterranean descent. Today however, because of generations of intermarriage, it is found among Americans of many other racial strains. The incidence of Cooley's anemia is rising. Let us not wait until it claims more lives than sickle cell anemia to mount an effective attack.

Until now, little Federal money has been spent in the fight against this dreaded disease. Today, however, we have before us legislation which represents a national commitment to combat this disease and eventually eliminate it. H.R. 14016 will provide for the Federal financial support so desparately needed for research on Cooley's anemia.

H.R. 14016 will provide for counseling, screening, and treatment programs by authorizing $7.1 million over 3 years. Also grants to public and nonprofit private organizations would be available under this bill.

The tragic consequences of this disease have been neglected too long. Strong support by the House for the Cooley's anemia legislation will show that this country has the ability and the concern to fight this killer disease. Your support for H.R. 14016 will lead the way for a national program that can meet the challenge of this critical health problem.

I would also like to include in the record of these hearings a letter written by Mr. John X. R. Basile, office of the executive vice president, UNICO National, expressing the strong support of his organization, for legislation to provide for the prevention of Cooley's anemia.[1]

STATEMENT OF HON. LOUISE DAY HICKS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF MASSACHUSETTS

Mrs. HICKS. Mr. Chairman, Cooley's anemia research desperately needs Federal financial support. This year, the Congress is taking the sorely needed first steps toward authorizing Federal funds for medical research and screening programs intended to assist the victims of sickle-cell anemia. This important legislation has had my support from the beginning.

But we must not stop there. Sickle-cell anemia is only one of the major genetic blood disorders affecting children in America today. Less known, yet equally crippling is Cooley's anemia. Medically termed Thalassemia Major and sometimes called Mediterranean disease, Cooley's anemia claims over 100,000 American sufferers, mostly children in this country. Cooley's children suffer malformed bone development which leads to brittle, easily broken bones, and alteration in facial appearance. Unlike normal children, these victims have no vitality and energy. Rarely does a victim of Cooley's anemia live beyond 20 years of age; and from the first year of life these victims must receive frequent blood transfusions to correct their anemia. Basic research on the problems of blood formation and destruction offers the only hope for sufferers of this disease.

At the present time, there is only one nongovernmental national source for extensive funding of research and training toward a cure for this disease. This is the Cooley's Anemia Blood and Research Foundation for Children, a private organization in New York City with branches in other major cities. Unfortunately, the foundation must rely heavily on moneys contributed from the private sector for its work, thus making long-range or extensive program planning difficult. Their research desperately needs Federal financial support.

---

[1] The letter referred to is printed on p. 14, this hearing, as an attachment to Mrs. Grasso's statement.

Last year, the Federal Government provided only $630,000 toward research on Cooley's anemia. This year the Congress must do more. This year, the Congress must act to provide Federal financial assistance in order to initiate a long-term program of research and training.

H.R. 14016 will provide this assistance. H.R. 14016 will provide $7.1 million over 3 years for counseling, screening, and treatment programs for Cooley's anemia. H.R. 14016 will make available grants to public and nonprofit private organizations studying and researching Cooley's anemia. And H.R. 14016 will provide programs to inform and educate the public about the disease.

It is my hope that we in the House of Representatives will recognize our ability, and more importantly, our responsibility, to wage an effective attack on Cooley's anemia. The provisions authorized under H.R. 14016 will introduce a long overdue response to this critical health problem.

I urge the committee to support this legislation.

Mr. ROGERS. The Department of HEW will be represented in their testimony by the Honorable Richard L. Seggel, the Deputy Assistant Secretary for Health Policy Implementation, Office of the Assistant Secretary for Health and Scientific Affairs, accompanied by G. Donald Whedon, Director of the National Institute of Arthritis and Metabolic Diseases.

Mr. Sopper, we welcome you too.

STATEMENT OF RICHARD L. SEGGEL, DEPUTY ASSISTANT SECRETARY FOR HEALTH POLICY IMPLEMENTATION, OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY DR. G. DONALD WHEDON, DIRECTOR, NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, HEW; AND DALE SOPPER, HEALTH LEGISLATIVE ASSISTANT, OFFICE OF THE DEPUTY ASSISTANT SECRETARY FOR LEGISLATION, HEW

Mr. SEGGEL. Mr. Chairman and members of the subcommittee, I am pleased to appear before you today to discuss the problem of Cooley's anemia which is also known as Mediterranean anemia, and most specifically H.R. 14016 and several identical bills, the National Cooley's Anemia Control Act. I will use this occasion, also, to discuss the activities of the Department related to Cooley's anemia.

Before discussing the bill I would like to describe briefly the disease itself.

COOLEY'S ANEMIA

Cooley's anemia—Mediterranean anemia—is an inherited blood disorder which occurs primarily in persons of Mediterranean ancestry. In the United States most of the victims are of Italian descent or of Greek, Turkish, Southern French and North African origin. There are sporadic cases found in individuals of other origins, especially among the Chinese and Israelis.

As in many genetic diseases, those who inherit the gene from only one parent carry the trait but are usually free of symptoms, while

those who inherit the gene from both parents have overt clinical disease, that is, symptomatic Cooley's anemia.

Cooley's anemia is the most common of the thalassemias, a group of genetically determined blood disorders characterized by an inability to synthesize adequate amounts of hemoglobin, the substance in red blood cells which enables them to carry oxygen. Thus it differs from sickle-cell anemia, which is associated with the production of abnormal hemoglobin.

Cooley's anemia is characterized by the production of abnormally thin red blood cells, and by a profound anemia which appears soon after birth and becomes progressively more severe. The skin may appear jaundiced and the spleen and liver frequently become enlarged. In children a thickening of the bones at the base of the nose often occurs, producing a somewhat mongoloid facial appearance.

As a result of the chronic state of anemia, the children with this disease are greatly handicapped. They tend to be small for their age because bone growth is poor. The only effective treatment today is the proper administration of blood transfusions to alleviate the constantly recurring anemia. Some children require transfusions weekly; most need one or two a month. There is no known cure. The iron overload which results from the frequent transfusions is a very serious complication of the disease. There are agents that can remove this excess iron, but those now available are too toxic for widespread clinical use. Some children die within a few years, while others may live into their twenties.

The true incidence of Cooley's anemia is not known and obviously varies from area to area of the country depending upon the percent of population of Mediterranean origin. The best available estimates are that about 200,000 individuals in this country carry the gene. So far as clinical disease is concerned, there are 1,000 known cases in New York City. Other figures are not available.

The disease resembles sickle cell anemia in one important respect—individuals with merely the trait or minor form have a normal life span and enjoy normal health; however, those with the severe form of the disease, which occurs in about one-fourth of the children of parents who both are carriers of the trait, may succumb to the disease by the age of 20.

Diagnosis is simple in those who have inherited the gene from both parents. The marked anemia is obvious although certain laboratory tests are necessary to confirm the cause. On the other hand, diagnosis in those who inherited the gene from only one parent and therefore merely carry the trait is much more difficult and requires a number of hematologic tests including electrophoresis. There is no simple screening test for thalassemia, such as there is for sickle cell disease. The diagnostic problem is further complicated by the fact that more intermarriage with other populations has occurred among Americans of Mediterranean descent than among black Americans. Thus the incidence of Cooley's anemia, while properly a matter of concern, is likely to decrease.

OVERVIEW OF THE BILLS

Now I would like to turn to the bills before this subcommittee. H.R. 14016 and related bills would authorize programs for diagnosis, pre-

vention, and treatment of, and research in, Cooley's anemia. The bills authorize the Secretary of Health, Education, and Welfare to: make grants to establish screening, treatment, and counseling programs; make grants for research in the diagnosis, treatment, and prevention of Cooley's anemia; make grants for fellowships for training in diagnosis, treatment, and prevention; and carry out a program of information and education. A total of $2,375,000 would be authorized for fiscal year 1973 and the 2 succeeding fiscal years. Participation would be wholly voluntary and provision is made for confidentiality of information on those tested. The bill would also direct the Secretary to establish within the Public Health Service a program of screening, counseling, and treatment, using PHS facilities.

CURRENT RESEARCH EFFORTS

The NIH is presently funding 33 grants in Cooley's anemia, of which 13—totaling approximately $631,000—are directly related to the disease and 20—totaling approximately $669,000—are indirectly related. Taken together, these represent $1.3 million which bear directly or indirectly on the problem of Cooley's anemia. In addition, numerous other studies in hematology and genetics, while they may not deal directly with Cooley's anemia, are essential to provide a better insight into blood mechanisms or the genetic basis of inherited hematologic disorders such as Cooley's anemia. Several institutes are involved in the programs on Cooley's anemia and other forms of thalassemia.

Research at the NIH campus is shared between two institutes. The National Heart and Lung Institute intramural research program includes a clinical and laboratory study of the way blood cells are formed and maintained, and of the precise nature of dysfunction in thalassemia. Investigators of the Hematology Branch of the National Institute of Arthritis and Metabolic Diseases are also participating in this study.

DEPARTMENT POSITION

The administration is in agreement with the stated purposes of these bills to preserve and protect the health and welfare of all citizens. Adequate legislative authority, however, already exists for the execution of their various provisions. Thus the Health Services and Mental Health Administration presently has authority for the proposed service and education programs; the National Institutes has authority for research, research training, and education. We have opposed, and continue to oppose, proliferation of duplicative authorities and categorical programs. As you know, the President has recently proposed development of linkages among the profusion of health service programs sponsored by the Federal Government in the proposed Allied Services Act. While there is useful research being done on Cooley's anemia per se, it is expected that broadly based research in hematology, genetics, and inborn errors of metabolism will contribute to further understanding of the disease and development of methods of prevention, diagnosis, and treatment.

With respect to research proposed in the bills the NIH is, as I have indicated, supporting research on Cooley's anemia which is com-

parable to the levels proposed in the bills. I would underscore the fact that virtually all meritorious research proposals are currently being funded. We are encouraging interested researchers to apply for support. As I have pointed out, we can accomplish this without further legislation. A specific problem for us in this bill is the inclusion of time and dollar limits for Cooley's anemia research. The specified amounts tend to limit the flexibility desirable for exploiting new developments. The general practice of earmarking tends to discourage discontinuance of programs that have outlived their usefulness. We are reviewing our efforts in research training and education in order to determine whether or not additional emphasis is needed.

The question of service programs—screening, counseling, and treatment—is a more difficult problem. I think it is fair to say that the problem of Cooley's anemia does not parallel that of sickle cell disease in terms of the screening methods presently available, the research base needed for development of satisfactory treatment, and the identification of the population at risk. It is our belief that enactment of the screening, treatment, and counseling provisions of H.R. 14016 and the other bills before the committee would not, at this time, result in a significant decrease in the incidence of the disease, nor would it result in the alleviation of human suffering which is the goal of the bills' sponsors and which we share.

The provision in the bill that would require the Secretary to establish a program using the Public Health Service facilities for screening, counseling, and treatment for any person requesting these services is objectionable.

Such a provision would conflict with established policies for the use of Public Health Service facilities. Currently, the use of these facilities is limited to Federal beneficiaries such as Merchant Marine, the uniform services and their dependents. H.R. 14016 would make any person who requests these services a Federal beneficiary.

At this point, we feel strongly that further basic research should be carried out before the initiation of large-scale service programs, which, if undertaken now, would be based on much too limited knowledge and medical potential. We therefore recommend against enactment of H.R. 14016 and other identical bills.

Mr. Chairman, we shall be glad to answer any questions the committee may have.

Mr. ROGERS. Thank you very much.

Mr. Nelsen?

Mr. NELSEN. No questions. Thank you.

Mr. ROGERS. Mr. Kyros?

Mr. KYROS. Thank you, Mr. Chairman.

Mr. Secretary, did you take the same position on the sickle-cell anemia bill?

Mr. SEGGEL. We did.

Mr. KYROS. You feel then——

Mr. SEGGEL. May I say, sir, there are some differences in the two areas which we brought out in the statement. We did take the same basic position.

Mr. KYROS. Yes sir. I want to discuss those differences.

Your position is that as we are presently constituted within the National Institutes of Health we are doing sufficient research in hemoglobin and blood diseases to take care of Cooley's anemia?

Mr. SEGGEL. That is our position, sir.

Mr. KYROS. And you feel that this bill would merely cause another agency to be set up?

Mr. SEGGEL. Not an agency, sir. It is just that we dislike the idea of earmarking funds because if some breakthrough occurs we would want to go past earmarking in the bill.

On the other hand, if things don't work out it may not be indicated. We are arguing for administrative flexibility and the opportunity of scientists to make judgment when the opportunity is available to do some important research.

Mr. KYROS. Certainly, but we are also talking about, in the interest of public administration, how we get money out for programs. That is what we are also talking about this morning.

Mr. SEGGEL. Yes, sir.

Mr. KYROS. By earmarking something like sickle cell anemia for the first time, many Americans who had never heard of it before the last year or two realize that there is a problem here and we should be spending money in that area. Is that right?

Mr. SEGGEL. Yes, sir; but the administration did recommend an initiative in this area involving $10 million this year and $15 millon next year, under existing authority.

Mr. KYROS. Mr. Secretary, is there any question in your mind that it makes your job and my job easier and the chairman's job easier to get money for your health programs, when we specifically know what we are aiming for and when we can educate and alert the American citizens as to what is necessary? Isn't that right?

Mr. SEGGEL. That is a possible result depending on our total budget.

Mr. KYROS. Oh, no; there is no question about that. We put out nearly one and a half billion dollars for cancer this year. We would never have done that under any other circumstances except that the Congress and the executive and the public became alert to the problem. Isn't that a fact?

Mr. SEGGEL. Yes. I think the question here is what we could do with more money.

Mr. KYROS. Can you imagine how many people in the United States had heard of Cooley's anemia until just recently?

Mr. SEGGEL. Not many, I am sure.

Mr. KYROS. I know Mr. Ancher Nelsen has forebears from Israel and the Mediterranean but he never told me about Cooley's anemia before.

Mr. NELSEN. Denmark. The Queen is a Dane, so I am concerned.

Mr. KYROS. Seriously, you point out in your testimony that making tests to determine if someone has Cooley's anemia is difficult. It is difficult to screen people, especially when the trait has been passed on by one of the parents only.

Dr. WHEDON. If I might break in, Mr. Kyros, the recognition of the major form of the disease is relatively easy by physical examination. The degree of anemia is usually sufficiently severe that it is recognizable and the patient is brought to a physician for diagnosis.

The matter of screening involves the detection, primarily of the estimated 200,000 patients who carry the gene. These individuals do not have any clinical features more than perhaps the most minor and one is dependent on some laboratory tests, as was suggested, for example, for sickle cell anemia.

In sickle cell anemia the patients and the carriers bear a distinct abnormality in hemoglobin, hemoglobin "S." In this disease, Cooley's anemia, there has been hard work in trying to pick out distinct abnormalities in hemoglobin.

Some abnormalities have been found, but none that are characteristic or distinct. For example, some individuals have an increase in "F" hemoglobin which is fetal hemoglobin, a hangover from what is normal in early infancy.

Others have an increased amount of "A–2" hemoglobin, but none of these are specific. In other words, if you find an individual with increase in the "F" hemoglobin or increase in "A–2" hemoglobin, that does not mean that the patient has Cooley's anemia or the trait. That is why screening is difficult.

Mr. KYROS. In addition to screening of Cooley's anemia or Thalassemia being difficult, you have a situation where you said it affects a lot of people who lived or bordered the Mediterranean; is that right?

Mr. SEGGEL. Yes.

Mr. KYROS. Then you pointed out, on page 3 of your testimony, that these people are more apt to intermarry with other Americans than Americans of black descent. Isn't that right?

Mr. SEGGEL. That is right.

Mr. KYROS. So, this disease or its trait could be diffused even more largely among our population.

Dr. WHEDON. In the diffusion that would take place the likelihood would be that a person with a trait would marry someone who would not have the trait and therefore there would be the likelihood of some of the offspring bearing the trait but none of the children would have the disease so we look then from this estimation toward decreasing numbers of patients with the disease.

Mr. KYROS. You said "some of the offspring bearing the trait but none of the children." What does that mean?

Dr. WHEDON. I am sorry; I spoke too quickly. Some of the children might bear the trait but none of these children would carry the frank severe disease. In other words, the numbers of patients bearing the frank severe disease should gradually decrease just by the genetic aspects of the disorder and the gradual intermarriage.

Mr. KYROS. In any event, sir, we have not yet broken down all the causes and except for massive blood transfusions we have no cure for this disease. Is that right?

Mr. SEGGEL. That is right.

Mr. KYROS. We could use some research and some money to do that.

Mr. SEGGEL. Yes.

Dr. WHEDON. I would like to stress, if I may, that in my explanations I am not trying to diminish our feeling that greater effort should be made. We should not stop just because we have not as yet found a specific defect in the hemoglobin metabolism. I think through increased work we are going to find something specific.

We may come to a specific screening test that will be valuable. That is the purpose of a number of our grants.

Mr. KYROS. Thank you very much.

Mr. ROGERS. Dr. Carter?

Mr. CARTER. Thank you, Mr. Chairman.

Two hundred thousand people you estimate in this country carry the gene. Is that right?

Dr. WHEDON. That is the best figure that we have.

Mr. CARTER. 1,000 people in New York City have the disease, is that right?

Dr. WHEDON. That is what we understand.

Mr. CARTER. How many in the United States?

Dr. WHEDON. Dr. Carter, we don't have figures for that. We can only estimate that there are frankly on the order of perhaps 10,000 to 15,000 patients.

Mr. CARTER. 10,000 to 15,000 in the United States.

Dr. WHEDON. Admittedly that is not based on any careful epidemiologic survey.

Mr. CARTER. How many deaths do we have in a year from Cooley's anemia?

Dr. WHEDON. I don't have a clear figure for that at the present time.

Mr. CARTER. Do you have it for New York City?

Dr. WHEDON. No, sir; I think the fact is clear that these patients with the full disease are unlikely to live past the age of about 20. So that one could divide 1,000 by 20 and come up with a very approximate figure for the number of deaths per year. That would be 50 in New York City. That is a very rough calculation.

Mr. CARTER. The only treatment we have at the present time is to transfuse these people when they become anemic, is that correct?

Dr. WHEDON. That is correct.

Mr. CARTER. And the transfusions themselves present a problem, multiple transfusions?

Dr. WHEDON. They do because of the gradual storing up of excess iron.

Mr. CARTER. We have no safe way of getting the iron out of the body?

Dr. WHEDON. That would be one of the very useful things to be developed. I am sure that some of our investigators are looking for ways of doing that.

Mr. CARTER. Of course in screening, you do that by electrophoresis, is that correct?

Dr. WHEDON. Yes, sir.

Mr. CARTER. It is very difficult to find these people who bear the gene, is that correct?

Dr. WHEDON. That is correct as you will recall from the explanation I was giving Mr. Kyros.

Mr. CARTER. If you could do this, then they could be counseled and by marrying people who didn't have the gene the disease could be extinguished. Is that correct?

Dr. WHEDON. That is what we would predict, that the genes would be so gradually dispersed that the frank disease ought to disappear or very nearly so.

Mr. CARTER. That is all I have, Mr. Chairman.

Mr. ROGERS. Thank you.

How much intramural work and extramural work is done? I believe you have 33 grants.

Dr. WHEDON. Extramurally, Mr. Chairman, there are a total of 33 grants in NIH, 17 of which are in our Institute. The total funding in our Institute extramurally is about $600,000.

Mr. ROGERS. Extramurally?

Dr. WHEDON. Extramurally only.

Mr. ROGERS. What about intramural?

Dr. WHEDON. Intramurally the major effort is in the Heart and Lung Institute where Dr. French Anderson is conducting a study. He heads a group of hematologists. The total effort in that Institute is tallied at $125,000. Dr. Anderson has in association with him Dr. Shulman of our Institute, largely consultative in his efforts, and the effort that we provide from our Institute is about $33,000. So the total intramural NIH effort is about $160,000.

Mr. ROGERS. How many people are involved?

Dr. WHEDON. I would say altogether that there are three investigators, two of whom are senior full-time knowledgeable hematologists.

Mr. ROGERS. At the doctoral level?

Dr. WHEDON. Yes.

Mr. ROGERS. Two of them?

Dr. WHEDON. Three.

Mr. ROGERS. Three are at the doctoral level?

Dr. WHEDON. I would estimate that about six technicians are involved in this effort.

Mr. ROGERS. This specifically is on Cooley's anemia?

Dr. WHEDON. Specifically on Cooley's anemia. I must modify that to say, however, that the major efforts of Dr. Shulman, who is counted among those three professionals, are in other problems of hematology.

Mr. ROGERS. How much time does he devote to Cooley's anemia?

Dr. WHEDON. To Cooley's I would estimate approximately 10 percent of his time.

Mr. ROGERS. Do the other two investigators devote all of their time?

Dr. WHEDON. I am not absolutely certain of that but I know it is a very major part of their effort.

Mr. ROGERS. That is not a very major effort on the part of the Government, is it, to have three investigators of whom one spends 10 percent of his time?

Dr. WHEDON. I think, Mr. Chairman, it is a matter of balance of effort.

Mr. ROGERS. I understand that. I understand you have lots to do. I am just saying this is not a very significant program.

Dr. WHEDON. I would agree, it is not large.

Mr. ROGERS. Now, I think it would be well for the record to give us the specific figures for Cooley's anemia, the people working on it, the degrees, who are working with them, what are the specific projects they are working on, what progress they are having and how long it has been going and what are the prospects?

Dr. WHEDON. We will be delighted to do that.

(The following information was received for the record:)

GRANTS (BY INSTITUTE) GROUPED UNDER THE CATEGORIES OF PRIMARY AND SECONDARY EMPHASIS GRANTS

The NIH is presently funding 33 grants in thalassemia research. Twenty-six grants totalling an estimated $1,032,900 are considered to give primary emphasis to research on thalassemia. Seven individual grants and portions of two larger grants totalling an estiamted $1,117,256 are considered to give secondary emphasis to thalassemia research.

Several Institutes at the NIH are involved in programs on thalassemia. The following information represents a list of grants (by Institute) grouped under the categories of primary and secondary emphasis grants.

PRIMARY EMPHASIS

Intramural Research

Research conducted at the NIH is shared among three Institutes. The National Heart and Lung Institute's intramural research program includes a clinical and laboratory study of the way blood cells are formed and maintained. The laboratory is engaged in studies aimed at a basic understanding of how hemoglobin is synthesized, a topic of particular relevance to thalassemia. The investigators have succeeded in making hemoglobin in a system without living cells. They are seeking means of controlling the synthesis of hemoglobin in an effort to increase the amount of normal and fetal hemoglobin in thalassemic cells. The propects are that within the next few years, the work in this laboratory will progress to a point warranting clinical studies, with a corresponding expansion of the effort and increase in support. At the NHLI, French Anderson, M.D. and Arthur Neinhuis, M.D., aided by four technicians, conduct research on thalassemia. N. Raphael Shulman, M.D. of the NIAMDD collaborates part-time in their studies. The current funding level for this project is approximately $158,000 ($125,000 in NHLI and $33,000 in NIAMDD).

The National Institute of Child Health and Human Development's intramural project includes research which focuses on the molecular basis of certain inherited anemias such as thalassemia. Specifically, the investigators are using synthesized globin-specific DNA that has been tagged with radioactive tracers in the hope of determining how messages to produce globin are processed within the mammalian cell. Attempts are also being made to determine whether the defect in the thalassemic cell is caused by the synthesis of inadequate amounts of normal m-RNA or by the production of defective m-RNA for globin. To date, accomplishments include the use of a special enzyme, reverse transcriptase, to synthesize a major portion of the globin gene. This will ultimately increase the understanding of cellular control mechanisms in mammalian development.

Dr. P. Leder and four additional investigators are involved in this research. The current funding level is approximately $200,000.

Extramural Research

National Institute of Arthritis, Metabolism, and Digestive Diseases.—The NIAMDD is presently funding 19 grants in Cooley's anemia, of which 16 (totalling an estimated $548,829) are directly related to the disease and 3 (totalling an estimated $163,965) are indirectly related. Taken together these represent an estimated $712,794 which bear directly or indirectly on the problem of thalassemia.

Grant Number.—AM 745. *Principal Investigator.*—John Harris, Metropolitan General Hospital, Cleveland, Ohio. *Title.*—"Study of Erythrocyte Production and Destruction." *Funding.*—$39,842. *Duration.*—Now in 18th year of support—runs through 11/30/75.

Grant Number.—AM 15234. *Principal Investigator.*—Helen Ranney, E. J. Meyer Memorial Hospital, Buffalo, N.Y. *Title.*—"Studies of the Properties of Hemoglobin." *Funding.*—$67,655. *Duration.*—Now in 15th year—runs through 5/31/74.

Grant Number.—AM 8154. *Principal Investigator.*—John Bertles, St. Luke's Hosp. Center, New York, N.Y. *Title.*—"Genetic Control of Hemoglobin Synthesis." *Funding.*—$30,517. *Duration.*—In 8th year—runs through 8/31/73.

Grant Number.—AM 12467. *Principal Investigator.*—Herbert Schwartz, Stanford, California. *Title.*—"Formation of Hemoglobin and Other Hemo Proteins." *Funding.*—$33,321. *Duration.*—In 10th year—runs to 5/31/7.

Grant Number.—AM 9805. *Principal Investigator.*—Brawase Wasi, Siriraj Hospital, Bangkok, Thailand. *Title.*—"Thalassemia and hemoglobinopathies"—Only grant related to iron overload but no longer studying chelating agents. *Funding.*—$17,300. *Duration.*—In 6th year—runs through 8/31/72.

Grant Number.—AM 10485. *Principal Investigator.*—Robin H. Bannerman, State University of New York, Buffalo, New York. *Title.*—"Hemoglobin metabolism in thalassemia". *Funding.*—$46,465. *Duration.*—In 6th year—runs through 5/31/72.

Grant Number.—AM 15035. *Principal Investigator.*—Sherman M. Weissman, Yale University, New Haven, Connecticut. *Title.*—"Hemoglobin MREA in thalassemia". *Funding.*—$18,305. *Duration.*—In 2nd year—runs through 3/31/74.

Grant Number.—AM 15074. *Principal Investigator.*—J. David Haywood, University of Washington, Seattle, Washington. *Title.*—"Intermediate steps in hemoglobgin synthesis". *Funding.*—$25,053. *Duration.*—In 5th year—runs through 7/31/72.

79-753 O—72——5

Grant Number.—AM 15929. *Principal Investigator.*—David G. Nathan, Childrens Hospital Med. Ctr., Boston, Massachusetts. *Title.*—"Molecular Basis of Thalassemia". *Funding.*—$28,900. *Duration.*—In 1st year—runs to 5/31/77.

Grant Number.—AM 12401. *Principal Investigator.*—Ronald F. Rioder, Downstate Medical Ctr., Brooklyn, New York. *Title.*—"Protein synthesis in erythroid precursors". *Funding.*—$8,980. *Duration.*—In 6th year—runs to 3/31/76.

Grant Number.—AM 12895. *Principal Investigator.*—George R. Honig, University of Illinois, Chicago, Illinois. *Title.*—"Regulation of hemoglobin synthesis". *Funding.*—$27,985. *Duration.*—In 4th year—runs to 11/30/76.

Grant Number.—AM 12896. *Principal Investigator.*—Elias Schwartz, Thomas Jefferson University, Philadelphia, Pa. *Title.*—"Heme and globin synthesis in infants and children". *Funding.*—$35,803. *Duration.*—In 4th year—runs to 4/30/77.

Grant Number.—AM 13532. *Principal Investigator.*—Michael L. Freedman, NYC Medical Center, New York, N.Y. *Title.*—"Control of polyribosomes in human reticulocytes". *Funding.*—$19,700. *Duration.*—In 3rd year—runs through 10/31/74.

Grant Number.—AM 13983. *Principal Investigator.*—Haig H. Kazazian, Jr., Johns Hopkins Hospital, Baltimore, Maryland. *Title.*—"Genetic control of hemoglobin synthesis". *Funding.*—$39,855. *Duration.*—In 3rd year—runs through 10/31/74.

Grant Number.—AM 14324. *Principal Investigator.*—Lawrence S. Lessin, George Washington University, Washington, D.C. *Title.*—"Erythropoiesis—structural basis of hemolysis." *Funding.*—$52,680. *Duration.*—In 5th year—runs through 3/31/74.

Grant Number.—AM14923. *Principal Investigator.*—Michael D. Garrick, State University of New York, Buffalo, N.Y. *Title.*—"Molecular basis of differential gene expression." *Funding.*—$8,251. *Duration.*—In 5th year—runs through 7/31/72.

A breakthrough in the Cooley's anemia picture, which was then shrouded in darkness, came in 1963 when it was first demonstrated that the basic defect of the disease is impaired synthesis of the Beta polypeptide chains which are part of the hemoglobin molecule. Defective synthesis of these Beta chains impedes the production of sufficient new hemoglobin for the young red blood cells which are continually developing in the bone marrow to take the place of old red blood cells [which, on the average became senescent and drop out of the circulation after a life span of about 120 days].

Since then the respective rates of synthesis of Alpha and Beta chains have been worked out and the locus of their production within the cell has been ascertained.

Also, the precise intracellular mechanism is now understood. Genetic material from the nucleus of a developing blood cell sends a "messenger" chemical compound to specific areas (ribosomes) within the cytoplasm of the cell which act as production machinery for the Alpha and Beta protein-like chains. These chains, in turn, become part of hemoglobin—the red, oxygen-carrying material in red blood cells. In the past two years, further details of this production have been elucidated and factors have been singled out which, apparently, are responsible for the imperfect initiation and follow-through of Beta chain production in Cooley's anemia.

In addition, the transmission electron microscope has now permitted investigators to trace the formation of intracellular inclusions found in red blood cells in Cooley's anemia and other hemoglobinopathies and their migration to and fixation to the cell membrane. The regional membrane alterations, and the changes in osmotic and mechanical fragility that result from this, help explain the premature fragmentation and eventual sequestration of those imperfect cells by the spleen. Also, recently the scanning electron microscope has given research workers a 3-dimensional look at the pitting and fragmentation that takes place within these imperfect cells in Cooley's anemia and has helped explain their premature destruction which leads to the profound anemia which characterizes this disease.

National Institute of General Medical Sciences

Grant Number.—GM 17702-02. *Principal Investigator.*—Dr. Jarvis E. Seegmiller. *Title.*—"Program in Human Biomedical Genetics." *Sub-project Title.*—Genetic Regulation of Hemoglobin Structure and Synthesis. *Investigator Concerned with Thalassemia.*—Dr. Harvey A. Itano. *Funding* (sub-project alone).—

$93,247 (direct costs)—This is a program-project. Only one of several projects is concerned with hemoglobinopathies. *Duration.*—6/1/71 to 5/31/75.

The objectives of this research are to understand the mechanisms regulating the rate of synthesis of the various polypeptide chains of hemoglobin, a problem directly related to thalassemia. Currently, a family with two genetic abnormalities in hemoglobin synthesis (hereditary persistence of fetal hemoglobin, and B–thalassemia) is being studied. In addition, Dr. Itano is exploring the use of animal models, such as genetic variants of rabbits, for their relevance to the study of the control of the synthesis of the subunits of hemoglobin.

Grant Number.—GM 15419–05. *Principal Investigator.*—Dr. James V. Neel (after 10/1/72. Dr. Myron Levine). *Title.*—"Program Project in Cellular and Biochemical Genetics." *Sub-project Title.*—Biochemical Genetics of Abnormal Human Hemoglobin and Albumins. *Investigator Concerned with Thalassemia.*—Dr. Donald Rucknagel. *Funding.*—$97,883 (direct costs)—This is a part of a larger program-project (total direct costs—10/1/71–9/30/72) $631,690. NIGMS Program Administrator. Dr. George Woolley. *Duration.*—The project has been funded since 10/1/67. NIGMS expects to fund this project for at least an additional five years, beginning 10/1/72.

The thalassemias are a collection of inherited diseases of regulation of hemoglobin synthesis. Our understanding of these complex and still poorly understood entities is in part due to studies dealing with the interaction of thalassemias with various mutant forms of hemoglobin. Dr. Rucknagel has taken a lead in studies of this type. For example, in current studies, isotopically tagged amino acids are incorporated into the hemoglobin of a patient with both sickle cell trait and α-thalassemia. The intent is to determine the mechanism whereby the α-thalassemia gene decreases the proportion of sickle cell hemoglobin below that found in simple sickle cell trait. Dr. Rucknagel is also analyzing the distribution of α-thalassemia in Thailand (where the disease is common), and correlating it with other red-blood cell markers.

Primary Emphasis (Thalassemia)

Grant Number.—GM 14552–06. *Principal Investigator.*—Paul A. Marks, Columbia University, New York, N.Y. *Title.*—Normal/Abnormal Cell Growth Multidisciplinary Study. *Investigators Concerned with Thalassemia.*—Drs. Arthur Bank, Luis Dow and Richard Rifkind. *Funding.*—$98,946 (direct costs). All of the research concerns normal and abnormal erythroid cells. *Roughly half (ca $50,000) is concerned* directly with the regulation of hemoglobin synthesis, the structure of thalassemia cells, etc., and thus is *primarily thalassemia research.* The residue of the research can be considered of secondary relevance, and contributory. *NIGMS Program Administrator.*—Dr. Paul Bowman, RGB, NIGMS. *Duration.*—The current project period is 9/1/–8/31/73. A competing continuation application has been reviewed, and there is a high probability that the project will be funded for an additional five years, beginning 9/1/73.

This group in collaboration with two other groups (Spiegelman at Columbia, Leder at NIH) has recently demonstrated that purified reverse transcriptase can transcribe messenger RNA from globin to make a synthetic DNA specifying the information for hemoglobin synthesis. Preliminary information suggests that this synthetic DNA can be used as a sensitive probe for detecting and quantitating human globin on RNA. Thus, one may be able to decide in the β thalassemia syndromes whether there is a deficiency of the mRNA for β chains, or whether defective RNA messengers are produced.

This research program is considered to be in the vanguard of very good research on the formation of red blood cells and hemoglobin. Through the combined use of morphology (light and electron microscopy) and molecular biology, additional insights into Cooley's anemia can be expected. In this highly sophisticated and active field, the group may well make its more significant contributions in the medical application of laboratory findings.

Division of Research Resources

Grant Number.—RR–72, Thomas Jefferson University. *Investigator's Name.*—Elias Schwartz, M.D. *Title.*—"Iron Absorption in Cooley's Anemia." *Period of Actions.*—Fiscal year 1970. *Patient Days.*—0. *Cost.*—0.

Although this protocol has been approved, there have been no patients actively studied to date.

Grant Number.—RR–73, University of Texas Medical Branch. *Investigator's Name.*—William C. Levin, M.D. *Title.*—"Erythrocyte metabolism in thalassemia

and hemoglobinopathies." *Period of Action.*—Fiscal year 1970. *Patient Days.*—44. *Cost.*—$4,969.80.

This protocol is investigating the composition and function of certain enzymes and lipids within red blood cells in patients with thalassemia and other anemias. Accomplishments have not been identified to date in the Annual Report.

Grant Number.—RR–86, Children's Hospital of Los Angeles. *Investigator's Name.*—Carol Hyman, M.D. *Title.*—"Preventing intertransfusion anemia in patients with thalassemia major." *Period of Action.*—Fiscal year 1970. *Patient Days.*—214. *Cost.*—$54,993.72.

The prognosis for growth, development, and eventual maturation and survival into adulthood of children with Thalassemia Major is very poor. Because there is extensive destruction of their abnormal red cells, these patients have a tendency to develop hemosiderosis, a disease characterized by accumulation of iron pigment in vital organs. The development of this complication is further enhanced because these patients are treated with multiple blood transfusions. To postpone the development of transfusion hemosiderosis in these patients, it has been a practice to give the least number of transfusions necessary to maintain cardiovascular function. Unfortunately, failure to maintain normal blood hemoglobin levels severely interferes with normal growth and development. Investigators at this institution are attempting to determine whether use of more frequent transfusions can afford normal growth and cardiovascular function without entailing the devastating complications of hemosiderosis. Thus far, all patients have shown marked improvement in general well being and activity since their intertransfusion anemia has been prevented. Thus far, there has been no acceleration of the extensive organ damage normally associated with hemosiderosis.

In addition to the above studies, extensive investigation is under way concerning the genetics of the molecular structure of fetal hemoglobin in thalassemia. These studies suggest there is a genetic basis for some observed variations in the molecular structure in fetal hemoglobin and patients with thalassemia. Furthermore, microscopic studies have suggested the possibility of vitamin E deficiency. The relationship of vitamin E deficiency to the pathophysiology of thalassemia will also be studied in depth.

Grant Number.—RR–128. *Investigator's Name.*—David G. Nathan, M.D. *Title.*—"Thalassemia and sickle-cell anemia." *Period of Action.*—Fiscal year 1970. *Patient Days.*—65. *Cost.*—$18,183.75.

Investigators at this institution have extensively studied several important features of thalassemia and the hemoglobinopathies. First, they have been able to confirm that the inclusions found in the red cells of patients with thalassemia damage the red cell membrane, resulting in removal and destruction of these cells. Secondly, they have been able to measure the rates of production of alpha and beta chains, the components of normal hemoglobin, with such precision that the diagnosis of the various forms of alpha and beta thalassemia, together with interacting thalassemias, can be made with ease. Finally, they have initiated important studies of the role of B-chain messenger RNA (a nucleic acid that regulates B-chain synthesis) in the pathogenesis of thalassemia. They have demonstrated that there is decreased beta messenger RNA available for beta chain production. They have also shown that its primary structure is entirely normal Thus, they have concluded that beta thalassemia is due to a quantitative decrease in messenger RNA, rather than structural abnormality. These studies will hopefully provide the basis for future therapeutic intervention and genetic reconstitution in individuals affected with these disorders.

Grant Number.—RR–645, Columbia University. *Investigator's Name.*—Arthur Bank, M.D. *Title.*—"Studies of thalassemias, hemoglobinopathies, and aplastic anemias." *Period of Action.*—Proposed fiscal year 1971. *Patient Days.*—0. *Cost.*—0.

Experiments have shown that β chain production in β thalassemia appears to decrease with erythroid cell maturation, and several mechanisms have been postulated which could account for these findings. It has also been demonstrated that α-chains synthesized in excess of β chains in patients with β thalassemia are destroyed intracellularly, most likely by the action of proteolytic enzymes. Current studies in thalessemia are investigating the role of initiation in normal and abnormal erythroid cells; in addition, experiments are in progress to quantitate and characterize the messenger RNAs in these cells. These studies should further clarify the nature of the genetic defect in thalassemia, and may have great significance in our understanding of other genetically controlled defects

in protein synthesis in man as well. The rates of globin chain synthesis in patients with abnormal hemoglobins is being investigated as well. These subjects are ideal for studying the mechanisms responsible for the differing rate of synthesis of normal proteins as compared to that of closely related mutant proteins.

SECONDARY EMPHASIS (ALL EXTRAMURAL)

The following are grants awarded by the NIH for research in basic hematology and genetics. While not dealing directily with thalassemia (Cooley's anemia), the studies are essential to provide a better insight into blood mechanisms or the genetic basis of inherited hematologic disorders such as Cooley's anemia.

National Institute of Arthritis, Metabolism, and Digestive Diseases

Grant Number.—AM 13431. *Principal Investigator.*—Edward Burka, Thomas Jefferson Univ., Philadelphia, Pa. *Title.*—Biochemical Determinants of Red Blood Cell Differentiation." *Funding.*—$34,903. *Duration.*—in 16th year—runs to December 31, 1973.

Grant Number.—AM 13431. *Principal Investigator.*—Irving London, M.I.T., Cambridge, Mass. *Title.*—"Metabolism of Erythrocytes." *Funding.*—$122,000. *Duration.*—In 16th year—runs to December 31, 1973.

Grant Number.—AM 780. *Principal Investigator.*—Rose Schneider, Univ. of Texas, Galveston, Texas. *Title.*—"Hemo-variants in Relation to Disease." *Funding.*—$40,738. *Duration.*—In 21st year—runs to August 31, 1972.

(See previous NIAMDD statement for discussion of accomplishments and prospects.)

National Institute of General Medical Sciences

Grant Number.—GM 15253–05. *Principal Investigator.*—Arno G. Motulsky. *Title.*—"Genetics in Medicine: Gene Action in Man." *Sub-titles Relevant to Thalassemia (and relevant Investigators).*—Hemoglobin Chain Initiation: Yoshida; Structural and Functional Studies on Hemoglobin Variants: Stammatoyannopoulos. Nute; Population Studies, Red Blood Cells: Fraser, Stammatoyannopoulos, Nute; Comparative Sequence Analysis of Hemoglobin (Nute).

Funding.—Total current funding (direct costs) is $397,486. This is a large program-project; emphasis on hemoglobin and red blood cell research can be expected to be about ⅓ of the total activity; *hence, about $150,000.*

The project will be funded for an additional five years, effective 6/1/72. Funding level will be approximately $900,000 per year (direct costs), of which hemoglobin and red blood cell research can be expected to be about 25–35% of the total activity.

NIGMS Program Administrator.—Dr. George Woolley.

This is a broad program on genetic disease, with much of the emphasis on diseases of red blood cells. Among the current activities are:

1. The identification of different types of thalassemia by means of qualitative analysis of hemoglobins, family and clinical studies, and red cell staining for HbF.
2. The exploraton of the possibility that a structural mutation accounts for some cases of beta thalassemia. This has not yet been ruled out.
3. Population studies in Greece and Cyprus, including an evaluation of the impact of genetic counseling practices (these are places with high incidence of alpha and beta thalassemia).

The prospects for continued excellent work in this area, and at this institution are excellent.

National Institute of Child Health and Human Development

Grant Number.—HD–0254. *Principal Investigator.*—Bernstein, Seldon E., Jackson Laboratory, Bar Harbor, Maine. *Title.*—"Studies of Neonatal Blood Disorders." *Funding.*—$33,947. *Duration.*—In 1st year—runs through November 30, 1975.

Grant Number.—HD–4130. *Principal Investigator.*—Basch, Ross S., N.Y.U. Med. Ctr., New York. *Title.*—"Pathophysiology of Fetal Hemoglobin Synthesis." *Funding.*—$32,394. *Duration.*—In 1st year—runs through December 31, 1972.

Grant Number.—HD–6533. *Principal Investigator.*—Gabuzda, Thomas G., Lankenau Hospital, Philadelphia, Pa. *Title.*—"The Synthesis of Fetal and Adult Hemoglobins." *Funding.*—$49,507. *Duration.*—In 1st year—runs through August 31, 1972.

The extramural projects are concerned with the genetic, morphologic, and biochemical regulatory mechanisms that control erythropoiesis, and with the abnormalities of hemoglobin synthesis in mammals. Several approaches to this problem are being used and include analysis of the action of mutant genes that alters normal growth and development of blood-forming tissue; the study of the role of cyclic-nucleotide dependent protein kinase and erythroid cell differentiation; and the use of short term cell cultures of human fetal hematopoietic tissue and cell free systems for the synthesis of human fetal hemoglobin.

National Cancer Institute

Grant Number.—CA 01074–22. *Principal Investigator.*—Elizabeth S. Russell, Jackson Laboratory, Bar Harbor, Maine. *Title.*—"Physiological Genetics of the Mouse." *Funding.*—$110,049. *Duration.*—September 1, 1971–August 31, 1972.

Highly congenic mice with and without mutant genes with clear cut effects will be used to analyze gene action leading to at least six different hereditary anemias. Such studies will add to the knowledge of gene-action pathways. Certain of the mouse anemias show great similarity to human hematological disorders such as erythrogenesis imperfecta or thalassemia.

Grant Number.—CA 06551–09. *Principal Investigator.*—Timothy R. Talbot, Jr., The Institute for Cancer Research, Philadelphia, Pa. *Title.*—Program I—Studies of Susceptibility to Cancer in Man Specific Project #3—Relation of Inherited Antigens and of Antibody Formation, to Cancer Susceptibility in Man. *Funding.*—$581,111. *Duration.*—September 1, 1971–August 31, 1972.

The objective of this program is to test the hypothesis that susceptibility to persistence of Australia antigen is under genetic control and is associated with susceptibility to leukemia and Hodgkin's disease. Aspects of this hypothesis will be tested in patients who receive many transfusions (hemophilia and thalassemia) and therefore have a high risk of exposure to Australia antigen.

Grant Number.—CA 12394–02. *Principal Investigator.*— Nicholas L. Petrakis, University of California School of Medicine. *Title.*—"Genetical Epidemiology of Cancer." *Funding.*—$112,031. *Duration.*—May 1, 1972–April 30, 1973.

This research project deals with the genetical epidemiology of cancer and seeks to define the variation in susceptibility to cancer in terms of multiple polymorphic genetic markers. Populations to be studied include various racial and ethnic groups (White, Negro, Oriental, Indian and Latin-American) who exhibit differing rates of cancer, as well as individual patients with specific type of cancer. It is hoped that significant associations will be found between genetic markers and cancer types will help to define high-risk individuals as well as provide clues to etiology and prevention.

National Heart and Lung Institute

The NHLI supports several studies related to the structure and function of the hemoglobin molecule and the manner and circumstances of its synthesis. The investigators approach this problem from different angles. Many involved in the project listed collaborate rather closely, particularly through the exchange of materials. All of the studies contribute the type of fundamental understanding essential to any rational approach to therapy.

Grant Number.—HL 2558. *Principal Investigator.*—Walter A. Schroeder, California Institute of Technology, Pasadena, California. *Title.*—"Structure-function relationships in the hemeproteins." *Funding.*—$65,837. *Duration.*—In its 16th year.

These fundamental studies of hemoglobin structure have been supported by NHLI for 16 years. One of the current interests is the structure of fetal hemoglobin from patients with thalassemia.

Grant Number.—HL 5168. *Principal Investigator.*—Titus H. J. Huisman, Medical College of Georgia, Augusta, Ga. *Title.*—"Inhomogeneity of Hemoglobin and Myoglobin Types." *Funding.*—$71,598. *Duration.*—In its 13th year.

This is another study of the structure and function of hemoglobin molecules, including hemoglobins derived from patients with thalassemia. This program has been supported for 13 years.

Grant Number.—HL 6374. *Principal Investigator.*—Allan J. Erslev, Jefferson Medical College, Philadelphia, Pa. *Title.*—"Expansion of research in a hematologic center." *Subtitle.*—Abnormal Hemoglobins. *Funding.*—$78,232. *Duration.*—In its 12th year.

This program project grant supports core laboratories used by a number of investigators, some of whom are interested in problems directly related to Cooley's

anemia. Such ongoing studies include work on erythropoietin, the substance that simulates red blood cell production; work on the types of protein that make up the hemoglobin molecule in patients with thalassemia; and studies on the synthesis of hemoglobin.

Grant Number.—HL 14131. *Principal Investigator.*—Paul R. McGurdy, D.C. General Hospital, Washington, D.C. *Title.*—"Abnormal hemoglobin syndromes." *Funding.*—$22,557. *Duration.*—In its 13th year.

This grant, now in its 13th year, supports studies on bone marrow in thalassemic patients, as well as work on the structure of the hemoglobin molecule. These studies may lead to a better understanding of why some individuals may have a relatively mild form of Cooley's anemia.

Grant Number.—HL 14492. *Principal Investigator.*—James W. Bacus, Rush-Presbyterian-St. Luke's Med. Ctr., Chicago, Ill. *Title.*—"Pattern recognition of peripheral blood cells." *Funding.*—$23,950. *Duration.*—In its 1st year.

This project is an attempt to develop automated computer recognition of blood cells, both normal and abnormal. Cells from patients with Cooley's anemia are included.

Mr. ROGERS. Also, are you doing anything for any screening? Do you have any specific grants or programs to determine how to screen?

Dr. WIEDON. A number of the projects are involved in the study of abnormal hemoglobins.

Mr. ROGERS. I understand, but are you geared to that purpose specifically?

Dr. WIEDON. I am sure that is in the minds of those working on it because if they could detect other subgroups of hemoglobin they might come up with a specific screening test.

Mr. ROGERS. I think it would be well to set that out for us in the record if you could.

(The following information was received for the record:)

DEVELOPMENT OF SCREENING METHODS IN COOLEY'S ANEMIA AND RELATED THALASSEMIAS

The following workers are known to be searching for screening methods which do not involve expensive and complicated laboratory procedures like electrophoresis, or which do not give false positive or negative results: Dr. Elias Schwartz (NIAMDD grantee) who is now planning a screening program in Philadelphia; Dr. Conconi in Ferrara, Italy (who will be funded by NIAMDD); and Dr. Wasi in Thailand (NIAMDD grantee). Dr. Howard Pearson of Yale (not an NIH grantee), who is now developing a new method and has started a pilot screening study, has not yet reported to the scientific community on his new method and findings. Publication of his method and its reliability or presentation thereof to a scientific meeting is eagerly awaited by fellow scientists; his method can then be subjected to critical evaluation by other physicians, and, if found reliable, would be adopted.

Mr. ROGERS. Also, I notice you don't think anybody ought to get any screening by the Public Health Service.

Mr. SEGGEL. Yes, sir.

Mr. ROGERS. You don't think if we have the technique they should use it.

Mr. SEGGEL. We don't have the technique right now. We feel that the Public Health Service hospitals should be restricted to Federal beneficiaries.

Mr. ROGERS. Even though they might be able to do this?

Mr. SEGGEL. If it becomes a community responsibility and it is part of an ongoing community system——

Mr. ROGERS. This is a national responsibility we are talking about, your responsibility.

Dr. WHEDON. I think there is much greater capability among the grantees of our institute in the medical centers around the country. The Public Health Service hospital system is now very small. If there should be a capability of doing a good screening technique and system, the manpower, the capability is in the medical centers scattered throughout the many States, not just in a few Government hospitals.

Mr. ROGERS. You could use techniques for the screening process.

Dr. WHEDON. If the screening tests were available.

Mr. ROGERS. You would not have to have a doctor to do that?

Dr. WHEDON. That is right.

Mr. ROGERS. You would not have to go to a medical center to do that, I would hope.

Dr. WHEDON. The patients are spread throughout the country although they seem to be localized in the East. The Public Health Service system is simply not large enough to cover the patients.

Mr. ROGERS. In its present being I would agree because we only have 30 clinics and eight hospitals. I am very much aware of the Public Health hospital system and how it has been degraded. I understand that. I believe the Department is not aware however, from your testimony, where you say that the limited facilities are limited to Federal beneficiaries such as Merchant Uniform Service and their dependents.

That is not a proper statement since the Emergency Health Act has passed. I presume the leadership in the Department knows that. You are aware of that, aren't you?

Mr. SEGGEL. Yes.

Mr. CARTER. Mr. Chairman, on that very thing, the employees of the Public Health Service are in the areas of need but how does it affect the Public Health Service hospitals?

Mr. ROGERS. They are authorized to be used in that program. I am sure the Department is aware of that.

Mr. SEGGEL. Of course the thrust of the effort is to get the doctors, and other health personnel as you well know, out in the underserved areas.

Mr. ROGERS. Like in Baltimore with the Baltimore hospital, like in San Francisco where the hospital is there and the city tried to get you to do that. I won't pursue that. I would hope that you would correct your statement in your prepared testimony.

(The following statement was subsequently received for the record:)

Mr. Seggel's statement referred to current policies for using the PHS hospitals. It is, of course, true that the Department is authorized to use these hospitals for the Emergency Health Personnel Act, but it does not, as a matter of policy, use them for this purpose.

Mr. ROGERS. Are there any other questions? If not, thank you very much for being here. We appreciate your testimony.

Mr. SEGGEL. Thank you very much.

Mr. ROGERS. The next witness is Dr. Howard Pearson, Chief of Pediatric Hematology, Yale-New Haven Hospital.

The committee welcomes you and we will be pleased to receive your statement.

If you like your statement will be made a part of the record without objection. If you highlight it for us it will be helpful.

STATEMENT OF DR. HOWARD A. PEARSON, PROFESSOR OF PEDIATRICS, HEAD, PEDIATRIC HEMATOLOGY DIVISION, YALE-NEW HAVEN MEDICAL CENTER

Dr. PEARSON. Chairman Rogers and members of the subcommittee, my name is Howard A. Pearson, professor of pediatrics and head of the Pediatric Hematology Division, Yale-New Haven Medical Center.

It is a pleasure to be here to discuss thalassemia, especially before the subcommittee which is responsible for the important legislation intended to attack the multiple problems of sickle-cell anemia. Thalassemia is a term which describes a group of inherited diseases whose common characteristic is a diminished production of hemaglobin, the protein which contain iron and which is responsible for the very basic life process of transporting oxygen from our lungs to all other body tissues.

As has been said in thalassemia there is no chemical or structural abnormality in the hemoglobin molecule but rather a quantitative deficiency. The consequence of this inadequate production of hemoglobin is anemia. There are two forms of this anemia. One of these is Cooley's anemia which is of such a profound degree that without treatment it is incompatible with life although many patients live to young adulthood. The other form, thalassemia minor, is a mild anemia that causes few, if any symptoms, to most carriers and which is usually only detectable by special blood tests.

The major form of thalassemia was first recognized in 1925 by a Detroit pediatrician, Dr. Thomas B. Cooley, in a small group of small Italian children. These children—like others with the major form of the disease—had severe anemia, massive enlargement of their spleens, and deformities of their bony structure, including striking changes in the skull producing a distinctively abnormal facial appearance.

It may seem unusual for a disease that was doubtless very common in Italy and Greece for thousands of years should be described first in Detroit in 1925. The best explanation for this delay in recognition appears to be that in the old world, anemia, enlarged spleens and early death of infants were attributed to such common diseases as tuberculosis and malaria. Ironically, there are some who now postulate that the genetic deficiency leading to Cooley's anemia—like that leading to sickle-cell anemia—may, in the minor form conferred some adaptive advantage in ages past for our ancestors to withstand malaria. Only when transplanted to the American scene and in an age of scientific medicine, however, did the true and unique nature of Cooley's anemia become apparent.

In the American melting pot many different ethnic groups have been found to have the genetic trait for thalassemia. As people have emigrated from the lands in this thalassemia belt—which includes Italy, Greece, the several Mediterranean islands, the Middle East, parts of India, China, Thailand and the Philippines—they have brought this now useless and potentially destructive gene with them. It can be found in descendants of Scandinavian immigrants, in the Irish, Jewish, black American and other populations of this country, but tends to reach its highest frequency in the United States in those areas where there are

significant concentrations of Italian and Greek Americans. Therefore this tends to be an urban disease, with many cases in the cities of Northern and Eastern America.

The kind of research that could be done to attack the problem of thalassemia may be described in three categories. First, fundamental research into the biochemistry and biochemical genetics of thalassemia is needed. The precise nature of the genetic abnormality in thalassemia has not been identified or characterized; such definition, of course, would enhance the possibility of correcting the disease at a very basic level. Furthermore, understanding of the genetic nature of thalassemia would have important implications in understanding other human genetic defects, such as hemophilia and other inborn errors of metabolism.

Second, research needs to be done into the clinical management and therapy for patients with thalassemia major, to find the best way to help the victims of that disease. Most of these patients have symptoms before the age of 2 years, and require regular blood transfusions thereafter to correct their anemia and sustain their life processes until they die, as much as 20 or 25 years later. This lifetime prospect is, as I am sure this subcommittee can understand, a staggering one for the families involved, and poses unique problems for the institutions that care for children with thalassemia major. By the time these children reach their late teen years they have—if still alive—received many hundreds of pints of blood, have usually required surgical removal of their spleens, and have been hospitalized on many occasions for the numerous and often unpredictable complications of the basic disease.

A consequence of the many pints of blood with which these patients must be transfused is the buildup of an enormous amount of the iron inevitably contained in the blood which becomes deposited in the patient's body and vital organs, including the heart. Once iron has been deposited in these tissues it cannot be removed by any normal process of the body. This accumulation of iron ultimately causes liver failure, failure of the pancreas and endocrine organs and failure of the heart and finally death.

Research should be directed, therefore, into the development of chemical agents that would enhance removal of iron from the tissues, and excretion of that iron from the body. Despite the obvious need for this type of drug which would avoid the fatal side effects of the prolonged blood transfusions, there is, to my knowledge, no concerted program for development, or research into the pharmacology or biochemistry of agents which would remove this deposited iron.

Finally, research is needed into methods of detection of the carriers of the genetic trait for thalassemia, in order that individuals whose children would be at risk of inheriting this disease can be identified and appraised of that risk.

At the present time there are really no accurate statistics concerning the number of people with thalassemia major or minor in the United States. By extrapolation of data from Italy and Greece, it could reasonably be anticipated that between 5 and 10 percent of the perhaps 15–20 million Italian and Greek Americans would be affected. The only survey that has been done on a wide scale in the United States was performed in Rochester, N.Y., in 1945, before the advent of mod-

ern diagnostic tests. This showed that one in 20 Italian Americans was affected. The data are very poor, however, and it is anybody's guess just how many people have or could have this condition in America.

One reason for this dearth of information is that in the past the definitive test for thalassemia was expensive and not suited for screening programs. At Yale-New Haven Hospital, in cooperative work with the Connecticut chapter of the Cooley's Anemia Blood and Research Foundation for Children, we have recently completed a pilot screening program for thalassemia in several urban Greek American communities. Aside from the data—which showed a 7 percent prevalence of the thalassemia trait, or minor form of the disease—this work demonstrated that simple and inexpensive but reliable screening tests are available, and that programs can be established that include education, screening, and genetic counseling.

Whatever the actual numbers of people with this disease, however, we now have the scientific methodology and genetic information to prevent new cases of thalassemia major in the next generation in this country. Federal support for research, screening, and related as proposed in this act are surely justified in order to prevent the massive burden this disease brings to its victims and their families.

Thank you again for this opportunity to testify; I would be glad to answer any questions members of the subcommittee might have.

Mr. ROGERS. Thank you very much, Dr. Pearson.

Mr. Kyros?

Mr. KYROS. Thank you, Mr. Chairman.

Dr. Pearson, I think your testimony is very clear, and I understand that you fully support the bill H.R. 14016.

Dr. PEARSON. Yes, sir.

Mr. KYROS. I am glad to see my colleagues, Congressman Giaimo and Congresswoman Grasso here.

One thing you point out sharply is that at the present time there is no established center for doing this screening and performing these tests.

Dr. PEARSON. These are being done on a purely research and pilot basis at the present time.

Mr. KYROS. You said you are doing it with Cooley's anemia at the Research Foundation for Children in New Haven?

Dr. PEARSON. I am doing it at my hospital in cooperation with Cooley's Anemia Blood and Research Foundation for Children.

Mr. KYROS. Each of these blood tests requires electrophoresis?

Dr. PEARSON. There are simpler ways. If one is to have a screening test, electrophoresis, at least for a quantative measurement, is no really applicable. One has to find a simpler test than this and we think this is available.

Mr. KYROS. What I didn't quite understand from the prior testimony by the Deputy Assistant Secretary of Health Policy is that there seemed to be no sense of urgency, in that we should not permit any of these traits to be transmitted by intermarriage to people in the United States.

I don't see any sense of urgency in his testimony. It seems to me there should be, should there not?

Dr. PEARSON. I think we have today the identification of those Americans which are of greatest risk for carrying thalassemia. Two or

three, four or five generations from now that identification will no longer be possible.

I think many of us don't know the nationalities of even our grandmothers. A generation from now that opportunity may be lost. I think there is urgency about it today.

Mr. KYROS. So we should screen them, identify them, diagnose them, and at the same time do the research which will give us some kind of cure.

Dr. PEARSON. Particularly ancillary research for which is developing and testing iron removing agents which is a compelling need today.

Mr. KYROS. Tell us about the horrible process of continuing transfusions for somebody who gets Cooley's anemia, the present method of treating them.

Dr. PEARSON. At present our children come into the hospital once a month for transfusions of blood.

Mr. KYROS. Can you look forward as a scientist and say with research, even as we say with regard to cancer, that there are answers ahead that we don't know anything about yet?

Dr. PEARSON. I certainly hope so. I can't see today where the breakthrough will be. I would hope that this would be true.

Mr. KYROS. Is it not so that the only way to get public support for this kind of program so that we can spend money, is to let the public know that these kinds of things exist.

Dr. PEARSON. We are surprised how few people living within the Italian and Greek community have heard of thalassemia.

Mr. KYROS. I never heard of thalassemia until sickle-cell anemia came up. Then I had not heard of sickle-cell anemia and I have been sitting here with Chairman Rogers the last 6 years. I thought I knew a little bit about health.

If Americans know about these diseases don't you think they would be more willing to spend a few million dollars to do the research, diagnosis, and treatment for them?

Dr. PEARSON. Yes, sir.

Mr. KYROS. Thank you very much.

Mr. ROGERS. Thank you.

Dr. Carter?

Mr. CARTER. Thank you, Mr. Chairman.

What should we do to eradicate this disease?

Dr. PEARSON. I would make an informational program that would reach those groups of Americans who are greatest risk today, this would be the Italian-Greek communities, making them aware of thalassemia, the availability of tests and the genetic implication of those people identified as having it.

I would not tell anyone whom to marry or whether to marry. As I talk to parents of my patients who have one of these children about the enormous implications this means for their next 20 or 30 years, they say they wished they had known. They would perhaps have done the same thing but at least they would not have gone with their eyes closed. It is a hard question to answer.

Mr. CARTER. Of course that question is up to them. If they make the proper decision there is no question but what the disease would be

eliminated; is that right?

Dr. PEARSON. Yes, sir.

Mr. ROGERS. Thank you very much.

As I understand it you feel that there is an adequate and quick screening process.

Dr. PEARSON. This is what our pilot study would indicate. We hope to expand this on a larger scale. We have in series now about 350 people and have encountered no false negative test results and have few false positives.

Mr. ROGERS. Is it difficult?

Dr. PEARSON. No, sir.

Mr. ROGERS. How much does it cost?

Dr. PEARSON. One needs a machine which most of our community hospitals do have. This is an electronic cell counter which automatically measures the volume of the red cell or MCV.

In the thalassemia trait red cell is uniformly reduced in size. This can be measured electronically. There is a strong correlation between small red cell size and thalassemia that——

Mr. ROGERS. I understood from the HEW testimony they didn't know that we had any quick and easy test. I wish you would let them know.

Dr. PEARSON. We have not published our work yet.

Mr. ROGERS. I wish you would let them know. I think it is very important. We will ask them to look over this transcript. I would think if they have a man there on top of this he ought to be aware of this. I am surprised that they are not knowledgeable.

Let me ask you this. Have you submitted a request for a grant to do research in this pharmacology of the biochemistry of agents that could remove the deposited iron?

Dr. PEARSON. No, sir.

Mr. ROGERS. Do you know anyone who has?

Dr. PEARSON. No, sir.

Mr. ROGERS. Can you encourage anyone to do it?

Dr. PEARSON. I would wonder whether on the shelves of our biochemical and chemical firms there might be agents that today have the ability to do this. The current agents we have don't remove sufficient iron to really make their regular use worthwhile but conceivably there might be other agents extant and particularly ones that could be given orally.

Mr. ROGERS. Has anyone contacted the pharmaceutical companies to request it?

Dr. PEARSON. Not to my knowledge.

Mr. ROGERS. Well, this committee will do it. We will have the staff make an inquiry of the pharmaceutical companies. I don't know why the institutes don't do this. We are going to have to get people to employ more practical approaches.

With a simple inquiry we might find these things. It is disturbing I think to hear about these programs that are supposed to be going on, yet they won't even take the practical steps of asking people who may already have an answer.

Thank you.

I think your testimony is most helpful and particularly to know that we can screen them at little cost right now and the Department does not even know.

Dr. PEARSON. Thank you, Mr. Chairman.

Mr. ROGERS. The next witness is Dr. James A. Wolff, Columbia-Presbyterian Medical Center, Babies Hospital in New York.

Dr. Wolff, we welcome you to the committee.

We will make your statement part of the record.

Without objection we will be pleased to receive your comments.

STATEMENT OF DR. JAMES A. WOLFF, PROFESSOR OF PEDIATRICS, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, AND DIRECTOR OF PEDIATRIC HEMATOLOGY, BABIES HOSPITAL, COLUMBIA-PRESBYTERIAN MEDICAL CENTER, NEW YORK CITY

Dr. WOLFF. Thank you, Mr. Chairman.

It is a pleasure to be here and to testify concerning thalassemia.

Let me introduce myself, I am Dr. James A. Wolff, professor of pediatrics, College of Physicians and Surgeons, Columbia University, and director of pediatric hemotology, Babies Hospital, Columbia-Presbyterian Medical Center, New York City.

Dr. Pearson has already told you a good deal about the population genetics of this disease. I know that Dr. Nathan will discuss the synthesis of hemoglobin in this disease and some of the pathogenic mechanisms in regard to thalassemia.

I would like to confine my remarks to a discussion of the management of the disease, of those patients who have thalassemia major, as we have had considerable opportunity in the past to be involved with this in our institution.

Our Pediatric Hematology Clinic has been concerned with the problem of the management of children and adolescents with thalassemia for many years.

Our roster of severely affected patients—those with a double-gene defect, the children with thalassemia major, who require frequent tranfusions and very careful supervision, is relatively large. We have, therefore, been able to conduct a number of investigations concerning the optimum intervals between transfusions, the indications for removal of the spleen, the value of chemical agents which remove iron from the body, and the adverse effects of both excess accumulation of iron and inadequate oxygen delivery to the tissues. We believe that considerable progress has been made in the past 20 years in the management of our patients, but also that much still remains to be done if the life expectancy of these youngsters, now still so relatively short—and as Dr. Pearson said, individuals with thalassemia major do die in their adolescence or early adult life—is to be increased.

In addition to the expanding program of clinical research in the management of the patient with the major form of the disease, we have enlisted the help of paramedical personnel to provide genetic counseling, our Social Service Department to aid the families with their economic and social problems, which compound with the years, and our psychiatric staff to provide psychological support to these families.

Before going on to the elaboration of the cost of this program I would like to say that we think some progress has been made in the

management. We have the Chelation program, the use of compounds which will remove iron from the body, which has already been mentioned. We have used a substance called desferal (deferroxamine) which is put out by the Ciba Chemical Co. We have been fortunate in having this material available to us without charge to our patients from the company over the past 7 years. As Dr. Pearson has already mentioned, we have found that this compound is not valuable to us when we administer it to children who already are seriously iron-overloaded, who have lived with the disease for a number of years and who have had frequent transfusions.

We have more recently attempted to use this compound in children who have not previously been transfused, in other words, at the time that the diagnosis is made. Our data on this is not sufficient at the moment to say what the outcome will be although we are hopeful it may make more of a dent in the iron overload problem than it has in those who have been seriously overloaded before it is used.

Now the cost of operation of a clinic such as ours has become prohibitive as a private undertaking. For example, the estimated cost for clinic and hospital admissions for one child with thalassemia major, who requires transfusions at 3-week intervals throughout life, is approximately $71,830 from birth to possible death at age 20 years. I should like to elaborate on this estimate. Each clinic visit, including a complete blood count, costs $29.50, a total of $9,830; each transfusion, blood and service charges for administration, costs $60, a total of $20,400; the average patient will have one brief admission to the hospital each year for careful reevaluation, each admission costing about $1,200, a total of $21,600; and possibly four prolonged admissions in the last 2 years of life, each admission averaging about $5,000, a total of $20,000. There are many more unexpected medical expenses not listed, for instance, the cost of hospitalization for splenectomy if the child is splenectomized. I would estimate that the total medical cost would be well over $100,000 at current prices. I must add that we have not been able to get Federal funding through the Institutes of Health for the care of children with thalassemia, for the management of this disease. We have made attempts to ask for aid in this regard and have not been successful.

There is no question in my mind that without major Federal funding, these unfortunate children will continue to die in almost all cases before reaching adult life and that their families will continue to be torn apart by the strains placed upon them by the ravages of this disease.

Mr. ROGERS. Thank you very much, Dr. Wolff for a very helpful statement.

Mr. Kyros?

Mr. KYROS. Dr. Wolff, how many patients do you treat? For example, what is your current patient load of people who have thalassemia major?

Dr. WOLFF. Our current patient load is slightly over 20. We unfortunately lost two of our older children who died. We ran between 20 and 25 patients with thalassemia major.

Mr. KYROS. Is it consistent with what has been described here that this disease occurs in those people who came originally from the Mediterranean?

Dr. WOLFF. Our patients are entirely of either Italian or Greek ancestry.

Mr. KYROS. I don't know if you have had a chance to read Congressman Giaimo's bill which we are discussing today.

Dr. WOLFF. Yes, sir.

Mr. KYROS. Would this be a help in treating those patients? It provides for programs of treatment.

Dr. WOLFF. Yes, sir. I think this would be very helpful to us because I think this is the one area where we not only have not found funding but we are perhaps unlikely to find funding in the future through the Institutes.

Mr. KYROS. I imagine at Columbia you have examined other areas where you could possibly try to find this kind of treatment?

Dr. WOLFF. Yes, sir.

Mr. KYROS. You can not find treatment, is that right?

Dr. WOLFF. That is correct.

Mr. KYROS. If there is nothing else in the bill, there is money to treat and take care of those patients you currently have in your hospital.

Dr. WOLFF. And for whom we hope we will be able to do more if we have more funds to expand our activities.

Mr. KYROS. Now apparently the children come to you as young children, is that right?

Dr. WOLFF. Yes, sir.

Mr. KYROS. Is it a fact that at the time, the family usually doesn't have the kind of money and help to take care of these kinds of diseases?

Dr. WOLFF. Most of our families are not in an economic position to handle this even at the start. Almost any family is unable to keep up with the kind of example that they have as time goes on.

Mr. KYROS. Is it your judgment, Doctor, that H.R. 14106 is absolutely needed if you are going to carry out the kind of work you are doing in treating people with thalassemia major?

Dr. WOLFF. Yes, sir; I consider it essential.

Mr. KYROS. Thank you, Doctor.

Mr. ROGERS. Dr. Carter?

Mr. CARTER. Thank you, Mr. Chairman.

What is the most apparent solution to this problem?

Dr. WOLFF. At the moment I really can't give you a straightforward answer to that, sir, but I think in the long run the more we know about the basic mechanism of the disease the more likely are we to eradicate it.

The second approach obviously is the one that Dr. Pearson has enlarged upon and that is genetic counseling. One could eradicate the disease in a relatively short period of time if one could prevent the gene from becoming homozygous; spread it throughout the population so that chance of two individuals with the genetic defect marrying and having offspring would be decreased.

On the other hand, we are hopeful that we can do something for the management of the patient and this has been our approach. I think this is not the final solution to the problem although until the gene can be diluted sufficiently, so that it is no longer a problem in the population, we would like to do what we can to make the lives of these children more bearable and to increase their longevity, which I think we can do.

Mr. CARTER. Certainly I agree with Dr. Pearson that the elimination of the disease could be done by identification of those who bear the gene and then by counseling.

Of course if they take the advice the disease would be eliminated in the years to come. Of course such treatment as we could give these patients should be given as I see it, but it may take a lot of research really to effect a cure.

Certainly we can do things to be helpful.

Dr. WOLFF. I don't think this is the most likely answer to the problem, that is in the treatment of the disease, but I think we may be able to extend the life of the patient considerably and we have already made inroads into the beneficial management of the disease in that we know, for instance, that our newer method of transfusion and the intervals that we use have greatly reduced the unfortunate side effects of the disease. For instance, the characteristic facial appearance of an older individual with the major form of the disease.

Mr. CARTER. Deposits of iron?

Dr. WOLFF. No, this is due primarily to changes in the bones as a result of efforts of the bone marrow to respond to the poor production of hemoglobin that is inherited in the disease and therefore results in anemia.

As a result of these efforts there is expansion of the marrow and one gets characteristic changes in the configuration of the bone which leads to the facial appearance which is very characteristic of this disease.

With the use of treatment with transfusions as is customary in most clinics today we can eliminate this kind of stigma of the disease, also the size of the very large livers and spleens that these patients develop can be lessened by increased frequency of transfusion.

So we have already made useful inroads into the management of the disease.

Mr. CARTER. I think it is fine that you have done this and right that you should go ahead. To me the basic thing is to get rid of the cause of the disease through identification of the carriers and counseling that we wish that these persons would not marry.

Dr. WOLFF. Yes, sir; I agree with you. However, I think that even though Dr. Pearson has expressed urgency about the need for counseling and for attempts to dilute the gene, even this is going to be a slow process.

In the meantime, we have to do what we can to make life more livable for the children with the disease.

Mr. CARTER. I agree with you. No one would disagree with that. That is a very extreme problem of research as I see it which will be very difficult of accomplishment.

The other solution is apparent, though it may take a generation or so to accomplish.

Thank you.

Mr. KYROS (presiding). Thank you very much, Dr. Wolff.

Your testimony will be very helpful to the committee.

Our next witness is Dr. David G. Nathan, Children's Hospital, Boston, Mass.

If you wish, Dr. Nathan, you may summarize your testimony and we shall make your prepared statement a part of the record.

STATEMENT OF DR. DAVID G. NATHAN, CHIEF, DIVISION OF HEMATOLOGY, CHILDREN'S HOSPITAL MEDICAL CENTER, BOSTON, MASS.

Dr. NATHAN. I would like to do that. In fact if I could just not give my statement but simply——

Mr. KYROS. You are from Harvard Medical School?

Dr. NATHAN. Yes, I could not help that.

What I would like to do then is to present my statement to you and perhaps show you the slides of the disease so that you have some firmer idea what it is we are talking about.

(There was a slide presentation.)

Dr. NATHAN. I simply want to show you what the problem is.

On the right is the blood film of a parent of a child with thalassemia. This blood film looks a great deal like the blood in iron deficiency.

Mr. KYROS. What are the round circles?

Dr. NATHAN. On the left the little round circles represent very young red cells in the blood of a patient with thalassemia. Notice how very abnormal those cells are. They are very pale. They have very little hemoglobin in them. The patient is trying to make more cells and therefore pouring out into his blood immature red cells.

The benign blood film of the parent is very deceptive. It is almost indistinguishable from simple mild iron deficiency but the combination of two such parents produces that severe change on the left.

Why is this patient so terribly anemic? (Slide.) If you look at the bone marrow with a special stain of the bone marrow cells something very funny about the marrow cells is seen.

Notice the big black deposits in two or three of the cells. That is half of a hemoglobin molecule. What has happened in this disease is that half of the hemoglobin is not being made due to the genetic abnormality, but the other half is being made. That half instead of being nice solid red hemoglobin falls out of solution as big stones in the red cells.

As a result the red cells not only don't have enough hemoglobin in them, they are destroyed very rapidly because they contain these big rocks of unmatched hemoglobin. (Slide—Fig. 1.)

The next slide shows this in the spleen of a patient from whom we took the spleen out.

On the upper left you see one of the red cells containing big precipitates of half of a hemoglobin molecule, the half that we call the alpha chain. These patients don't make the beta chain of hemoglobin. Look how distorted some of these cells are in the spleen.

On the lower left one of the distorted cells is caught between two spleen cells and is being destroyed in the spleen. Therefore there are two major problems in these cells.

First, beta chains of hemoglobin are not being made because of the genetic defect. Second, alpha chains are being made and they are precipitating in the cells and cause this tremendous destruction of cells.

Now, what does that do to the patient? (Slide.)

Let us look at the next slide. Here is a little girl in one early phase of this disease. She is 5 years old. It began at birth. We are showing

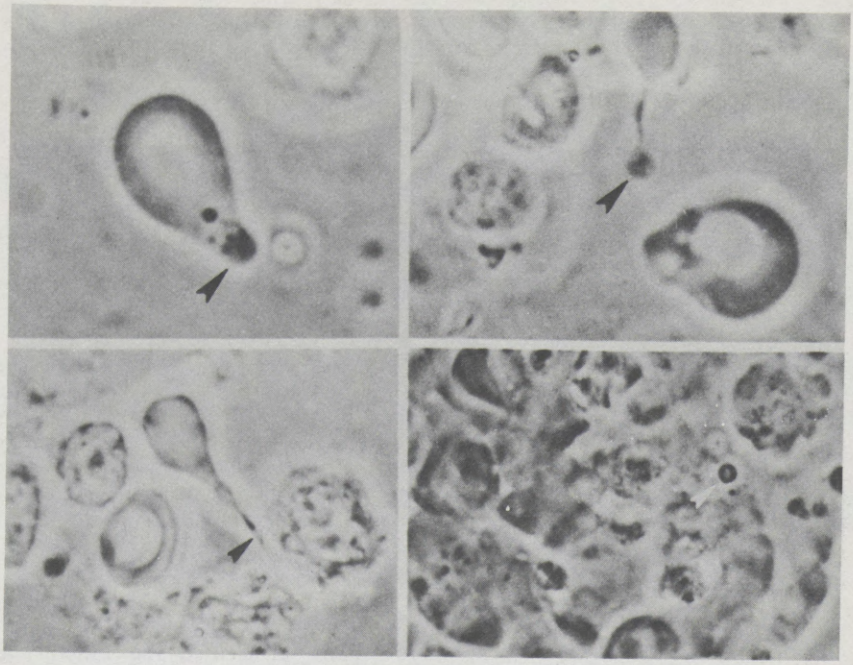

FIGURE 1.—Wet preparation of scrapings of splenic pulp of a patient with homozygous beta thalassemia viewed with phase optics. Note "teardrop" red cells with inclusions at their tips (arge arrows). One cell appears to be attached between two spleen cells (small arrow). Also note inclusions (white arrow) lying free within splenic pulp.

you this little girl because she still has some fat on her bones. She still is a child who is doing reasonably well. She is not ravaged by the disease but her spleen shown on the right drawn on the surface of the body to show you where it is inside, and her liver on the left, are really very enlarged. Her heart is drawn on her chest and that is getting very large. She certainly is not well.

She is in the early phases of this disease, is receiving transfusions but this photograph was taken before we recognized that giving more transfusion might shrink these organs.

Mr. KYROS. Her stomach is distended because her organs are larger?

Dr. NATHAN. That is correct.

Let us see what happens on the next slide.

This poor little boy is 15 years old. Note that he has had retarded sexual development. He is tiny. He has a green hue to his skin. I think if you were to look at this child you would think that this child has cancer. Indeed he does have a disease characterized by massive turnover of red cells which are made and destroyed like tumor cells. They are literally eating up his body and taking away his nutrition.

We have taken his spleen out. We are giving him transfusions but note his boney deformity, the changing of the whole appearance of his face, he is shrunken and small and he is just going to die because we are unable to sustain him.

Now, the next slide shows some X-rays of what happens in this disease and what can be done for the patients if you treat them early enough.

Look at the skull film on the left—figure 2 in this text.

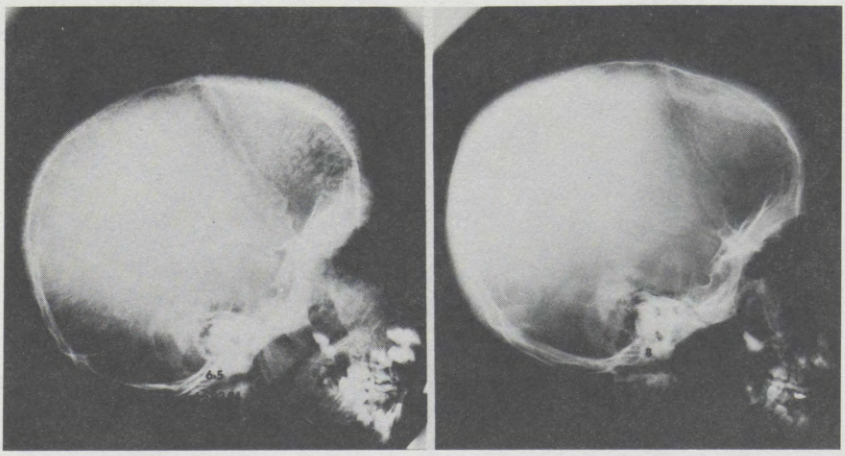

FIGURE 2.—Roentgenograms of the skull of a patient with homozygous beta thalassemia at the age of 6½ years (left), before splenectomy and transfusion therapy, and at the age of 8 (right) after splenectomy and transfusion therapy.

When this boy came to us he had never had any blood for his thalassemia. He only had two grams of hemoglobin. The normal is 15. His bones were becoming motheaten, and remarkably weakened.

On the right 2 years later we had transfused him. We improved the bone growth and calcification has occurred.

The chest bones of this boy are thin. His heart is large. After transfusion his heart is smaller and the bones have grown solid.

Look at the arms.

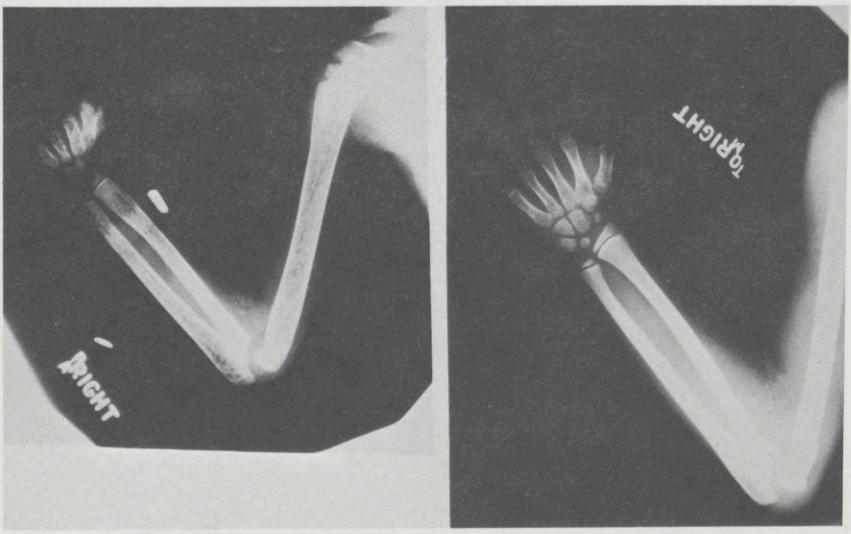

FIGURE 3.—Roentgenograms of the right arm of child with homozygous beta thalassemia. Note growth and recalcification after transfusion therapy.

This boy had 15 fractures. His bones looked like they were riddled with tumors, and in a sense they were. It is bone marrow that is growing abnormally. We transfused him and this treatment started growth and reclacification of his bones.

In defense of the NIH, it is programs like the blood resources program of the NIH which make it possible to develop better methods for transfusion. That program is working on such programs very hard.

Now in research there are several possibilities that we are working on. You heard about trying to get rid of iron. That is a tough one, a very hard problem. We are also trying to work on the basic problem of this disease because although you can talk about dilution of the gene and talk about people not marrying, the facts are that there is not a single genetic disease that we have ever been able to stop in this country by genetic counseling.

Although it is an important facet of research it is not the only answer and cannot be.

Mr. KYROS. Why is it not an answer?

Dr. NATHAN. It certainly is an important thing to try. Obviously Dr. Carter is correct, if you could get people not to reproduce it would work but we are talking about massive numbers of people. I realize it is hard to imagine in this country when we talk about 20 people in one clinic and 30 in another.

I should point out though that in Thailand, there are 322,000 patients with one of the major thalassemia diseases—in a country of 30 million. That is of course a very concentrated area. It is when you get into large numbers that it becomes very difficult effectively to counsel.

So research must go on to understand this genetic disease. Furthermore, the NIH representatives who spoke to you are quite right, research in one area affects another. This is a genetic disease. Cancer is a very special form of genetic disease. What we learn in thalassemia is applied in many different areas such as the cancer problem.

In the area of genetic engineering our laboratory, the groups in New York and here at the NIH have been working with some effect. I heard Dr. French Anderson's effort described as insignificant. I would like for the record to point out that it is anything but insignificant. The NIH work has been outstanding in this field.

Mr. KYROS. I did not hear anyone here describe it as insignificant. The chairman has suggested that it was not enough.

Dr. NATHAN. I understand. I just want to clear the record on that point.

In the three laboratories that I mentioned genetic message for hemoglobin has been quantitated. From this work we know now or have excellent evidence that the gene product is normal in kind in thalassemia but decreased in amount. Thalassemia is the only disease that I know of in which that sort of information has been generated. This is very important because if it were possible to stimulate that gene by some drug or agent the product would be normal. Whereas in sickle hemoglobin the more you might simulate the gene the more abnormal protein would be made because there is mutation in the structure of the gene in sickle-cell disease.

Mr. KYROS. Incidentally, thalassemia sounds like a sea or ocean.

Dr. NATHAN. It means the sea in us, the Mediterranean. Those of us who are from the Mediterranean have the disease.

Mr. KYROS. I hope not.

Dr. NATHAN. Or might have it, I should say.

Now another approach. I showed all those alpha chains that are precipitating and causing a great deal of the trouble. Maybe we can design drugs that will specifically inhibit the production of those alpha chains and cause less of those inclusions. That is being worked on.

Finally there is the area of prenatal diagnosis. If you can't do effective genetic counseling premarriage, can one do an effective job of prenatal diagnosis after marriage in this disease?

There is some very exciting work in this area going on at Johns Hopkins and we think our own work is moving along now to the point where actually chemically the diagnosis of hemoglobinopathy can be made in a 6 centimeter fetus. That would be around 18 to 20 weeks.

However the acquisition of a blood sample presents a technical problem that is as yet unanswered. But things are moving.

So, it is with the feeling that the patients need help and that the field is moving that I support the bill.

I understand the position of the NIH testimony here. I don't want to leave without saying that I really do understand it very well. I think it is terribly hard now for the NIH to cope with the problem of categorical research the way it is moving.

On the other hand if we are going to have categorical research then this is a very important category. I back it from that point of view very strongly.

(Dr. Nathan's prepared statement follows:)

STATEMENT OF DR. DAVID G. NATHAN, CHIEF, DIVISION OF HEMATOLOGY, CHILDREN'S HOSPITAL MEDICAL CENTER, BOSTON, MASS.

I am Dr. David G. Nathan, Chief of the Division of Hematology of the Children's Hospital Medical Center in Boston and Associate Professor of Pediatrics, Harvard Medical School.

I am pleased to present my point of view on thalassemia to this committee and to lend support to Congressman Giaimo's effort to call your attention to the importance of this disease.

Indeed if the NIH is going to embark on further funding by special category of disease, it is our duty to present the facts clearly to you and to show you why the illness which we discuss today is so important. In the next few minutes I will try to do so. You have already heard an overview of the clinical problems of thalassemia presented to you by Dr. Pearson, and an explanation of the effects and the costs of maintaining a large clinic of patients with thalassemia by Dr. Wolff. I would like to devote my remarks to the future of research in this problem as I see it so that you can have a clearer picture of where we hope to go with this disorder.

Of course you must first ask how many people actually have severe homozygous thalassemia in the United States and in the world, and unfortunately I am not able to give you an accurate estimate. This is because we do not have as yet a simple and inexpensive method by which we can define the heterozygous state of this disorder. As you know from your examination of the sickle cell anemia problem, the gene frequency for the sickling phenomenon is easily defined by population surveys using a simple and reasonably definitive test for the trait.

Simple Mendelian genetics permits one to calculate with reference to sickle cell disease that if the trait (i.e. the heterozygous state) has an incidence of 10% among American Blacks, then 1 in 400 American Blacks will have homozygous sickle cell anemia. This amounts to a population of approximately 50–60,000 patients. The thalassemia gene is concentrated with a particularly high incidence in individuals of Mediterranean origin, those originating in the Middle East, and in the Orient as well as in certain parts of Africa. The incidence of the trait in American Blacks has been estimated at approximately 1%. This means that approximately 1 in 4,000 American Blacks have homozygous thalas-

semia for a total incidence of perhaps 6,000 patients. Careful surveys of the thalassemia genes have been performed in Thailand where the incidence is extraordinarily high. In that small country of 30 million people there are no less than 20,000 estimated patients with homozygous beta thalassemia and a total of 322,000 people with serious other thalassemia disorders. If these patients received adequate treatment the massive drain on the resources of this small country would be beyond calculation. Certain Italian-Americans suffer with an incidence of thalassemia which is equal to that of sickle cell anemia in the Black. Thus 1 in 400 Italian-Americans of origin from the Po River delta or Sicily would be expected to have homozygous disease. Approximately one half that is observed in Greeks or Greek-Americans and Americans of pure Indian, Sudanese, Turkish and Sephardic-Israeli origin.

Thus America the "melting pot" must accept responsibility for the improvement of the lot of these patients. In addition, research on thalassemia, which is fundamentally research on the gene itself, must lead to better understanding of the cancer problem which is also increasingly recognized as a very special form of an acquired genetic disorder.

The clinical aspects of thalassemia point the way toward future curative research in this field. The first slide shows two blood films taken from (on your right) the mother or father of a patient with homozygous thalassemia whose blood film is shown on the left. Note that the two smears look very different. The mother or father, shown on the right, does have somewhat small red cells, and they are not as fully filled with hemoglobin as are normal cells, but they might well be missed in a cursory examination as being anything but normal. However, careful and, I'm afraid, somewhat expensive electrophoretic analysis of the hemoglobin of such an individual shows the characteristic abnormalities of thalassemic red cells. On the left is the patient who has inherited the thalassemia gene both from the father and from the mother. Notice that his red cells, though they appear large, are actually plate-like, flat, and poorly filled with hemoglobin. These cells are shaped in a bizzare manner. They are removed at a rapid rate from the circulation. They are destroyed rapidly in the bone marrow as well.

Why are they destroyed so rapidly? (Slide off please) This was discovered as a result of basic research into hemoglobin. Hemoglobin is a protein made in the bone marrow but comprised of two parts which we call alpha and beta. In each hemoglobin molecule there are two alpha and two beta chains. In the ordinary form of homozygous beta thalassemia, beta chains are produced at a very low rate. For this reason the total amount of hemoglobin accumulated in the cell is small. But alpha chains are produced at a normal rate. These accumulate and have no beta chains with which to match. As a result they precipitate within the cells and form large inclusions. These are shown in the bone marrow on the next slide. This is a slide of the bone marrow cells from a patient with homozygous thalassemia. This is a special stain to bring out the very large inclusions in the developing red cells in the bone marrow. Notice that there are large black inclusions present in several of these cells. These are the precipitated alpha chains which have no beta chains with which to mate. The next slide shows the fate of red cells which contain such inclusions. This slide represents a suspension of red cells found in the spleen of a patient with homozygous beta thalassemia. Note that these markedly distorted red cells contain large black inclusions of alpha chains which have precipitated in the cell.

On the lower right, one of the inclusions can be seen lying free in the splenic pulp, and in the other panels the inclusions can be found in the red cells themselves. Note on the lower left two spleen cells that have actually trapped a thalassemic red cell by one of its elongated processes in which there is an inclusion clearly demonstrated. In fact these cells with alpha chain inclusions become trapped by the clean-up cells of the body the so-called reticuloendothelial cells which line all the blood channels, and they are destroyed. As a result there is an enormous loss of newly synthesized red cells that are actually destroyed by the extra alpha chains which they produce. What does this marked destruction of blood do to the patient? This can be shown on the next slide. The little girl has homozygous beta thalassemia. She is only four years old so she has not yet been destroyed by the ravages of the disease. But we have drawn on the surface of her body, her heart, her liver, and her spleen. Note that they have become gigantic. The spleen and liver have enlarged from the hypertrophy which is associated with the destruction of red cells, due to the alpha chain accumulation, and the

heart is enlarged because of her severe anemia which is a result of both the failure to accumulate hemoglobin in the cell and the destruction of cells by virtue of the accumulation of alpha chains. As she grows older the tragedy continues.

The next slide shows a boy, unbelievably aged 16; no sexual maturity has occurred. We have already tried to help him by removing his spleen—thus the scar on his abdomen. Note the green death-like hue to his skin, the marked weight loss, the protuberant teeth, the peculiarly shaped nose and jutting forehead of a markedly expanded bone marrow. This boy's red cells are turning over so rapidly in his bone marrow and in his body that they behave like a cancer consuming all his body energy as he wastes and waits a lingering death. The next slide shows what happens to the bones in this disease in a boy like the one we just showed you. On the left the moth eaten skull due to markedly expanded bone marrow again looking like a cancer due to the marked expansion of the bone marrow which is trying to keep up with the demands for more red cells. On the right is shown what we can do with transfusion therapy in just such a boy if we treat him early enough. If we give him enough blood we can in fact restore his bone marrow to normal by reducing the demands on his bone marrow by transfusion. This is of course a limited form of therapy which cannot go on for too long.

On the next slide the X-rays of such a boy's chest. Notice before transfusion therapy his markedly enlarged heart and his eroded thinned out ribs. If we showed this rib cage to many cancer specialists, they would say he might be riddled with tumor, but notice what we can do with transfusion. On the right after two years of transfusion therapy his heart is smaller, his bones have begun to recalcify. The next slide shows the arms of such a boy. Note on the right the poorly shaped very thin bones. This particular child had at least 5 major fractures before he came to our attention. With transfusion therapy he has begun to grow and his bones have begun to recalcify. Thus the major goal of research in this disease is to deal with the marked unbalance of hemoglobin synthesis which occurs in this disorder. There are too many alpha chains produced for the number of beta chains produced, and as a result the disease is not only due to a failure to accumulate hemoglobin in the cell, it is a disease characterized by massive turnover of cells within the bone marrow. Where is the research leading us as we deal with this problem? There are five major approaches. First, of course, is the desirability to improve blood banking and blood transfusion techniques and to design drugs to rid the body of the excess iron which is given to the patient in the form of transfusion. In fact a great deal of work continues to be done to develop so called chelating agents which will remove iron from the body.

The work of the Blood Resources Program of the National Institutes of Health is of great importance to the thalassemia patient because it is in that program that better ways to deliver transfusions are being funded by the National Institutes of Health. A second approach to the thalassemia problem might be to take the bull by the horns and to transplant bone marrow into these patients; to give them normal erythroid cells from a non thalassemic individual. This is a field in which further study of the immunology of bone marrow transfusion is absolutely imperative. At the moment the risks of bone marrow transfusion are so great that they cannot be warranted in this disease. But we have hopes that after a solid base of investigation of bone marrow transfusion, thalassemic patients may benefit. Third, we must deal with the promising area of genetic engineering. In our laboratory, in New York, and here at the NIH important discoveries have been made this very year. We have been able to show that the genetic message produced by the beta thalassemia gene is decreased in amount and not in function. You see there are two different kinds of genetic abnormalities. In the first, and in fact more common type, a gene produces an abnormal product such as sickle hemoglobin. In thalassemia, the product that is produced is normal but is decreased in amount.

This is due not to an abnormality of the structure of the genetic message, but of the amount that is produced. This is a hopeful piece of evidence because it means that if we should be able to stimulate the gene by a particular kind of drug, the product of the gene would itself be normal and would restore the ability to produce a normal protein. Clearly stimulation of the gene would be useless if the product of the gene, the message itself, were abnormal and would not stimulate hemoglobin production. This recent work on the genetic message has been based in part upon the use of viral reverse transcriptase about which

you have heard so much in the past year. Although this enzyme has been associated recently with the cancer problem, it has been used in this research to deal with this very important inherited disease. This illustrates the importance of broad research, the sustaining of efforts in many areas in order to deal with diseases with which we have so much difficulty at this time.

The fourth approach is a somewhat indirect one. If we cannot increase the production of beta chains in patients with beta thalassemia, can we decrease the production of alpha chains and thus reduce the amount of inclusion which forms in them and is responsible for their rapid destruction. Recently our laboratory in conjunction with the group at the Massachusetts Institute of Technology have in fact found ways to depress alpha chain synthesis with various agents. Admittedly this is now at the cost of a decrease in the total production of hemoglobin and it is only done in broken cells rather than in intact cells. We are in hopes that future research will allow us to suppress alpha chain production selectively so that inclusion formation can be reduced in this disease and hence the transfusion requirement.

Finally we are adopting methods by which we can detect thalassemia in fetuses of only 3 months gestation. You can imagine the agony in families in whom 3 patients with homozygous beta thalassemia have been born. This in an unparalleled tragedy in the life of the family, and mothers constantly come to us asking whether the pregnancy which they carry has thalassemia or not. Clearly if we could find a way to detect this disease by prenatal diagnosis, we could help such mothers to have healthy babies rather than babies with homozygous beta thalassemia. Work at Johns Hopkins and in our own laboratory has already produced hope that a method for the diagnosis of homozygous sickle cell disease can be established in utero. We are now working hard on all the facets of the method and hope to adopt it for thalassemia as well.

These then are the present areas of research in this disease. In the meanwhile we must cope with the patients that we have. We must offer them some sort of a useful life, and help their families to sustain their care. It is with these patients in mind that I lend my support to Congressman Giaimo's bill. For if we cannot have a system by which medical research flowers for its own sake with the confidence that from research in many different fields will come the answers which we all crave, if we must clearly define the goals of each category of research, then I plead that this particular category is well worthy of your attention and of the resources of this country. I should end by saying that the entire world really looks to the United States for this kind of research. It is expensive, it is difficult, it requires many years of training. It requires the kind of commitment that has characterized the National Institutes of Health and the National Science Foundation. With these resources and the intelligent pleadings of organizations such as the Cooley's Anemia Foundation, we must in the future offer significant improvement not only to these patients but to patients with genetic disorders of many kinds. Thank you.

Mr. KYROS. Dr. Nathan, that is a thoroughly balanced statement and I couldn't agree with you more. I am just delighted that we were able to put your testimony on record. I wish we were able to put the pictures of the slides in the record because I think every one should be aware of them.

Mr. Chairman?

Mr. ROGERS. I have no questions.

I apologize for having had to leave for a time.

Mr. KYROS. We will recess the committee for about 15 minutes before we receive testimony from Dr. Zaino and Dr. Miller.

(Whereupon, a recess was taken.)

Mr. ROGERS. The subcommittee will come to order, please. Other members will be coming back.

The next witness is representing Cooley's Anemia Blood and Research Foundation for Children, Dr. Edward Zaino, who is chairman of the medical advisory board, and Mr. Edward Paradiso, who is the president of Cooley's Anemia Blood and Research Foundation for Children.

We welcome you gentlemen to the committee. Your statements will be made a part of the record at this point without objection. The committee will be pleased to receive your comments.

STATEMENTS OF DR. EDWARD C. ZAINO, CHAIRMAN, MEDICAL ADVISORY COMMITTEE OF THE COOLEY'S ANEMIA FOUNDATION; AND EDWARD D. PARADISO, PRESIDENT, COOLEY'S ANEMIA BLOOD AND RESEARCH FOUNDATION FOR CHILDREN, INC.

Dr. ZAINO. Mr. Chairman, members of the subcommittee, my name is Edward C. Zaino. I am chairman of the medical advisory committee of the Cooley's Anemia Foundation.

As you have learned today, Cooley's anemia is also known as thalassemia major. It is a fatal congenital disease of children associated with a severe anemia, it does not respond to any medication. Most of the present medicine available for the treatment of anemias are not only of no value but, medicines, especially those containing iron in any form are dangerous to the infant.

Unless careful blood tests are done, the anemia may look like an iron deficiency anemia. Many of the infants are usually erroneously treated first with iron for varied and prolonged periods of time before the condition is diagnosed. Under the microscope, the blood cells may look like the so-called widely publicized "tired blood" cells. The body is unable to produce normal quantities of blood and absorbs large quantities of iron. The iron is not utilized, it is heavily deposited in the vital organs as the heart, liver, thyroid, pancreas, adrenals, pituitary, and bone marrow as well as the spleen.

The spleen becomes markedly enlarged and in most infants it requires surgical removal. These children are stunted in growth because of the severe anemia, and they usually die with heart failure. The heart failure is related to the massive amounts of iron deposited in the heart. Life can only be maintained by frequent transfusions usually on a monthly basis.

As you have also learned today, Cooley's anemia is inherited as the double dose of the gene defect. Each of the parents is a carrier carrying the defect, in a single dose. The parents are thus known as Cooley's anemia trait or thalassemia minor. Most of the individuals with the trait lead a normal life without even knowing that they have the condition. If they are mildly anemic, they also will be unsuccessfully treated with iron. The traits seldom require blood transfusions. While this disorder is worldwide, the heaviest concentration is seen in the Mediterranean region. It is thus also known as Mediterranean anemia. However, it is now an American disease. The children we are treating are American born, of American parents, whose parents in turn, have been born in the United States.

I, therefore, recommend the following considerations:

(1) Massive countrywide public education.

(2) Screening of the population, particularly those at high risk, to determine the exact incidence of the disease and to uncover the traits.

(3) Patient services—

(*a*) Countrywide donations of blood so that blood will be available on a routine and regular basis for patients with Cooley's anemia.

(*b*) Establishment of transfusion clinics where patients may be treated without hospitalization.

(*c*) Subsidization of hospital costs depending on the family's ability to pay when hospitalization is necessary.

(*d*) A plan for the payment of laboratory and possibly physicians' fees once the diagnosis of Cooley's anemia has been made.

(4) Genetic counseling.—There is no way to prevent the disease except by diagnosing it and giving genetic counseling.

(5) Research to further delineate the abnormality and to find a cure for this abnormality.

(6) The $7.1 million as indicated in H.R. 14016 should be considered as a minimal estimate, the subcommittee should consider the magnitude of the needs and arrive at what they feel is the best amount on the basis of their findings.

For these reasons, the National Cooley's Anemia Control Act must be passed. I might add that a commitment has been made for sickle cell anemia. I think it is an excellent commitment. I endorse it wholeheartedly. I feed the same sort of commitment should be made towards Cooley's anemia.

Mr. ROGERS. Thank you very much.

Mr. Paradiso.

STATEMENT OF EDWARD D. PARADISO

Mr. PARADISO. Chairman Rogers and members of the subcommittee, my name is Edward D. Paradiso, and I am national president of the Cooley's Anemia Blood and Research Foundation for Children, Inc. In addition to the national foundation, I am representing the 12 chapters of the foundation now established across the country, from New England and the New York-New Jersey area to the midwest and to California.

As the father of two children with Cooley's anemia, I am particularly concerned about presenting the views of parents of children with Cooley's anemia and of the children and young adults with this disease.

I first learned about Cooley's anemia 22 years ago when our pediatrician told my wife and I that our daughter had this disease. He explained that it was a blood dyscrasia that had no known cure, and that the only known therapy was periodic and regular blood transfusion. He said that even the transfusions were "palliative" therapy, that Cooley's anemia was a terminal disease, and that it carried a life expectancy of from 10 to 12 years.

This was a terrible blow to us. Naturally, we sought other medical opinions, hoping against hope that our pediatrician had been wrong. A hematologist confirmed the diagnosis, however, and two other physicians in New York City did likewise. We decided, therefore, to learn more about this disease—Cooley's anemia—which our daughter had, and which has now become part of our lives.

Public and medical libraries were of little help; we found that blood transfusions were the only known therapy, and that surgical removal of the patient's spleen might help in some cases. My wife and I were already expecting another child at this time, and we went through many nightmarish months waiting to find if this second child would also have Cooley's anemia. Fortunately, our doctor was

able to tell us when our son was 3 months old that he did not have the disease.

Despite our private pact to have no more children—so as not to risk having another with Cooley's anemia—my wife and I were advised over the years that our chances of having another child with Cooley's were slim. Our third child, a daughter, did not have the disease, but our fourth, a son, did. If we had had information available then—information which every parent at potential risk has the right to know—we would not have gambled on having either a third or fourth child.

As our children grew, we discovered many of the other heartaches that come with Cooley's anemia. I can recall no more terrible feeling than bringing a child to the hospital for the blood transfusion therapy. As you approach the hospital, he asks pitifully, "Am I going to the hospital again for a transfusion?"—understanding even when very young what that means—and you have to tell him, "Yes, you are."

This isn't merely the ordinary young child's fear of doctors; it can be terror and unforgettable fear, especially in an impersonal atmosphere with personnel not specifically knowledgeable about the procedure and the possible complications. As a parent, you find yourself quietly checking the blood type, worrying about the possibility of transfusion reactions or hepatitis; you try not to alarm your child.

As the years go on, more questions appear, but few answers. Men trained to treat the disease are few and far between; research seems limited, and publicly available information nonexistent. Many of the answers and much of the help available came from the Cooley's Anemia Foundation, a group we first heard about 16 years ago. Without the accidental intervention of one researcher working under a grant from the foundation, for example, our oldest daughter's bone growth would have been interrupted, and her chance for normal activities lost forever. So many more questions arise—as I'm sure they would to you, were one of your children to have this disease—but so few answers are available, most of them coming through communication within this private foundation.

One of the hardest questions facing most parents is: "How are we ever going to pay the medical bills?" As you have heard today, the medical complications of this disease can be overwhelming, with many expensive hospital admissions. Many parents are not covered at all for those kind of expenses, even with apparently adequate hospitalization policies.

Last fall, for example, I met a family in Tennessee with two Cooley's anemia children. The parents of those children—aged 7 and 9 then—were indebted for medical bills of more than $8,000; can you imagine the individual burden facing those parents for the next decade or more? Another factor, of course, is that the parents of these children want to do everything they can to help themselves; they don't want handouts, and neither does our foundation want that.

Finally, as your children with Cooley's anemia grow older, there is the constant fear of prolonged illness and death that pervades family life. We know this disease will take our children at an early age—there is no escaping that—although we all try as parents to make their lives as free of sickness as possible, and are rewarded in often finding that the children with this disease are no less interested in life; they can

make their own contributions to a family, to friends and in many cases, to society.

There are so many problems to be dealt with in this disease, gentlemen of this subcommittee, that neither parents nor our foundation can do the whole job. There are jobs to be done for which Federal help is needed—in research, and especially applied or clinical research; in training of people who can work with the children who have this disease; in public information and education, including education of physicians, parents, and the public at large; in screening—the hope for preventing future cases, by making available information that a parent should have available.

We in this foundation can help; we work everyday to raise funds, provide patient services, fund research. But, we do now need your help as well, and therefore, urge you to consider and report a National Cooley's Anemia Control Act. Thank you for this opportunity to speak for the parents and children affected by Cooley's anemia.

Mr. ROGERS. Thank you very much, Mr. Paradiso and Dr. Zaino. We appreciate your presence here, giving us the benefit of your own personal experience. Mr. Kyros.

Mr. KYROS. Thank you, Mr. Chairman.

That was a very moving statement, Mr. Paradiso. What is the Cooley's Anemia Blood and Research Foundation for Children, Inc.?

Mr. PARADISO. It is a foundation founded some 16 years ago dedicated to the alleviation, the cure, the assistance of children suffering from Cooley's anemia.

Our main purposes are to supply blood for these children at no cost to the parents, wherever, however much they need it, at all times. We try in our small way, to raise some money so that we can sponsor research programs in various hospitals or provide money for fellowships for the study of Cooley's anemia.

Any grants which we have been fortunate to give, we have first screened through a medical advisory board consisting of some 16 or 18 of the finest hematologists and physicians throughout the country.

Mr. KYROS. You say you have four children, and two have Cooley's anemia. The two children are alive?

Mr. PARADISO. Yes, sir.

Mr. KYROS. What is the prognosis of the children who have the disease?

Mr. PARADISO. It is a terminal disease. At the moment, we don't know the life expectancy. We feel that the average case will probably run about 18 to 20.

Mr. KYROS. Have they been going to school normally?

Mr. PARADISO. Yes. My daughter, fortunately, she is 22 years old—she has completed college. She is working as a medical technologist.

I have a son who is 16. He is going to school. However, he ran into difficulties in trying to keep up with the children he is associated with in school. He goes to the hospital approximately every 4 weeks and receives 2 pints of blood. By the time he is ready to go to the hospital, he is feeling tired and beat.

Mr. KYROS. And your daughter, 22 years old?

Mr. PARADISO. The same way; she goes to the hospital every 4 weeks. She has to be careful when it comes to the end of the time that she does

not overstrain herself. Otherwise, she would not be able to go to work or whatever she is doing the following day.

Mr. KYROS. I certainly commend you, Mr. Paradiso for your testimony.

Mr. ROGERS. Dr. Zaino, are there any particularly encouraging breakthroughs that you see on the horizon?

Dr. ZAINO. I have been puzzled with this over the past 5 years. I can honestly say I don't; I haven't seen a breakthrough.

Mr. ROGERS. Are you doing a great deal of research yourself?

Dr. ZAINO. The research I am doing is in the field of screening. I certainly would support, in my small way, what Dr. Pearson has said about the electronic counter. I am interested in studying the red cells of patients with Cooley's anemia and the traits under the electronic microscope.

Mr. ROGERS. Thank you very much.

Dr. ZAINO. Thank you, Mr. Chairman.

Mr. ROGERS. Our last witness today, is Dr. Denis Miller, director of the Pediatric Hematology Clinic, New York Hospital-Cornell Medical Center. We welcome you to the committee. Your statement will be placed in the record, and we will be pleased to receive your comments.

STATEMENT OF DENIS R. MILLER, ASSOCIATE PROFESSOR OF PEDIATRICS, CORNELL UNIVERSITY MEDICAL COLLEGE, DIRECTOR OF PEDIATRIC HEMATOLOGY, NEW YORK HOSPITAL-CORNELL MEDICAL CENTER AND MEDICAL DIRECTOR, CHILDREN'S BLOOD FOUNDATION, INC.

Dr. MILLER. Mr. Rogers and members of the committee, my name is Denis R. Miller, associate professor of pediatrics at Cornell Medical College and director of pediatric hematology at the New York Hospital; I also serve as medical director of the Children's Blood Foundation.

I would like to summarize, if I can, and depart from my formal presentation and, to save time, try to cover some of the areas that have not already been mentioned.

As pediatric hematologist and director of the oldest and largest facility of this kind in the country for the specific diagnosis and treatment of thalassemia, I wholeheartedly support the legislation. In the discussion that follows, I will attempt to review some aspects of the nature of the thalassemia problem in this country and some of the specific needs in the field of patients' care, research, and training. Drs. Wolff, Nathan, and Pearson have eloquently stated the historical and genetic aspects of the disease.

To emphasize the eugenic scope of the thalassemia syndromes, the gene for thalassemia may interact with that for sickle cell trait, which occurs in approximately 1 in 10–12 black Americans, resulting in a moderately severe form of hemolytic anemia known as sickle cell-thalassemia disease.

The estimated gene frequency of B-thalassemia among American blacks is 1–2 percent. B-thalassemia may also interact with Hemoglobin C trait (gene frequency in blacks approximately 4 percent) causing Hemoglobin C-thalassemia disease.

Few large scale screening programs to detect thalassemia in this country have been mounted; if launched, these programs would add greatly to our knowledge about the frequency of this disease in our country. Such a screening program would also provide the basis for the proposed genetic counseling and educational programs outlined in H.R. 14016.

I won't discuss the pathophysiology which Dr. Nathan has reviewed with you, but I would like to discuss the clinical features and natural history of the disease.

The typical child with homozygous thalassemia is well for the first few months of life because of the presence of fetal hemoglobin. However, as gamma chain synthesis declines and beta chain synthesis (adult hemoglobin) fails to increase because of the underlying genetic defect, pallor, weakness, progressive anemia, and poor appetite become manifest. The spleen gradually enlarges and with expansion of all bone marrow cavities, marked changes in the bony skeleton occur, most marked in the skull, face, vertebrae, and long bones.

With severe anemia, frequent infections, poor growth and development, gall bladder stones, cardiac failure, leg ulcerations, and fractures may occur. Since the child with homozygous thalassemia is unable to maintain levels of hemoglobin compatible with normal life, blood transfusions are the cornerstone of therapy.

Splenectomy may decrease the frequency of transfusions in some patients, but following the procedure there is an increased risk of fatality secondary to an overwhelming bacterial infection. A number of programs to optimize transfusion therapy are currently under investigation in a number of centers, but definitive results must await many more years of followup with larger numbers of patients.

Although blood transfusions sustain life, the many complications of transfusion therapy contribute to the shortened survival of the afflicted patient who is between Scylla and Charybdis—he requires blood transfusions to live, yet the complications of chronic transfusion therapy eventually cause death.

These complications include iron overload of all tissues resulting in bronzed skin, cardiac and liver failure, diabetes mellitus, kidney failure, delayed secondary sexual development and stunted growth, hepatitis, transfusion reactions, and increased susceptibility to infection. Although life has been prolonged with carefully directed transfusion programs where patients receive total comprehensive care, few patients live beyond 25–30 years.

The oldest surviving patient in our large clinic which cares for 72 patients with thalassemia major, is 27 years of age. During that period he has had a splenectomy, multiple fractures, meningitis, pneumonia, pericarditis, is a diabetic and has received over 600 pints of blood. The cost of his transfusion maintenance program and general medical care, all performed on an outpatient basis is approximately $3,000–$4,000 per year.

Since some families have more than one affected child, few can afford the medical expenses of care for this chronic disease. In addition to the financial burden, the emotional burden on the child with a debilitating, deforming, and fatal disease is massive and is a challenge to those responsible for his care.

For this reason, the establishment of clinical centers where children may receive total care is essential if the life of children with thalassemia is to be made happier, more bearable and effective. The proposed legislation, in establishing treatment centers, is an obvious necessity if these goals are to be met. The screening programs have been well covered by Dr. Pearson.

The proposed legislation will help create and support thalassemia treatment centers, where total comprehensive care can be provided by well-trained, well-equipped staffs. In most private and Blue Cross and Blue Shield insurance programs, there is almost no coverage for outpatient therapy which is almost a necessity for children with thalassemia major, if at all possible.

This would include specific therapy of the primary disease with blood transfusions as often as every 2 to 4 weeks, and the use of chelating (iron binding) agents to decrease the severity of chronic iron overload; treatment of complications with the supportive assistance of a specific team of consultants from the following subspeciality departments: orthopedic and general surgery, gastroenterology, dental, cardiology, endocrinology, dermatology, psychology, psychiatry, and medical social service; adequate blood bank facilities equipped to supply blood components and frozen blood; an intensive education program for affected children and parents regarding the nature, needs and emotional adjustments of a chronic illness.

There are relatively few centers designed to provide total care for the patient with thalassemia; one such model is our clinic at the New York Hospital-Cornell Medical Center, which is supported by the Childrens Blood Foundation, a private philanthropic organization based in New York City.

I might add, as has been mentioned by other witnesses today, there are very few Federal funds for patient care. This clinic was founded in 1951 by Dr. Carl H. Smith and was the first outpatient facility of its kind in this country. Currently, we care for 72 patients with homozyous thalassemia who require approximately 1,300 patient visits per year.

As with other chronic diseases of childhood, such as leukemia and hemophilia, total health care for diseases such as thalassemia should be provided in pediatric centers capable of meeting the many difficult needs of these patients.

Dr. Nathan has summarized the research needs in this field. My last comment has to do with the information and educational materials. In view of the general public unawareness of the problem of thalassemia, an intensive informational and educational campaign would be required.

The use of mass media, films, symposia for health professionals and laymen, and pamphlets and other printed material currently not generally available would be essential if such a campaign is to be effective; if it is to be effective, the educational program must coincide with genetic counseling. Accordingly, the proposed appropriation of $25,000 per annum may be inadequate to meet the dual goals of reaching the susceptible high risk groups, screening them and providing genetic counseling and reaching the practicing physician and increasing his awareness of thalassemia, its diagnosis, treatment, and prevention.

In summary, I enthusiastically support this legislation which will provide funds where none currenty exist. Specifically, the support of patient care, screening and educational programs are desperately needed. I thank you for permitting me to testify.

(Dr. Miller's prepared statement follows:)

STATEMENT OF DENIS R. MILLER, M.D. ASSOCIATE PROFESSOR OF PEDIATRICS, CORNELL UNIVERSITY MEDICAL COLLEGE, DIRECTOR OF PEDIATRIC HEMATOLOGY, NEW YORK HOSPITAL-CORNELL MEDICAL CENTER AND MEDICAL DIRECTOR, CHILDREN'S BLOOD FOUNDATION, INC.

I. INTRODUCTION

Normal adult human hemoglobin is composed of 4 polypeptide globin chains, two alpha chains and two beta chains. Fetal hemoglobin is made up of two alpha and two gamma chains and a minor normal hemoglobin, hemoglobin A_2, is comprised of two alpha and two delta chains. The chains differ in the number and sequence of individual amino acids, but for normal life, adequate amounts of functioning hemoglobin must be available to transport oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs.

Cooley's anemia (or the thalassemia syndromes) encompass a broad group of inherited disorders of hemoglobin synthesis in which there is a specific impairment of production of one or more of the normal chains of globin. This results in a hypochromic (decreased pigment) microcytic (small red blood cells) anemia of varying severity associated with an alteration in the amount, composition, and type of hemoglobin within the red blood cell.

Depending upon the type of synthetic defect, the disorders may be classified as beta-thalassemia, the most prevalent type, alpha-thalassemia and rarely, delta-thalassemia. The homozygous form of beta-thalassemia is incompatible with life unless blood transfusions are administered. Stillbirth or early neonatal death occurs in homozygous alpha- thalassemia. Individuals with the heterozygous state (thalassemia trait or "carrier") may have a mild anemia or may be entirely asymptomatic.

The legislation being considered today proposes to provide funds for (1) thalassemia screening, treatment and counselling programs, (2) research in the diagnosis, treatment and prevention of these diseases, (3) training fellowships and, (4) educational programs for the health profession and general public. As a pediatric hematologist and director of the oldest and largest facility of its kind for the specific diagnosis and treatment of thalassemia, I wholeheartedly support the proposed legislation. In the discussion that follows, I will attempt to review the nature of the thalassemia problem in this country and the specific needs in the field of patient care, research and training.

II. THE NATURE OF THE PROBLEM

A. Historical and geographical aspects

In 1925 Dr. Thomas Cooley described an anemia peculiar to individuals of Green and Italian origin. Subsequently, the disease has been so thoroughly documented that thalassemia (from the Greek *thalassa* or sea, referring to the Mediterranean), is one of the first diagnostic considerations in an individual of Mediterranean ancestry who presents with a hypochromic anemia. Through genetic migration, thalassemia also occurs frequently in the Middle East, India, Southeast Asia, and in the United States among Italians, Greeks, Blacks and Orientals.

B. Gene frequency

In some parts of the world the gene frequency for thalassemia trait (the carrier or heterozygous state) may be as high as 20 percent, i.e., one in five individuals is affected. In Americans of Greek and Italian ancestry, the gene frequency is estimated as 0.04 or 1 in 25. In New York City alone, of 3,000,000 individuals of Greek and Italian ancestry, 120,000 may have thalassemia trait. In the ethnic "melting pot" of modern America, many third and fourth generation Americans may have little knowledge of their ancestry, and if they do, awareness of diseases relative to that ancestry may not be apparent since the laboratory means of detecting mild forms of hemoglobin abnormalities were not available prior to 1949.

To emphasize the eugenic scope of the thalassemia syndromes, the gene for thalassemia may interact with that for sickle cell trait, which occurs in approximately 1 in 10–12 Black Americans, resulting in a moderately severe form of hemolytic anemia known as sickle cell-thalassemia disease. The estimated gene frequency of β-thalassemia among American Blacks is 1–2 percent. β-thalassemia may also interact with Hemoglobin C trait (gene frequency in Blacks approximately 4%) causing Hemoglobin C-thalassemia disease. Few large scale screening programs to detect thalassemia in this country have been mounted and would add greatly to our knowledge about the frequency of this disease in our country. Such a screening program would also provide the basis for the proposed genetic counselling and educational programs outlined in HR 14016.

C. Genetics and pathophysiology

Affected individuals with homozygous thalassemia must inherit a thalassemia gene from both heterozygous parents. The gene controls the synthesis of globin chains. The structure for globin chains in thalassemia (i.e. the sequence of the individual links or amino acids in the chain) is normal but the amount of chain produced (alpha-chains in alpha thalassemia or beta-chains in beta thalassemia) is deficient. From recent exciting research it appears that the genetic defect in thalassemia is related to abnormal messenger RNA, resulting in decreased synthesis of normal globin chains, and an imbalance in globin chain production. The excess free chains which are unstable and insoluble within the red blood cell, adversely affect cell function and result in shortened survival of the red cells. Increased rates of red blood cell production results in expansion or utilization of every available site for blood production to keep up with the increased rate of destruction, a situation which produces many of the clinical features of the disease.

D. Clinical features and natural history of the disease

The typical child with homozygous thalassemia is well for the first few months of life because of the presence of fetal hemoglobin. However as gamma chain synthesis declines and beta chain synthesis (adult hemoglobin) increases, pallor, weakness, progressive anemia, and poor appetite become manifest. The spleen gradually enlarges and with expansion of all bone marrow cavities, marked changes in the bony skeleton occur, most marked in the skull, face, vertebrae and long bones. With severe anemia, frequent infections, poor growth and development, gall bladder stones, cardiac failure, leg ulcerations, and fractures may occur. Since the child with homozygous thalassemia is unable to maintain levels of hemoglobin compatible with normal life, blood transfusions are the cornerstone of therapy. Splenectomy may decrease the frequency of transfusions in some patients but following the procedure there is an increased risk of fatality secondary to an overwhelming bacterial infection. A number of programs to optimize transfusion therapy are currently under investigation in a number of centers but definitive results must await many more years of follow-up with larger numbers of patients. Although blood transfusions sustain life, the many complications of transfusion therapy contribute to the shortened survival of the afflicted patient who is between Scylla and Charybdis—he requires blood transfusions to live, yet the complications of cronic transfusion therapy eventually cause death.

These complications include iron overload of all tissues resulting in bronzed skin, cardiac and liver failure, diabetes mellitus, kidney failure, delayed secondary sexual development and stunted growth, hepatitis, transfusion reactions, and increased susceptibility to infection. Although life has been prolonged with carefully directed transfusion program where patients receive total comprehensive care, few patients live beyond 25–30 years. The oldest surviving patient in our large clinic is 27 years of age. During that period he has had a splenectomy, multiple fractures, meningitis, pneumonia, pericarditis, is a diabetic and has received over 600 pints of blood. The cost of his transfusion maintenance program and general medical care, performed on an outpatient basis is approximately $3,000–$4,000 per year. Since some families have more than one affected child, few can afford the medical expenses of care for this chronic disease. In addition to the financial burden, the emotional burden on the child with a debilitating, deforming and fatal disease is massive and is a challenge to those responsible for his care. For this reason, the establishment of clinical centers where children may receive total care is essential if the life of children with thalassemia is to be made happier, more bearable and effective. The proposed legislation, in establishing treatment centers, is an obvious necessity if these goals are to be met.

III. SPECIFIC PROPOSALS IN H.R. 14016

A. Screening, counselling and treatment

1. *Screening and counselling.*—Because of the relatively high gene frequency among certain ethnic groups and because of the disastrous consequences of thalassemia, large scale screening programs among susceptible population groups, as proposed in HR 14016 will hopefully increase public awareness of the problem and provide genetic counselling to individuals who are carriers of thalassemia. In order of priority, the groups to be screened should include 1) high school students, 2) young couples, 3) children of primary school age and 4) pre-school children and infants greater than 6 months of age. Tests to detect thalassemia in the newborn are difficult and not amenable to large scale screening programs. Antenatal detection of thalassemia is also in the embryonic stages of development although hope for the future is promising in the light of recent research activities. (Science 174:689, 1971).

2. *Treatment.*—The proposed legislation will help create and support thalassemia treatment centers, where total comprehensive care can be provided by well-trained, well-equipped staffs. This would include specific therapy of the primary disease with blood transfusions as often as every 2 to 4 weeks and the use of chelating (iron-binding) agents to decrease the severity of chronic iron overload; treatment of complications with supportive assistance of a specific team of consultants from the following subspecialty departments; orthopedic and general surgery, gastroenterology, dental, cardiology, endocrinology, dermatology, psychology, psychiatry and medical social service; adequate blood bank facilities equipped to supply blood components and frozen blood; and intensive education program for affected children and parents regarding the nature, needs and emotional adjustments of a chronic illness. There are relatively few centers designed to provide total care for the patient with thalassemia; one such model is our clinic at The New York Hospital-Cornell Medical Center, which is supported by The Childrens Blood Foundation, a private philanthropic organization based in New York City. This clinic was founded in 1951 by Dr. Carl H. Smith and was the first out-patient facility of its kind in this country. Currently we care for 72 patients with homozygous thalassemia who require approximately 1300 patient visits per year. As with other chronic diseases of childhood, such as leukemia and hemophilia, total health care for diseases such as thalassemia should be provided in Pediatric Centers capable of meeting the many difficult needs of these patients.

B. Research

A number of important recent developments in thalassemia research have provided us with clues to the etiology of this inherited disorder. The proposed legislation, by providing $1,700,000 per annum for research grants and contracts to study diagnosis, treatment and prevention of thalassemia would aid considerably in the folowing areas: 1) the determination of the exact nature of the biochemical defect and the role of messenger RNA; 2) explorations into possible means of biochemically reengineering the abnormal gene in this disease; 3) antenatal diagnosis; 4) evaluation of chelation programs to decrease iron overload; 5) development and expansion of blood bank facilities to provide the best available product for the affected patient, e.g. frozen blood; 6) investigations of the pathology and pathologic biochemistry of iron overload; 7) effect of disease on growth and development, other organ function and malfunction; 8) hematologic reconstitution with transplantation.

C. Training

The proposed appropriation of $150,000 per annum would provide stipends for approximately 10 fellowships for training in thalassemia. This would appear adequate and realistic considering the number of institutions actively engaged in thalassemia treatment and research today, most of which have general training grants. The special merit of this program is to provide financial support for special trainees solely interested in pursuing research and clinical experience in thalassemia.

D. Information and educational materials

In view of the general public unawareness of the problem of thalassemia, an intensive informational and educational campaign would be required. The use of mass media, films, symposia for health professionals and laymen, and pamphlets and other printed material currently not generally available would be essential if such a campaign is to be effective. Accordingly, the proposed appropriation of $25,000 per annum may be inadequate to the dual goals of reaching

the susceptible high risk groups, screening them and providing genetic counseling and reaching the practicing physician and increasing his awareness of thalassemia, its diagnosis, treatment and prevention.

In summary, I enthusiastically support this legislation which will porvide funds where none currently exist. Specifically, the support of patient care, screening and educational programs are desperately needed. I thank you for permitting me to testify.

Mr. ROGERS. Thank you very much, Dr. Miller, for a very excellent statement.

Mr. Kyros?

Mr. KYROS. Thank you, Mr. Chairman.

Dr. Miller, is it a fact that presently the National Institutes of Health, with the research programs that they are carrying on, nevertheless, do not cover the many comprehensive steps you want taken in regard to Cooley's anemia?

Dr. MILLER. I think things are somewhat fragmented in that where there may be funds available for basic research, and very important and necessary research to understand the pathophysiology and genetics of this disease, what is lacking, really, is patient care, support for children and families who cannot afford a very expensive and, now, chronic therapy which persists for 15, 20, 25 years.

Genetic counseling programs have not been specifically funded. Large-scale screening programs have not been specifically funded, and patient care has not been funded.

Mr. KYROS. Except for those three items, screening, counsel, and patient care, would you say that the research should continue under that same formula of broad basic research as done by the NIH, or should Congress categorically put funds also into specific research for Cooley's anemia?

Dr. MILLER. I think in a disease like thalassemia, there is a happy marriage between what happens at the bedside at the clinic, and what happens at the laboratory bench. One cannot do laboratory research without taking care of patients. There is an important blending. One cannot operate in a vacuum without the other.

I think, wherever there are more funds available for disease that cries out for more research, for more knowledge and thalassemia certainly satisfies that, the more money available for all the activities, the faster we will learn more about the nature of this disease and how better to control it and treat it.

Mr. KYROS. There is nothing inconsistent with having categorical research in thalassemia while at the same time continuing in NIH all kinds of hematology and epidemiologic research on blood and related disease.

Dr. MILLER. I would agree.

Mr. KYROS. I think your testimony is most comprehensive and enlightening, and I thank you very much.

Mr. ROGERS. Doctor, let me ask you this question: I notice you say antenatal detection of thalassemia is also in the embryonic stages of development, although hope for the future is promising in the light of recent research activities. Then you give a quotation from "Science" or a citation. What is that citation?

Dr. MILLER. Dr. Nathan touched on this, but it was possible in the fifth month of gestation to detect synthesis of the beta hemoglobin chain. He also alluded to some of the work he is doing here. If it were possible to detect the abnormality of hemoglobin synthesis in early

gestation, it would be possible for, again, parental decisions to be made but, at least, one could be aware of a serious life-threatening and fatal situation before an infant is born.

I think genetic counseling is a better way to get at this problem. We are now capable of detecting many metabolic diseases through the use of sampling of amniotic fluid and, in this case, sampling actual blood from the fetus.

Mr. ROGERS. Are you aware of Dr. Pearson's screening technique?

Dr. MILLER. I became much more aware of it in the informal discussion at the break.

Mr. ROGERS. You know, we are always told that the scientific community is in such close touch that they know what is going on everywhere. They always tell us, you know, we don't need to change anything, we will just do the publishing bit. I have been concerned about that for some time. I think we may have to set up a commission or something to keep on top of what is actually happining.

Dr. MILLER. I think in all of our laboratories, we are working on potentially exciting areas. We are not exactly sure in the preliminary stages whether the data will confirm our original impressions.

Until that happens, until we have more solid feeling about what we are doing, we tend to work on it more, get stronger data, and then present it. At the time of a formal presentation in a scientific meeting, the rest of us find out what our colleagues are doing. I think it is justified in a way, because it avoids a great deal of premature pronouncements and, what may be unscientific material.

Mr. ROGERS. I can understand that, except for this: If a national institute finds that there is a breakthrough, or it would appear to be a breakthrough, even though you are not ready to publish, they ought to be able to go in and exploit that area quickly. For instance, in Boston, on lung cancer, it appears that we are making some progress there.

I am not sure it is being exploited. They are going to wait 2 to 3 years to publish. They may have to wait 5 by the time the investigator thinks in his own mind it is safe to publish. Maybe if they had someone come in and check this out and do some more research, and encourage more research, you could get it quicker and save lives. We have to change this technique somehow. I think publishing is a necessary part of it, but I think perhaps a better technique could be worked out.

Thank you very much for being here. I believe that concludes the number of witnesses. We are grateful to all of you. The committee recognizes the seriousness of this disease. We appreciate those who have taken the leadership in this area, particularly our colleague, Congressman Giaimo who has brought this to the committee's attention very dramatically.

Thank you all for being present. This concludes our hearing.

(The following letter was received for the record:)

YALE UNIVERSITY,
SCHOOL OF MEDICINE,
DEPARTMENT OF PEDIATRICS,
New Haven, Conn., May 30, 1972.

Hon. PAUL ROGERS,
Chairman, Public Health and Environment Subcommittee, Interstate and Foreign Commerce Committee, House of Representatives, Washington, D.C.

DEAR CHAIRMAN ROGERS: A pilot program for detection of thalassemia trait and related blood conditions has been conducted in several Greek-American communities in Connecticut. This program has been completed with no outside fund-

ing, as part of the research activities of the Division of Pediatric Hematology, Department of Pediatrics, Yale University School of Medicine.

The purposes of the program were (1) To access the validity and reliability of a simple inexpensive and readily available screening test for thalassemia trait. (2) To provide an estimate of the practicality and cost of a comprehensive program including educational, testing and counselling procedures. (3) To determine the prevalence of thalassemia trait in this community.

Although the final results of the program are not fully completed, sufficient data are on hand to permit specific conclusions.

(1) Determination of the erythrocyte mean corpuscular volume (MCV) with a commercial electronic blood cell counter (Coulter Model S) provides a reliable test for identifying individuals with thalassemia trait. An MCV of less than 78 cu μ is indicative of the reduced erythrocyte size characteristic of thalassemia trait. In our survey of more than 400 individuals there were *no* false negatives. A few persons with iron deficiency anemia also had low MCV's but in this population the incidence of the false positive result was less than 1% and was also important for the individual.

The Coulter Model S is widely used in community hospitals throughout the country. Electronic determination of MCV is rapid (about 15 seconds) is automatic, and inexpensive. Cost of materials is less than 5¢, and literally thousands of determinations can be performed in one day.

When an individual has been identifiied as having a low MCV, confirmatory studies are necessary. These can be performed on the same blood sample.

(2) Confirmatory tests for β thalassemia:

(*a*) Quantitation of Hgb A_2 by electrophoretic techniques

(*b*) Quantitation of Hgb F by alkali denaturation tests.

These tests identify instances of classical thalassemia trait, high fetal variety of thalassemia trait, and the Hgb Lepore variety of thalassemia trait.

(3) Confirmatory tests for α thalassemia trait and iron deficiency anemia.

If low MCV with normal levels of Hgb A_2 and F are documented measurement of serum iron binding capacity, will identify individuals with iron deficiency anemia. If iron studies are normal, family studies showing similar hematologic findings in a first degree relative confirm a diagnosis of *a* thalassemia trait.

This pilot program indicates: (1) The Greek-American community has been very receptive to a voluntary program for education, testing and counseling for thalassemia trait in their teenagers and young adults. The program appeared to evoke no anxiety or misunderstanding on the part of the community studied. (2) The program confirms the reliability of a simple inexpensive, and generally available laboratory procedure (electronic measurement of red cell MCV) as a screening test for detection of all cases of thalassemia trait with definite exclusion of 95% of the population who are not at genetic risk. Thus the more expensive corraborating tests such as hemoglobin electrophoresis only need to be performed on the small number of individuals with an abnormal screening result. (3) The prevalence of thalassemia trait in the American-Greek community appears to be about 7%.

I believe the study clearly indicates the feasibility of conducting comprehensive testing programs on a much more extensive scale in American communities at risk. Such programs would require federal funding.

I hope that you will be able to include this information in the hearing record on thalassemia.

Thank you very much for your interest in this matter.

Sincerely,

HOWARD A. PEARSON, M.D.,
Professor of Pediatrics.

(Whereupon, the committee adjourned at 1:10 p.m.)

○