S. HRG. 103-694

SICKLE DISEASE RESEARCH: AN UPDATE

OF THE

COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

ON

TO AWARD A GRANT TO THE LOUISIANA DEPARTMENT OF HEALTH AND HOSPITALS TO ESTABLISH AND CONSTRUCT THE NATIONAL CENTER FOR SICKLE CELL DISEASE RESEARCH AT SOUTHERN UNIVERSITY IN BATON ROUGE, LA, AND FOR RELATED FACILITIES AND EQUIPMENT AT SUCH CENTER

JULY 28, 1994

Printed for the use of the Committee on Labor and Human Resources

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SICKLE DISEASE RESEARCH: AN UPDATE

THURSDAY, JULY 28, 1994

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, DC.

The committee met, pursuant to notice, at 1:34 p.m., in room SD–430, Dirksen Senate Office Building, Senator Edward M. Kennedy (chairman of the committee) presiding.

Present: Senators Kennedy, Simon, and Wellstone.

OPENING STATEMENT OF SENATOR SIMON

Senator SIMON [presiding]. The hearing will come to order.

This is a hearing requested specifically by Senator Bennett Johnston, and we are pleased to have it. I am pinch-hitting temporarily for Senator Kennedy, who will be along before very long to join us for the hearing.

The hearing is about sickle cell anemia, a very major problem in our country, and the question is whether we are doing enough research in this field. In the whole field of science, there is no one in the U.S. Senate who is as knowledgeable as Senator Bennett Johnston. I have to say in candor, I do not know if that applies to sickle cell anemia, but I have worked with him on a variety of other scientific projects and have always been amazed at the depth of his knowledge.

One of the questions is whether we should be earmarking funds, and how do we make sure that we do the kind of research job that needs to be done.

So we are pleased to call on you, Senator Johnston, to open this up.

STATEMENTS OF HON. J. BENNETT JOHNSTON, A U.S. SENATOR FROM THE STATE OF LOUISIANA; AND HON. WILLIAM JEFFERSON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF LOUISIANA

Senator JOHNSTON. Mr. Chairman, thank you very much, and thank you for your very kind comments, which I appreciate.

Mr. Chairman, this bill would establish a sickle cell anemia research center at Southern University in Baton Rouge.

I have a written statement, which I would like to submit for the record.

Senator SIMON. It will be entered in the record.

Senator JOHNSTON. I think the members of this committee generally are familiar with the scourge of sickle cell anemia, which is

really the scourge of the African American community in this country.

The trait in the hemoglobin affects 10 percent of the African American population. Not that many are afflicted, but among that 10 percent, you never know where it is going to strike and when it is going to strike, and when it does, it is terribly severe, and it has just been a terrible thing for the African American community and one that cries out for research; there is not enough research being done.

The real focus, I think, of S. 1724 is not whether or not sickle cell anemia is serious enough to warrant the kind of Federal effort that this envisages. I think that question answers itself, and I think it is overwhelmingly in favor of the affirmative answer. Nor is it arguable that we know enough about it. I think we clearly need to do that.

The question is why Southern University. That, I think, is really the crux of this, and that was the question that submitted itself to the President who, on two occasions, endorsed and committed himself to a sickle cell anemia research center at Southern University in Baton Rouge. And it is a question that addressed itself to the Black Caucus in Congress, and the Black Caucus addressed the question, and every, single member of that Caucus—and I would like to submit for the record letter to Donna Shalala endorsing this research center, signed by each and every member of the Black Caucus, some of whom have in their districts institutions that do research.

So at least insofar as this administration and all of the members of the Black Caucus, they have made the determination that Southern is the appropriate spot.

So the question for this committee is why Southern. Well, we begin with the fact that Southern University is the largest historically black college or university in the country. It has 16,000 students, among whom are some distinguished graduates, some less distinguished—I am only kidding—my colleague, Congressman William Jefferson, seated beside me, is a graduate of Southern University undergrad and some other, much less distinguished, law school—Harvard, I think it was.

Thirty percent of the population of my State of Louisiana is African American, among which 10 percent have this sickle cell trait in their blood. That means 130,000 Louisianians have this trait.

More to the point, there has been a commitment by Southern University to fund this center. You will be hearing later from the president and the chancellor from Southern University, who will tell you more about that commitment, but suffice it to say that the State of Louisiana, through our Governor, and Southern University have committed to fund this institution, to keep its research funded as it goes on, and the legislature has voted $7 million which is now available in a fund for the construction. So that the commitment of the State of Louisiana, of Southern University, and of the legislature is complete and is not matched anywhere else in the country.

Now, what is their capability of doing this? Well, the legislation calls for, and there has been collaboration with Louisiana State University Medical School and Tulane University Medical School,

along with the other sickle cell anemia research institutions in the country, including NIH, Duke, and Children's Hospital of Philadelphia, which have all given resources and have, in the case of Tulane and LSU, committed to enter into cooperative agreements in setting up this institution, which in turn would draw upon the very best in research, the best experts in the country. The full-time faculty would be given tenure status at Southern University, to which Southern has committed.

So that what we have in effect is a total commitment from the administration, from the Black Caucus, from Southern University, from our Governor, from our legislature, and from the State of Louisiana to ensure that this institution would be the best and do the best kind of research that is possible to do.

Mr. Chairman, I do not think—I know—that there is no other institution that can make that statement. There are others that perhaps have, along with a lot of other research—NIH, for example, does very good research—but the African American community wants a place that they can identify as the clearinghouse where this is the principle endeavor, the principle focus, and the principal reason and raison d'etre is sickle cell research—not hundreds of other research endeavors, worthy though they may be, but one committed to sickle cell that they can claim as their own and that the State of Louisiana will fully support.

Mr. Chairman, I strongly urge this committee to act favorably upon this bill.

Senator SIMON. Thank you very much.

[The prepared statement of Senator Johnston follows:]

PREPARED STATEMENT OF SENATOR J. BENNET JOHNSTON

If you are an African American, and particularly if you are an African American parent, S. 1724 may be one of the most important pieces of legislation considered by the Congress this year.

S. 1724 establishes a national center for research on Sickle Cell Disease, a painful, life-threatening, inherited illness which affects African Americans almost exclusively. Approximately one in every twelve black Americans is born with the sickle cell trait; about one in every 400 has the disease.

Because it is genetic in origin, parents pass the disease to their children. If both parents carry the trait, one in four of their children, on a statistical basis, will have the disease. For thousands of African-American parents, the joy of childbirth is marred by fear, because in our present condition of medical ignorance, doctors do not know how to prevent the disease or cure it. The best they can do is treat patients for the excruciating pain which accompanies a disease crisis. Children afflicted with severe forms of the disease—about one case in four—do not usually live through adolescence.

No group of Americans should have to watch its children live and die in pain if there is anything the Congress can do about it. In this case, I believe that we can do something which will help those with the disease, and which will offer hope to those carrying the trait. We can establish a national center to serve as a resource for those affected by the disease and those trying to eliminate it: patients, trait-bearers, doctors, psychologists, counselors and researchers. This center would have three missions.

First, it would perform, or collaborate in the performance of research into the nature of the disease: a hemoglobin mutation which causes the distortion of red blood cells. Research will also be conducted in the areas of molecular biology and genetic engineering: including DNA manipulation.

The tragedy of sickle cell disease is that parents suffer as much as their afflicted children. The second function of a national center would be the examination of the psychosocial aspects of the disease, including the effectiveness of various counseling and education methods. Data from broad-based studies would be gathered to illu-

minate public policy issues such as the mandatory genetic testing of susceptible newborns.

Finally, a national center would function as a clearinghouse for all available information, both biomedical and psychosocial, about the disease. A national center is in a position to track ongoing research projects at universities and hospitals across the country, to organize their findings and disseminate this information, in an accessible form, to research scientists worldwide.

S. 1724 directs that this national center be located at Southern University in Baton Rouge, Louisiana. Founded 112 years ago, Southern is a land grant college with a distinguished teaching faculty. Its administration is committed to scholarship and the preparation of minority students for the professions, including medicine and the sciences. Southern is the largest predominantly African American university in the United States with over 16,000 students enrolled. Because its administration,faculty, students and alumni are all affected, directly or indirectly, by sickle cell disease, research performed at Southern will have an urgency and involvement not necessarily found at other institutions.

Location of the Center at Southern is supported by the State of Louisiana. Sickle cell disease is a serious public health problem for Louisiana's 30 96 minority population: one of every 10 African Americans in the state—130,000 people—carries the sickle cell trait. The Louisiana Legislature has indicated the strength of its commitment by appropriating $7 million for the project, contingent upon a three to one match from Federal funds.

Southern University is prepared, without reservation, to commit its resources and personnel to this project. The University will offer faculty appointments and a tenure track in order to attract qualified research faculty to the Center, and will encourage undergraduate students to work as research assistants. Realizing that there might be concern about establishing a biomedical research center at what is primarily a teaching institution, planners for the Center have made every effort to draw upon existing medical resources in Louisiana and in the sickle cell research community.

A team of eminent scientists with expertise in sickle cell research will act as a Technical Advisory Council to the director of the Center. A number of these experts including representatives of Sickle Cell Centers at NIH, Duke University and the Children's Hospital of Philadelphia have already participated in a planning session and submitted suggestions for projects to be undertaken by the Center.

Louisiana medical centers, including the Earl R. Long Memorial Hospital in Baton Rouge, the Louisiana State University centers at New Orleans and Shreveport and the Tulane University Medical Center, have indicated their support for the Center. They are willing to enter into collaborative arrangements to conduct clinical trials of the Center's research findings. Southern University's plan for a National Center is fully supported by the Louisiana community and, nationwide, by the sickle cell disease research community. It represents a systematic and well-thought-out attack on an important public health problem. Its research offers the possibility of finding a cure or, at the very least, a more effective treatment for an agonizing disease which targets a vulnerable segment of our population. It deserves the support of the Congress.

Senator SIMON. We are pleased to have Congressman Jefferson, who by now is a veteran in the House.

Mr. JEFFERSON. Thank you, Mr. Chairman. Good afternoon to you and to others who make up this committee.

I reluctantly admit that my Senator has covered just about everything that is important to be said here today and has covered it, I think, with a great deal of compassion and sincerity, which shows his strong commitment to this issue.

Those of us in Louisiana see him as a guy who works a lot of mundane little things, moving around the issues, and putting bills together. He exhibits his passion very carefully. But today, Mr. Chairman, I think we saw a dose of it, and I think that when he shows it, he really means it, and I am glad that he is working hard on this bill, which I think is worthy of all of our best efforts.

So I do appreciate the opportunity to appear before you today to give a brief statement in support of his bill, S. 1724, a bill to establish the sickle cell disease research center at Southern University.

I am in strong support of this legislation, and I hope that the Senate will pass this bill this year.

I want to commend you, Mr. Chairman, for your leadership in the area of medical research. You have been in the forefront in authorizing important research programs that will 1 day—and some have already done it—find cures for many of the diseases that are affecting millions of people around the world.

As a graduate of Southern University, as Senator Johnston has already informed you, which is the largest predominantly African American university in the country, I am proud that this center will be cited if this legislation passes—and we are hopeful that it will—at Southern University. Southern University has committed itself, its resources, and its personnel to seeing that this project is successful and that it produces a cure for this dread disease.

As Senator Johnston described in general, the sickle cell disease is a serious illness that disproportionately affects African American. One of every 12 African Americans is born with the sickle cell trait, and about one in every 600 develop the sickle cell disease. In my State, that means 130,000 people have the trait out of 1.3 million people, and approximately 4,000 people currently suffer from the disease in Louisiana.

Although the impact of this disease has been greatest in the African American community, it also occurs in other populations, including those of Puerto Rican, Cuban, Southern Italian ancestry, and more recently, other population groups.

Despite this well-documented data on this disease, despite its high incidence of occurrence and its spread to broader populations, there is no national research center seeking a cure for this deadly disease.

Mr. Chairman, sickle cell disease is a very painful disease caused by inadequate transportation of oxygen due to an abnormal type of hemoglobin molecule in the red blood cells. Even with medication, this disease will cause long-term suffering. Until recently, a person with this disease usually died before the age of 20. Victims of this disease have strokes, heart attacks, and other fatal illness due to oxygen loss.

We think it is time the Congress and the Nation make important steps to address this tragic oversight. The legislation before us today creates an excellent partnership between the Federal Government, State, and teaching universities in Louisiana. The State of Louisiana has already appropriated $7 million to match our request for a $21 million Federal grant from the Department of Health and Human Services.

Southern University has devoted significant resources toward the development of this research center, as Senator Johnston has talked about, and there will be a collaborative arrangement for joint research programs and projects between LSU, Tulane, and other medical and research institutions in our State and in our city.

Mr. Chairman, today, you will hear from a number of people involved in this project who are committed to making this national research center the best research facility on this issue in the world. I hope that you and the members of this committee will support this important bill.

Thank you very much for giving me this chance to appear before you.

Senator SIMON. I thank you both.

Let me just ask a question, and I am speaking for myself now and not for the chairman of the committee. How did you arrive at the $21 million figure? Ordinarily, in NIH grants, we have the peer review process. How do you handle that aspect of it to make sure that we really are spending our money wisely?

Senator JOHNSTON. First of all, they have formed a coordinating committee made up of researchers from all around the country—NIH, Children's Hospital of Philadelphia, LSU, Tulane, and Southern University has committed personnel to this—who have done the preliminary design upon which the $21 million—actually, it is $28 million, because the State of Louisiana has put up $5 million, and I think they have just appropriated an additional $500,000—so that comprises the $28 million figure.

Now, this will be a national center, drawing on the finest researchers from around the country. We do not intend to have this be an in-house research center, but rather a national center, funded, to be sure, by the State of Louisiana through the Southern University budget. But the researchers who are available from around the country will be those who do the work at Southern University.

Now, in terms of the peer review, Mr. Chairman, of course, it would be possible to say, well, let us do this research at NIH. But the legislature of NIH has not put up $7 million; the President has not committed to build this at NIH. The Black Caucus has not endorsed NIH. And I think it is because there is a particular feeling of—is the word "ownership" of this disease. I mean, this is a disease that afflicts African Americans, and Southern University is their institution, and there is that proprietary interest at Southern University. It is not just a Louisiana deal because it is endorsed by every, single member of the Black Caucus.

So I think that is the reason, rather than peer review. We expect the peers to be those who run the institution.

Mr. JEFFERSON. I would agree with what Senator Johnston has said, and in addition, I would say that there is nothing inconsistent about what we are doing here and the idea of peer review. There can be peer review of this proposal, and there can be done peer discussion about the funding levels. If someone wants to quibble about whether it should be lower or higher. So this does not prevent a real examination of whether this proposal ought to go forward as it is presented or whether it ought to be rearranged. But it does set a framework within which this discussion can take place, and that is really all that we are asking to have done here.

Senator SIMON. All right. I was not suggesting that it ought to be NIH, but simply that we ought to have some mechanism so that we make sure—and I do not mean this disrespectfully to Southern University—that we are really putting this where we ought to be putting the money.

Senator JOHNSTON. Oh, yes; we solicit that, we seek that, because indeed, we do want to make it a national institute of the very highest quality. So, yes, on oversight, during the construction, during the formulation of the research projects, we very much seek

that, and if the legislation should more explicitly say that, we would welcome that.

Senator SIMON. And real candidly, I was drafted at the last minute to preside here, as both of you understand, although I have been interested in this subject for a long time. And we appreciate your testimony. It is a worthy cause, and it sounds like something that we ought to be looking at very, very carefully.

I appreciate your being here. Thank you.

Senator JOHNSTON. Thank you, Mr. Chairman.

Mr. JEFFERSON. Thank you, Senator.

Senator SIMON. Our next witness is Dr. Claude Lenfant, Director of the National Heart, Lung, and Blood Institute at NIH. We are pleased to have you here, Dr. Lenfant, speaking in behalf of your institute.

Please proceed.

STATEMENT OF CLAUDE LENFANT, M.D., DIRECTOR, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE, NATIONAL INSTITUTES OF HEALTH

Dr. LENFANT. Thank you very much, Mr. Chairman.

I am very pleased indeed to be here. As you just noted, I am Claude Lenfant, and I am director of the National Heart, Lung, and Blood Institute, which is one of the institutes at the NIH which has just been discussed.

My institute is responsible for the sickle cell disease program that we are supporting, and the invitation which I received from Senator Kennedy was to discuss with you the sickle cell disease center that the National Institutes of Health supports.

I cannot think of a better way to present to you the national network of sickle cell disease centers that we are supporting than by telling you about the research accomplishments which have been realized since the creation of this network in 1972.

With your permission, I would like to take you very briefly through two charts which I have here. I hope you can see my little pointer here, with the red dots.

Senator SIMON. Yes.

Dr. LENFANT. OK. At the bottom, we have a span of three decades, from 1970 to the year 2000. Here, what you have is the research progress which has been accomplished during that period of time since we have been supporting the center and where we expect to go. You can see for each decade some very significant achievements which have been accomplished which have led us to where we are today.

Senator SIMON. Is the red line dollars spent?

Dr. LENFANT. The red line represents the progress which has been made and the accumulation of knowledge which is going to eventually bring us to a cure of this condition.

Senator SIMON. How do you measure that? When you put it on a graph, it looks very precise.

Dr. LENFANT. It is not that precise. It is a symbolic representation of the progress. What I am attempting to show you is that in the early 1970's, when the center network program was created, our knowledge was very low, very rudimentary, and over the years, with very significant support from the Congress, our knowledge has

increased to bring us close to what we believe is a cure for this disease. It is in sight. I cannot tell you whether it is going to be in 3 years or in 4 years, but I can tell you without any hesitation that it is in sight.

And basically, what you see on these charts is the history of the basic research that has been done—very basic research at the cellular, at the molecular level. And in fact, I am sure, Senator, you hear in Congress and elsewhere the term, "molecular medicine." Today, medicine is seen at the molecular level. And it may be of interest to you that the term, "molecular medicine," was invented in relation to all the discoveries and the advances which have taken place relative to sickle cell disease. In fact, the gene which controls this disease and which controls the hemoglobin, which we all have in our red cells, is really the gene about which we have the most knowledge today.

The second chart brings you the clinical research and the advances which have taken place during that period of time. Here, during the first decade, you can see great advances in comprehensive care, treatment of eye abnormality—in fact, I should tell you, Senator, that a great deal of the work concerning the eye abnormality comes from investigators from Chicago, from your State; at this point in time, we are no longer supporting them, but when they were supported by the Institute, we were extremely proud of the very remarkable work which came from Chicago.

I would like to underscore susceptibility to infection. So many of these children who are born with sickle cell disease are at very high risk of pneumococcal infection, which is a respiratory system infection, and would die from that. But through the research that has been done, we have found ways to prevent this complication, and we can see, as we move along from the 1970's to now, all the advances which have been made in prenatal diagnosis, in the prevention of stroke, which is a complication of this condition, the development of prophylactic penicillin to treat this infection that I was mentioning, the development of methods for newborn screening so we can identify babies born with the sickle cell trait and prevent occurrence of complications, and so forth.

Now, to finish my remarks, I would like to return to the first chart and tell you that the basic research that is ongoing today is bringing us to, if you will, the eve of finding a cure for this condition. And I am focusing most specifically on bone marrow transplantation and gene therapy, two therapies, two approaches, that the Congress hears a lot about from the research community.

Bone marrow transplantation is not yet used in many children. In fact, only 14 cases have been completed in the whole world—I believe, 6 in Europe and 8 in this country—with very, very interesting results. Gene therapy is also something which is getting to be in our possibilities, and n fact, within a couple of weeks, the National Heart, Lung, and Blood Institute is going to initiate a national program of gene therapy research for the cure of sickle cell disease.

We think that the prospects from these two therapeutic approaches are just enormous, and we are very confident that within some period of time—but again, I have to tell you I cannot say whether it will be in 2 years, 5 years, or 10 years—but we know

where to go, and we have the opportunity to do it, we have the basic science which permits us to reach the goals that we want to reach.

So when I was asked to come here and tell you about this national network of sickle cell research centers that has been supported by the Congress since 1972, I thought the best way to present that to you would be to say here are all of the things which have been accomplished, and this is where we are today and what we expect to accomplish within an attainable period of time.

I would be glad to answer questions, Mr. Chairman.

[The prepared statement of Dr. Lenfant follows:]

PREPARED STATEMENT OF CLAUDE LENFANT, M.D.

Mr. Chairman and members of the Committee, I am Dr. Claude Lenfant, Director of the National Heart, Lung, and Blood Institute (NHLBI), a component of the National Institutes of Health (NIH). I am pleased to appear before you today to present testimony about our research program in sickle cell disease and, in particular, about the Comprehensive Sickle Cell Centers grant program.

BACKGROUND

To place my testimony in context, let me review some basic facts about sickle cell disease, the most common serious inherited blood disorder seen in this country. It is characterized by recurrent bouts of pain called "crises," chronic anemia related to accelerated destruction of red blood cells, increased susceptibility to certain infections, and acute or chronic damage to various organs. Sickle cell disease results when the gene for defective ("sickle ") hemoglobin is inherited from both parents. In the United States, it occurs predominantly, but not exclusively, in persons of African ancestry; about 50,000 to 60,000 African Americans are affected. Medical costs for patients with sickle cell disease can be extremely high, quality of life is impaired, and loss of time from school or employment is common. Thus, sickle cell disease is a problem of significant psychological, social, and economic importance.

President Nixon's health message to Congress in 1972 identified sickle cell anemia as a major neglected health problem. The National Sickle Cell Anemia Control Act, subsequently passed by Congress, provided authorization to establish programs of research, research training, and demonstration service activities related to the diagnosis, treatment, and control of sickle cell anemia. The NIH was designated as the lead agency for the National Sickle Cell Disease Program, and the NHLBI was assigned responsibility for research and development activities and for coordination across federal agencies. The National Sickle Cell Disease Advisory Committee was appointed by the Secretary, Department of Health, Education, and Welfare, and charged with making recommendations on program direction and policy. The committee articulated the overall goals of the program as reduction of the frequency, morbidity, and mortality of sickle cell anemia through a program of research and development and demonstration activities in education, testing, counseling, patient referral, and rehabilitation.

THE COMPREHENSIVE SICKLE CELL CENTERS (CSCC) PROGRAM

HISTORY AND ACCOMPLISHMENTS

Among the advisory committee's first recommendations was a program of comprehensive centers focusing on the range of problems associated with sickle cell disease. The Comprehensive Sickle Cell Center (CSCC) program was established in fiscal year 1972 as a direct result of this recommendation. The program began operation with a total of 10 centers and increased to 15 centers in fiscal year 1973. The Institute has consistently supported 10 centers since fiscal year 1977, each for a five-year award period. Continued funding for the CSCC program was ensured in 1983 by the passage of Public Law 97-414, which directed the Secretary of Health and Human Services to "provide for the development and support of not less than 10 comprehensive centers for sickle cell disease."

The goals of the CSCC program are to conduct basic and clinical research to improve the diagnosis and treatment of sickle cell disease and prevent its complications. The program encompasses both scientific investigation and service so that advances in research on sickle cell disease can be translated readily into practice and

incorporated into the health-care delivery system. Each sickle cell center is comprehensive in that it integrates and coordinates fundamental and applied research with clinical applications and trials to assess various modes of therapy, with demonstration projects that address methods of disease diagnosis and approaches to patient counseling and education, and with training programs for health-care professionals and allied personnel that focus on the specific problems associated with sickle cell disease. By requiring each center to be comprehensive, the NHLBI ensures that a variety of models based on this approach are developed. Furthermore, by allowing each center to select its own area or areas of primary emphasis, the Institute encourages development of specialized expertise in individual centers that can serve as a shared resource for the entire program.

This unique program concept of interrelated investigational and service components has been noteworthy for accomplishments made possible by the synergistic interaction of scientific investigators and a well-informed patient population. Through this support mechanism, the scope and quality of research and clinical studies have increased markedly. Highly effective,innovative programs in education, diagnosis, counseling, and patient care have been created where none existed before. The program has proven successful in attracting talented scientists into studies related to sickle cell disease by providing challenging environments conducive to cross-stimulation and synergism between specialties. Collaborative efforts among center projects-and between centers enhance research productivity, facilitate technology transfer between research and clinical components, and ensure a knowledgeable study population through education and counseling.

The CSCC program has contributed to many important advances in understanding molecular mechanisms and the pathogenesis of sickle cell disease. Investigations conducted in the centers have led to: progress in basic sickle cell research and in management of sickle-cell-related complications; better understanding of gene expression and regulation of fetal hemoglobin synthesis; a scientific foundation for clinical trials of hydroxyurea as a therapeutic approach; modern DNA techniques for prenatal diagnosis of sickle cell disease; identification and classification of over 300 abnormal hemoglobins; and guidelines for ocular sequelae of sickle cell retinopathy. Clinical investigations have shed light on the natural history of sickle cell disease and provided a basis for the ongoing collaborative national study on the clinical course of sickle cell disease. The current centers have implemented additional collaborative clinical research protocols in preoperative transfusion therapy, pain management, acute chest syndrome, and use of magnetic resonance imaging to diagnose and follow the progression of cerebral and skeletal events.

REVIEW PROCEDURES

The continued quality of the Institute's CSCC program is ensured by a careful and thorough process that includes review and approval of the program concept by the National Heart, Lung, and Blood Advisory Council, peer review of individual grant applications, and internal review within the CSCCs. Grant applications in response to announcements for CSCC support are subjected to a multistage review process that parallels that for review of other large program grant applications. For example, in the most recent competition for CSCC grants (for funding in fiscal years 1993 through 1997), 20 applications were received and given an initial review by the parent peer review committee, a group of 18 expert scientists and clinicians convened by the NHLBI. Seventeen applications were recommended for further consideration. All were site visited by teams that included at least two representatives from the parent committee, as well as scientists, clinicians, educators, and other consultants with expertise in areas proposed by the applicants. Reports and recommendations of the site visit teams were then referred back to the parent committee for consideration at a second review meeting. Applications were evaluated according to a number of criteria, including the qualifications, experience, and commitment of the center director and senior personnel; the scientific merit and quality of the proposed projects; the adequacy of laboratory and health-care facilities and access to patients; the overall structure and management of the center, including scientific and fiscal management, integration of the parts, and quality control; the institutional commitment to the program; and the appropriateness of the budget. The parent committee voted a numerical priority score for each application, reflecting its overall merit. Reports and recommendations of the parent committee were then conveyed to the National Heart, Lung, and Blood Advisory Council for final review and consideration.

As with all NHLBI-supported programs, the review process does not terminate with award of the grant. Each of the CSCCs is required to submit an annual progress report for review by NHLBI program staff. NHLBI staff members also visit

each of the centers during the middle period of the grant cycle to provide constructive guidance and work with center staff to determine what improvements might be possible in their programs.

NHLBI Research in Sickle Cell Disease: Past, Present, and Future

The CSCC program has been and will continue to be an important element in our national strategy to reduce the burden of sickle cell disease. However, I want to emphasize that it is but one part of a much larger effort. For the past 22 years, the NHLBI has initiated and supported a broad-based program of basic and clinical research in sickle cell disease with the goal of reducing deaths and improving the quality of life for patients and their families. We believe our approach to achieving this goal has been logical and stepwise. It began in the laboratory, with studies at the most fundamental level of the red blood cell, moved to research on globin gene expression and regulation, progressed to epidemiologic studies of the natural history of sickle cell disease and, today, also encompasses clinical trials of potential therapeutic agents.

Let me give you a brief history of sickle cell disease research and summarize its most important advances. This information provides a context in which to view the contributions of the CSCC program, and offers important insights into where we have been, where we are now, and where we will be in the future as we move rapidly toward the twenty-first century.

In the 1970s, basic research supported in scientific laboratories throughout the country brought a tremendous revolution in our understanding of sickle cell disease at the molecular level. One of our earliest Institute initiatives focused on research to determine the mechanisms that regulate the 'switch" from fetal to adult hemoglobin during infancy. It had been recognized for some time that sickle cell patients who were fortunate enough to have inherited a tendency to continue producing fetal hemoglobin beyond the first year of life had relatively benign disease. Therefore, it seemed logical to pursue therapeutic modalities that would enable patients producing adult sickle hemoglobin to "switch back" to producing normal fetal hemoglobin. This research catalyzed the field of molecular biology, and became the cornerstone for development of therapeutic approaches based on increasing the level of fetal hemoglobin in patients with sickle cell disease- -work that continues to this day.

In 1977, sickle cell anemia became the first human disease to be described at the level of DNA and RNA. Breakthroughs that rapidly followed introduced gene mapping into prenatal diagnosis, and made it possible to use placental tissue rather than fetal blood samples. This substantially increased the safety of prenatal diagnosis for sickle cell disease, and rapidly led to the application of molecular genetics for prenatal diagnosis of other inherited diseases.

Very early on, it became apparent that, although much was known about the molecular basis of sickle cell disease, little was known about its natural history or clinical course. Only the sickest patients were described in the medical literature, and most clinical reports of patient outcomes were anecdotal and retrospective. There was, consequently, a poor understanding of the variable severity of the disease. In 1979, the NHLBI responded to the need for epidemiologic and clinical information with the Cooperative Study of Sickle Cell Disease (CSSCD).

The CSSCD—a large scale, multi-institutional study—recruited over 4,000 patients of all ages, from newborns to people in their sixth decade. The study clarified issues of growth and maturation patterns among children with sickle cell disease; defined causes of death in the pediatric population, showing longer survival rates than had been reported previously; described the epidemiology of painful episodes and documented, for the first time, that the frequency with which such "crises" occur is a predictor of premature death in adult patients; and pointed out the risks of alloimmunization for sickle cell patients receiving repeated blood transfusions. Most recently, exciting new data from this study showed that average survival of patients with sickle cell anemia has increased to 48 years of age for women and 42 for men. Previously, it was thought that the average patient rarely lived beyond 20 years of age. These findings, recently reported in the New England Journal of Medicine dated June 9, have provided renewed impetus for the search for long-term therapeutic agents to improve the quality of life for sickle cell disease patients.

As mentioned earlier, the CSCC program has had a major impact on the management of sickle cell disease. The centers have served as models for a revised management approach that places the central focus on the patient. Care that was previously fragmented, impersonal, and episodic has been replaced with a team approach, involving a cadre of trained personnel that include not only the clinician, but the nurse, social worker, psychologist, nutritionist, counselors, and allied health professionals.

In the mid-1980s, an NHLBI-supported clinical trial demonstrated the value of prophylactic penicillin in preventing major infections in infants and young children. Before that time, approximately 30 percent of sickle cell deaths occurred before five years of age, most in children under the age of two. Pneumococcal infection was the major cause of mortality in these early -years. Prophylactic penicillin has thus been among the most dramatic contributions to saving lives. This trial also provided the impetus for recommending that all newborns be screened for sickle cell disease. Infants at risk could then be referred for comprehensive care, and prophylactic penicillin therapy could be given by three months of age. Sickle cell disease is now included in the screening programs of more than 40 states.

Unfortunately, many children with sickle cell disease are faced with crippling central nervous system (CNS) complications, including strokes. Chronic transfusion therapy to maintain the level of sickle hemoglobin below 30 percent is, however, extremely effective in preventing the recurrence of strokes in such children. Current and future emphasis is on preventing the initial strokes by early detection of narrowed cerebral vessels and implementing therapy prior to CNS damage.

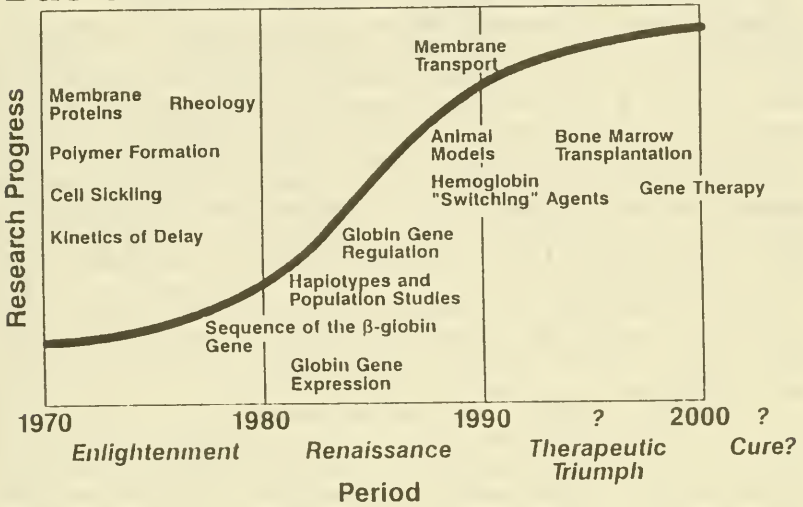
We see a new era of optimism for treating sickle cell patients. We are on the threshold of moving molecular medicine even closer to the bedside. The NHLBI is currently supporting a multicenter clinical trial using hydroxyurea in 21 centers around the country. Approximately 300 severely affected adult patients are enrolled. Now entering its third year, this trial is investigating one of many agents identified as able to "turn on" the production of fetal hemoglobin in patients with sickle cell anemia. If efficacy and safety are proven, hydroxyurea will be the first agent to become available as an effective therapy for sickle cell disease. Erythropoietin, a hormone, also significantly increases fetal hemoglobin synthesis. The recent availability of recombinant erythropoietin, a major scientific advance, made it possible to use this drug in combination with hydroxyurea. This combination approach offers the possibility that lower doses of hydroxyurea can be-used to achieve the required therapeutic levels of fetal hemoglobin.

Because we recognize that this approach will not achieve therapeutic levels of fetal hemoglobin in all patients, parallel research efforts to seek other strategies are continuing. Looking into the future, gene therapy and bone marrow transplantation appear to offer the best hopes for a cure of sickle cell disease. Bone marrow transplantation has been successfully used by several investigators in Europe, as well as a small number in the United States. Although early reports are promising, patient selection, donor availability, and complications of the procedure continue to be potential problems that prevent widespread use of this therapeutic modality today. Gene therapy research is advancing, with the possibility of inserting normal genes for hemoglobin production into the bone marrow precursor or stem cells, thus leading to the production of normal hemoglobin. This approach is receiving active attention by many researchers around the country and is the subject of a targeted research program recently initiated by the NHLBI.

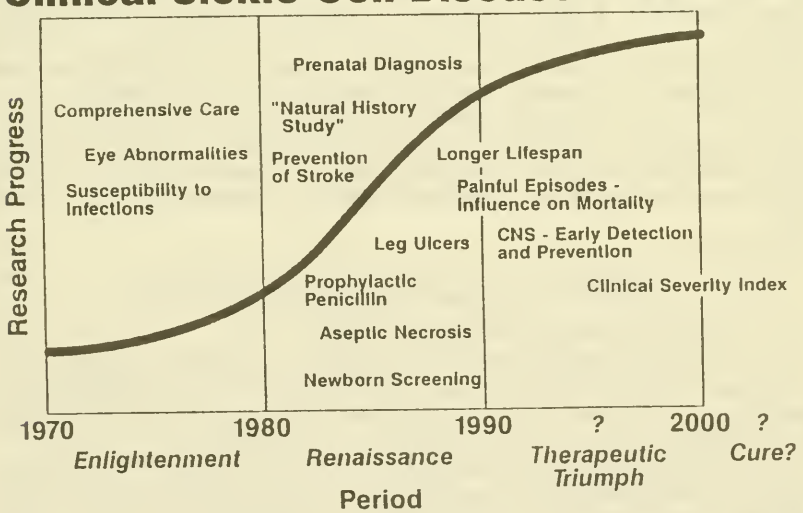
A number of opportunities exist for further advances in sickle cell disease research. What needs to be done was best stated by the Sickle Cell Task Force on Investigator-Initiated Research. Its report defined areas of research that currently hold the greatest promise for achieving a cure for sickle cell disease, including: development of mice that serve as models of sickle cell disease, improved understanding of factors important in the switch from fetal hemoglobin to adult hemoglobin, targeted studies of methods for gene insertion into primitive blood cell precursors, and fundamental studies of red cell structure and metabolism. Also recommended were epidemiolcgic investigations of the role of clotting and clot dissolution in sickle cell crises and additional studies on the natural history of sickle cell disease. The NHLBI is strongly committed to a balanced and innovative approach to achieve our national goal of reducing the personal and public health burden of sickle cell disease.

I would be pleased to answer any questions the Committee may have.

History of Basic Sickle Cell Disease Research



History of Clinical Sickle Cell Disease Research



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Senator SIMON. Thank you.

We now have 10 sickle cell centers.

Dr. LENFANT. That is correct.

Senator SIMON. How would the center that is now being proposed for Southern University differ from those centers?

Dr. LENFANT. Well, I should say to you, Mr. Chairman, that we have not seen a detailed description of the proposal that would be presented by the university. I have heard the two previous witnesses, and many of the things which they have discussed, describing research that would span from very basic to clinical, describing supports to the community and to the patients, treatment, care, counseling, and all of these things, there is a very remarkable similarity between what I think I have heard here and what our centers are now supporting.

Senator SIMON. We will have to make a decision on this, obviously. If you were a member of the U.S. Senate, would you vote for it? Is this a wise way to invest the money in terms of achieving the breakthrough?

Dr. LENFANT. That is a very difficult question. Let me answer it this way, if I may. The more research we support, the faster we are going to get where we want to be. Just a few months ago, I testified before the Appropriations Committee of the Senate for my budget, and Mr. Harkin asked us, if you had so much more money, what would you do? And my answer is basically the answer that I am giving you today, that we know where to go, and we know we are going to reach it; if I have more money, I will reach it faster. I think that is a decision which is not within my purview.

Senator SIMON. I understand. We thank you very, very much. Senator Kennedy and other members of the committee may have some questions for you.

Dr. LENFANT. I will be here, Senator, for the duration of the hearing.

Senator SIMON. Thank you. And they may be submitting some in writing. Senator Kennedy had planned to be here by now.

My difficulty right now, frankly, is that I am supposed to be at another meeting. I think what we had better do is recess temporarily until Senator Kennedy gets here, or another member of the committee can get here. So we will take a temporary recess at this point.

[Recess.]

OPENING STATEMENT OF SENATOR KENNEDY

The CHAIRMAN. We will come to order.

I am enormously grateful for the understanding and patience of our witnesses this afternoon on a subject which is of enormous importance to all of us on this committee and something which I have been involved in for a very extensive period of time.

As the Senate schedule has indicated, we are caught in this situation of advancing the hearing and sharing the leadership in chairing the hearing, so we are very, very grateful to all of those who have testified and for the testimony we will receive.

I will put my full and complete statement in the record, and we will utilize the time we do have to hear from some very special people.

[The prepared statement of Senator Kennedy follows:]

PREPARED STATEMENT OF SENATOR KENNEDY

Despite the unprecedented growth in scientific knowledge and the ability of medical science to diagnose, prevent, treat, and cure many illnesses, sickle cell disease continues to devastate the lives of tens of thousands of Americans.

Sickle cell disease affects an estimated 50,000 African Americans. It is a hereditary illness that occurs in 1 out of every 625 African American infants born in the United States. The death rate for the disease during infancy can be as high as 30 to 35 percent if treatment is delayed or inadequate. Those living with the disease own have frequent attacks of severe pain. They suffer strokes at an early age and endure debilitating joint and bone disease.

The severity of the symptoms and life expectancy vary considerably. Some patients survive beyond middle age. But many die in childhood, and many others die in infancy. Treatment for this chronic illness is expensive and the disease places a heavy psychological burden on patients and caretakers alike.

The disease was first diagnosed in the United States in 1910 by Dr. James Herrick. The discovery was made on a dental student from Grenada, rather than on the thousands of African Americans with the disease. It was called sickle cell anemia because of the characteristic sickle shape of the red blood cells in patients with the disease.

Ih 1949, Dr. Linus Pauling discovered the association of sickle cell anemia with an abnormal form of hemoglobin, and later won the Nobel prize for his work in this area. Eight years later, the molecular basis of the disease was discovered in one of the landmark breakthroughs in the field of human genetics. Dr. Vernon at Massachusetts Institute of Technology demonstrated that the hemoglobin in patients with sickle cell anemia differed from normal hemoglobin by a single amino acid substitution on the beta chain of the protein. In 1977, Dr. Bernard Forget identified the particular gene responsible for the disease.

Patients with the disease inherit a sickle cell gene from both parents. If each parent has a sickle cell gene, one-quarter of the children on the average will inherit both genes and will have the disease.

Half of the children will inherit one of the genes. They will be carriers of the genes, and can pass it on to their own children. Their condition is called sickle cell trait, and 8 percent of African Americans have it. The sickle cell gene has persisted in operation even though a double dose of the gene is so lethal, because the red cells of individuals sickle cell trait are less vulnerable to the malaria parasite.

In spite of the remarkable knowledge that science has gained as a result of sickle cell research, there has been a continuing perception over many decades that U.S public health policy has not given enough priority to prevention of the disease and treating those who suffer from it. The perception is especially troubling because of the racial nature of the disease.

In 1971, in response to these concerns, I joined Senator John Tunney, Senator Ed Brooke, and other Senators in sponsoring the

National Sickle Cell Anemia Act, which was signed into law by President Nixon the following year. I still regard it as one of the most important health bills I have ever introduced.

The Act contained numerous provisions on screening, counseling, research and training. It included programs to educate the public about the disease and to facilitate early diagnosis, and effective treatment.

In 1972, the National Institutes of Health established the Sickle Cell Disease Branch of the National Heart, Lung and Blood Institute. In the years since then, Congress has enacted legislation to strengthen basic and applied research, to provide more extensive testing, counseling, and treatment and to expand public information and education programs.

An important provision in the Orphan Drug Act of 1983 provided support for the establishment of 10 Comprehensive Sickle Cell Centers around the country. These national centers are now well-established. They are located in Alabama, Georgia, Massachusetts, North Carolina, Pennsylvania, and Tennessee, and two centers are located in New York and California these centers are at the cutting edge of research on the disease, and there each receive Federal support of $1 to $3 million a year. Since 1972, the Federal grant has spent $610 million on sickle cell research, and the amount for the current year in $46 million.

The developments over the past two decades have seen significant improvements in the treatment of patients with the disease. Thirty years ago, 50 percent of patients with the disease died before the age of 20. Today, 50 percent live past the age of 50. Much of the recent progress has come from research conducted by the ten Comprehensive Sickle Cell Centers around the country and from research supported by the Sickle Cell Disease Branch of the National Heart, Lung and Blood Institute. These Centers have successfully brought together experts in basic science, clinical research, and psychosocial research to address the multitude of problems faced by those with the disease.

In the important effort to find a cure for the disease, promising research is being carried out in bone marrow transplantation and gene therapy. In addition, promising new anti-sickling drugs are being tested.

In spite of these advances, much remains to be done. Our hearing this afternoon will assess the effectiveness of all aspects of our current efforts, identify unmet needs, and try to develop a strategy to achieve more rapid progress in the coming years.

I look forward to the testimony from our witnesses today, and to working closely with my colleagues on the committee and in the Congress to achieve this goal.

The CHAIRMAN. Shawnita Agnew is an honor student at English High School in Boston. In September, she will be a freshman at Fisher College. She is a team leader in sickle cell support for children, and she will share her experience with sickle cell disease. Her mother is here as well, Ms. Sharon Agnew Stewart, who is a sickle cell counselor.

We also welcome Lillian McMahon, who is director of the Comprehensive Sickle Cell Center at Boston City Hospital and has successfully brought together experts in basic science research, clinical

research, and psychological research, to address the many problems faced by those who have the sickle cell disease.

We also welcome Dr. Ernest Turner, who is director of the Comprehensive Sickle Cell Center at Meharry Medical School in Nashville, TN. Clinical studies at Meharry have vast improved the understanding of sickle cell disease and its treatment; and Dr. William Moore is vice chancellor for Academic Affairs at Southern University, and is the principal investigator at two research centers, minority institution projects funded by NIH.

Shawnita, we are glad to hear from you. We know that you have endured a good deal of personal discomfort in joining us here today, and we are also very mindful that it is difficult to share one's health experiences and needs publicly, so we are certainly grateful to you for your willingness to be here and for all the good things that you do. We want you to know that the best way we can thank you is to redouble our energy and commitment in terms of both the research and, hopefully, solutions, to some of these challenges.

We are thankful to you for being here today, and we look forward to hearing your comments. So if you would like to make a statement, we would be glad to hear from you now.

STATEMENTS OF SHAWNITA AGNEW, HONOR STUDENT, ENGLISH HIGH SCHOOL, BOSTON, MA; LILLIAN McMAHON, M.D., DIRECTOR, COMPREHENSIVE SICKLE CELL CENTER, BOSTON CITY HOSPITAL, BOSTON, MA; ERNEST A. TURNER, M.D., DIRECTOR, COMPREHENSIVE SICKLE CELL CENTER, MEHARRY MEDICAL SCHOOL, NASHVILLE, TN; WILLIAM E. MOORE, M.D., VICE CHANCELLOR FOR ACADEMIC AFFAIRS, SOUTHERN UNIVERSITY, BATON ROUGE, LA; KWAKU OHENE-FREMPONG, M.D., DIRECTOR, COMPREHENSIVE SICKLE CELL CENTER, THE CHILDREN'S HOSPITAL OF PHILADELPHIA, PHILADELPHIA, PA; AND HON. CHARLES D. JONES, LOUISIANA STATE SENATOR

Ms. AGNEW. Hi. My name is Shawnita Agnew, and I am a young lady who lives her life every day with a disease called sickle cell anemia.

As a child, living with this disease was very hard for me. I really did not understand it as much as I do now. Many times, I would have to be admitted to the hospital with terrible pain in my legs, my back, my arms, and sometimes my chest. I would need to stay many days, weeks, sometimes months, with i.v. medication, oxygen, and sometimes, blood transfusions, until the pain was bearable enough to go home and later return to school.

As a child, I did not really understand why I could not participate with other children when they would swim, play running games, and so on. I could not get too hot or too cold, excited, or sad. It really confused me.

As I got older, I started to understand the disease more, but I still did not participate as much. But I started to learn to live with it. Together with other kids from Boston City Hospital, we formed a teen group for support with each other.

I will be working with this teen group and recruiting younger kids and helping them to understand and deal with the disease.

Now, being 18 years of age, I have really learned how to take care of my sickle cell anemia. When I swim, I know to keep warm. When I go out in the winter, I know to dress warm. When it is hot, keep cool, and drink a lot.

In September, I will be moving on to Fisher Junior College to study early childhood education, and I hope to become a teacher. I think I have improved 90 percent from what I used to be.

The model for our teen support group is "A Cure in My Lifetime." Please help us get there.

Thank you.

The CHAIRMAN. Thank you very much. We will come back to you for some questions.

[The prepared statement of Ms. Agnew follows:]

PREPARED STATEMENT OF SHAWNITA AGNEW

Senator Kennedy and members of the committee, hi, my name is Shawnita Agnew and I am a young lady who lives her life every day with sickle cell disease, which doesn't bother me any more.

As a child living with this disease was very hard for me. I really didn't understand it as much as I do now. Many times I would have to be admitted to the hospital with terrible pains in my body and needed to stay for days with I.V.'s, sometimes blood transfusions, and medications until the pain was bearable enough for me to go home and later on return to school.

As a child I really didn't understand why I couldn't participate with the other children when they would swim, when they would play running games, and etc. I couldn't get cold or hot, excited or sad, it really confused me. Any of these things could bring on a sickle cell crisis and I would end up in the hospital again.

As I got older I started to understand this disease more, but I still couldn't participate as much. But I started to learn to live with it. Together with other kids from Boston City Hospital and two other hospitals we formed a mutual support team for teens with sickle cell disease at the Boston Sickle Cell Center. Together we shared our experiences and learned more about the disease. Together we wrote a booklet for teens by teens on what it is like to have sickle cell disease. We worked on many art projects and Teens for Peace. I will be working with the Teen group this year in recruiting younger kids and help them understand and deal with their disease.

Now as me being 18 years of age I have really learned how to take cars of my sickle cell disease myself. When I swim I know to keep warm. When I go out in the winter time I know to dress warm. When it's hot I know to keep cool and drink too much. So basically living with sickle cell disease doesn't bother me now. I live my life as a regular life. It seems like I'm a normal person now. My mind has accepted the fact.

In September I will be moving on to Fisher Junior College to study Early Childhood Education and I hope to become a teacher. I myself think have improved 90 percent of what I used to be.

The motto of our Teen Group is "A Cure In My Lifetime". Please help us get there. Thank you.

The CHAIRMAN. Dr. McMahon.

Dr. MCMAHON. Thank you, Senator Kennedy.

I have to say that Shawnita did not mention that she is right now in the middle of a painful crisis. I offered to read her testimony here before the committee, but she was determined to come in spite of it to speak to groups of people who are important in maintaining research and treatment of sickle cell disease. Thanks, Shawnita.

We have travelled a long way since the age of 3, when she was diagnosed with sickle cell disease, and there have been many, many, many admissions for pain, for surgery, for infection, and a couple of near misses. So she has come a long way, and she did not

mention that she did receive the headmaster's award in her school, and many scholarships which will allow her to go to Fisher.

I want to thank you, Senator Kennedy, and the committee for inviting me here to speak about the Boston Comprehensive Center. The Boston Center is one of 10 national comprehensive centers in the United States, all of which work in an academic environment within a university and medical center, which is actually essential to bring both researchers and clinicians together so that research does not happen in a vacuum, in a laboratory, and clinicians are not delayed in delivering the most important findings of research to their patients.

So Boston Sickle Cell Center is particularly important that it has affiliated four medical schools—Harvard, Tufts, and Boston University—and our six research projects take place in six university-affiliated hospitals and one graduate school.

The Boston Center has really concentrated their research in red cell membrane, endothelial adhesion and hemoglobin switching. It is really impossible in 5 minutes to tell you the accomplishments of the center, but I will try to highlight them.

In red cell membrane, our investigators have focused on understanding the alterations of the red cell membrane which contribute to the disease. For example, one group of our researchers under Jiri Palek has discovered sites in the red cell membrane where the polymers of hemoglobin will penetrate, disrupt the membrane, damage it, and cause cell damage. This then causes sickling, causes the red cells to stick inside the lining of the blood vessels and occasions obstructions to blood flow and produces pain or organ damage. This is vital knowledge that has increased our overall understanding of the disease.

Another group of our researchers under Dr. Carla Brugnara has developed a novel approach in attempting to prevent the dehydration of the red blood cell which occurs in sickle cell disease. They began with the premise that a certain channel within the red cell called the Gardos channel, which is calcium-dependent, has a primary role in the potassium loss and dehydration of the red cells. They demonstrated in vitro that inhibitors of this channel actually would block the water loss from the red blood cells. And one such inhibitor, a drug called clotrimazole, which is a very common drug used in treating fungal infections in the general population and actually had concentrations lower than what is routinely used, is actually effective in doing this. They studied this in transgenic mouse model of sickle cell disease and demonstrated that indeed it is effective in preventing red cell damage. And on the basis of this very exciting and promising work, we are now embarking on phase one trials with patients with sickle cell disease, and Shawnita is one that is looking at joining one of these trials.

Another approach in research of our group has been in hemoglobin switching, one in which researchers look for drugs that will promote the bone marrow to increase production of fetal hemoglobin instead of sickle in patients with sickle cell disease. This prevents sickling.

Well, the study of hydroxyurea originated in Boston by sickle cell researchers, and this drug does indeed promote the bone marrow to produce cells with a greater amount of fetal hemoglobin and, in

selected patients who have been put on clinical trial, it decreases the tendency to sickle and ameliorates their disease. It actually diminishes the frequency and the intensity of the crisis.

There are further trials that are now taking place in a multicenter fashion.

Another drug that also promotes the increase of fetal hemoglobin is butyrate. Dr. Perrine, a researcher at the California center, has now transferred to our center and has been very important in the investigation of this drug, and clinical trials are now in progress with this drug in sickle cell disease and thalassemia.

Sickle cell disease is a disease that affects persons from birth as long as they will live. We are increasingly happy to see how much longer patients are living as a result of better medical care and translating research results into clinical care.

So as a result of the penicillin prophylaxis study which Dr. Lenfant mentioned, this was a landmark, multicenter study which demonstrated that administering penicillin twice a day to children prevents the mortality, which was as high as 30 percent, in the first 3 years of life and decreased the morbidity of infection. As a consequence of that, newborn screening has been instituted in a majority of the States in this country, so that our center was instrumental in establishing newborn screening in Massachusetts.

Babies, as soon as they are identified, are placed on penicillin, which will prevent that tremendous human loss which we saw before this study was published. In addition, in Massachusetts, in conjunction with the department of public health, we have arranged so that any family that does not have insurance or a way of buying penicillin will receive free penicillin for the first 7 years of life.

The Boston Center serves also as a resource to the New England area. When Rhode Island initiated newborn screening, it was the Boston Center that did newborn screening for Rhode Island until the New England Regional Newborn Screening Program took over this task. We are also a resource to New England States for testing, counseling and consultation.

In Rhode Island, we helped establish a sickle cell clinic in Women and Infants Hospital, and we continue to do testing for Maine, New Hampshire and Vermont. Outside the United States, we have served as consultation for the establishment of two clinics in England, and in Brazil, we continue to share our experience in basic and clinical research and educational materials, which I have helped to translate into Portuguese, in their efforts to establish screening and start sickle cell clinics.

The physicians of the Boston Sickle Cell Center are responsible for over 400 patients in the greater Boston area and serve as consultants for the entire State, and again, for the region. Our population is mostly African American, African, Haitian, Cape Verdean, Puerto Rican, and other countries from the Caribbean, Central America and South America. To better serve this population, we try to hire Spanish-speaking, Haitian-Creole-speaking, and myself, as both Puerto Rican and Portuguese, also help to address many of our patients needs and anxieties in their own language.

Recently, as you are well aware, we have a very significant number of refugees from Somalia, which are increasing in numbers,

whom we are now testing and will be counseling and enrolling any patient that we discover in comprehensive care.

Finally, because the ultimate goal of the combined efforts of all researchers in the 10 national centers is to find a cure, we are tremendously pleased to know that the National Institutes of Health will be funding three projects in gene therapy this year. We, along with other centers, are also participating in bone marrow transplantation studies for young patients with sickle cell disease.

There is so much more that I would like to tell you about my center, but I know there are other colleagues here who are equally eager to tell you about the accomplishments in their centers. Again, I thank you for inviting me here to tell you about this.

The CHAIRMAN. Thank you very much.

[The prepared statement of Dr. McMahon follows:]

PREPARED STATEMENT OF LILLIAN CALDEIRA MCMAHON, M.D.

Dear Senator Kennedy, thank you for inviting me to testify on the Senate Committee on Labor and Human Resources hearing on Sickle Cell Research next Thursday, July 28, 1994.

The Boston Comprehensive Sickle Cell Center is one of ten national comprehensive centers funded through the Sickle Cell Branch of the National Heart, Lung and Blood Institute. Each of the ten Sickle Cell Centers operate within the academic environment of a university and medical center which allows tar a productive collaboration between researchers and clinicians and for continuity of care of patients.

The Boston Sickle Cell Center is especially fortunate to have three medical schools, Tufts, Harvard, and Boston University, affiliated with our program. Our six research projects in red cell membrane, endothelial adhesion and hemoglobin switching are conducted in six university-affiliated hospitals and a graduate school, Northeastern University. This academic and clinical environment brings together a community of scholars, researchers, clinicians and other health professionals, which are vital to progress of sickle cell research and treatment of patients with sickle cell disease.

It is almost an impossibility to report to your committee the accomplishments of the Boston Sickle Cell Center in only five minutes allowed for this presentation. However I will attempt to highlight some of our achievements.

Investigators in the Boston Sickle Cell Center have focused on understanding how alterations in the red cell membrane contribute to the pathogenesis of sickle cell disease. Such knowledge could lead to the development of therapeutic strategies that prevent the dehydration that is such a critical determinant in the formation of intracellular sickle hemoglobin polymers. Even a modest reduction of the hemoglobin concentration inside the red cell could have a marked effect in inhibiting sickling.

Dr. Carlo Brugnara and co-investigators in the Boston Sickle Cell Center have developed a novel approach based on these principles. They began with the premise that the calcium dependent Gardos channel inside the red cell assumes a primary role in the loss of potassium and cell dehydration that accompanies sickling. They have demonstrated that, in vitro, inhibitors of the Gardos channel could block water loss from sickle red cells. One of these inhibitors, clotrimazole, a commonly used antifungal agent, was fully effective on sickle red cells at concentrations lower than that used in patients routinely treated with the drug. They then tested this drug in a transgenic mouse model of sickle cell disease and demonstrated the efficacy of the drug in vivo in preventing the dehydration of sickle red cells. On the basis of these exciting and promising findings, these investigators, in collaboration with another Boston Center investigator, Dr. Orah Platt, are embarking on a phase I clinical trial in patients with sickle cell disease.

Also in red cell membrane research Dr. Jiri Palek and collaborators discovered sites in the red cell where polymers of hemoglobin penetrate disrupting the membrane, causing breakage and cell damage, which in turn leads to stickiness of the cell inside the blood vessels and obstruction of blood flow all this resulting in pain to the patient and organ damage. This important work was published in the journal Science.

Research using the drug hydroxyurea originated in Boston by sickle cell researchers. Hydroxyurea promotes the bone marrow to produce greater quantity of red cells containing fetal hemoglobin and decreases the tendency of the. red blood cells to

sickle. The use of hydroxyurea in selected patients with sickle cell disease resulted in diminishing the frequency and intensity of their sickle cell crises. Further clinical trials continue in Boston and other Centers with careful monitoring of patients by sickle cell researchers and clinicians.

With the transfer of Dr. Perrine and her research project from the California Sickle Cell Center to our Center in Boston we are continuing the investigation of other drugs, such as butyrate, which also promotes the bone marrow to switch from producing sickle hemoglobin to producing more fetal hemoglobin. Clinical trials are now in progress with patients with sickle cell disease and with thalasseaia.

The Boston Center participated in the landmark multicenter study of penicillin prophylaxis in children with sickle cell anemia which demonstrated that administering penicillin twice daily to children with thin disease prevents the mortality which was as high as 30Q in the first 3 years of life and diminishes the morbidity caused by certain bacterial infections in children.

As a result of the findings of this study screening for sickle cell disease in newborns was instituted in most states in the U.S. As soon as babies are identified as having sickle cell disease they are started on penicillin prophylaxis, preventing the tremendous human loss we experienced before this study. The Boston Center was responsible for establishing universal newborn screening for sickle cell disease and other hemoglobinopathies in Massachusetts in 1988 and performed sickle cell screening of newborns for the state of Rhode Island as part of a Special Program of National and Regional Significance grant. We now serve as consultants to the Now England Regional Newborn Screening Program and are responsible for the medical care of babies identified through this program in Massachusetts. Once identified, newborns with Sickle call disease are started on penicillin prophylaxis and enrolled in a comprehensive medical care program. We continue to screen for the states of Vermont, Maine, and New Hampshire.

We serve as a resource for the New England states for testing, education and counseling, and for consultation concerning sickle cell patients. The Boston Sickle Cell Center participated in the establishment of the Sickle Cell Clinic in Women and Infants' Hospital in Rhode Island. Outside the country we assisted with consultation in the creation of two programs for screening and clinical management of patients with sickle cell disease in England, and share our experience in basic and clinical research, as well as educational materials with our colleagues in Brazil in their efforts to establish screening programs and start sickle cell clinics.

Boston Sickle Cell Center physicians deliver comprehensive medical care to over 400 patients with sickle cell disease. Our population is diverse and comprised of African Americans, Africans, Cape Verdeans, Haitians, Puerto Ricans and persons from other Caribbean, Central and South American countries. To best meet the needs of our patients the Boston Center has staff who speak Spanish and Haitian Creole. Myself, as being both Puerto Rican and Portuguese, am able to address many of our patients in their native language, which facilitates communication and helps ease patients' anxieties. There is presently a significant and increasing number of refugees from Somalia in Massachusetts which the Boston Center will test and counsel concerning sickle cell disease, and enroll in comprehensive medical care.

There is so much more that I would like to relate to you and your committee but I understand that my colleagues from two other Sickle Cell Centers are equally excited and eager to report the accomplishments of their Centers.

Finally, because the ultimate goal of our combined endeavors is to find a cure, we are tremendously pleased to hear that the Sickle Cell Branch will fund 3 projects in gene therapy this year.

Again I thank you for this opportunity to report some of the achievements of the Boston Sickle Cell Center to your Committee.

The CHAIRMAN. Dr. Turner.

Dr. TURNER. Thank you, Senator Kennedy, for the opportunity to speak before you and your committee this afternoon.

We have given you some written information, and I would like to focus my comments around three of the slides that I have prepared for you to try to give you an overview about our center. This also, I think, gives a better overview of all the centers in the United States that are currently funded by the NIH. This slide is the last one in my packet that gives you an overview of the program components that all of the centers currently have.

We are all involved in research activities, which includes both basic and clinical activities. We all serve as resources for our sur-

rounding communities and catchment areas. I am at Meharry Medical College in Nashville, TN, and I serve the 21 counties as my catchment area of Tennessee, and in addition to that, I serve as the consultant for the State of Kentucky, especially southern Kentucky, where we are responsible for that patient population.

In addition, all the centers have a major role in making sure that information is disseminated to the lay public and to our own colleagues, who many times are not aware of new developments that may happen in our centers and other research activities.

We have major psychological support in our institution in terms of research activities. We have a joint partnership with Vanderbilt University, where many of our psychological projects are conducted with their staff at Peabody Institution, which is a major institution that has been involved in research and psychological activities in the United States for many, many years.

We are involved in counseling, and we also have the State contract for making sure that individuals who are diagnosed with sickle cell trait in the State of Tennessee get information that is appropriate for the type of hemoglobin variant that they have.

We have not talked about yet in this hearing that there are over 700 known hemoglobins right now in the United States that are documented, recognized, and known. Thus, there is a wealth of information that needs to be translated to a variety of individuals. As was mentioned earlier, we have State newborn screening programs, and on a daily basis in our laboratory—I am the reference laboratory for the State of Tennessee—we are always getting this "alphabet soup," as I call it, and I am always getting calls to help someone understand what hemoglobin-D or J or H, or hemoglobin-Bart represents.

So we have a tremendous responsibility to make sure that the information that is there is translated to other individuals who may not be as familiar with this "alphabet soup," that I call the 700 types of variants that may be available.

What I would like to do in the next few minutes is talk about some of the accomplishments that have occurred at our center. For the past 20 years, Meharry Medical College has been involved in sickle cell disease research. We have come a long way. We started out as an infant, and I think we are now in the teenage stage of our activities at Meharry Medical College in the sense that we have taken our time to develop a center. There needs to be a critical mass that is there to carry on these kinds of activities, these very sophisticated and time-consuming activities that occur in the center itself. So we have a critical mass that has allowed us to develop basic research.

For example, many of us in this room know we now believe that the reason for the sickle cell gene mutation was protection against malaria. And we have been working with one of the membrane receptors, glycophorin, over the past 10 years, to help solidify that concept and also to look at how it can help us further develop strategies and treatment plans for individuals who have sickle cell disease.

We have also been involved in looking at mechanisms and manipulating systems that would help us to ultimately get closer to gene therapy—looking at the viruses that may possibly serve as

vectors that we could use to help us with a cure for sickle cell disease.

As I have already mentioned, we have a laboratory that is the State reference laboratory. We are a recipient and participate in the cap certification. In fact, we just recently sent out hemoglobin-Zurich as one of the unknowns to all the State laboratories; that came out of our laboratory, where we just cloned and sequenced the gene that was responsible for that hemoglobin-Zurich. And this is a very interesting hemoglobin that is not predominantly found in African Americans, but is found in individuals from Middle Europe, and individuals who may get exposed to certain kinds of oxidants, specifically sulphur drugs, may have occasion to become severely ill. So the family that we described is not an African American family; it is a Caucasian family from middle Kentucky, where we have now done pedigree studies and are looking at the extraction of this family back to Central Europe. So we have done some very interesting work in that area.

We are involved not only in the United States—as Dr. McMahon has said, she is involved in Brazil—we are involved in Peru. We have an ongoing relationship and have some AID grants in Peru. We have also translated with my help into Spanish information that is now being used in Peru from our center. So we are also involved on the international scene and have been involved with a number of other centers and countries in sickle cell disease.

I would really like for us to think of this as a global issue in many ways. As I mentioned, there are 700 different types of hemoglobins. There are many people who are now getting involved in this arena. And as the world gets smaller, we are starting in our area to see other kinds of hemoglobins that we did not have information on. For example, hemoglobin-E is now one of the most frequently diagnosed hemoglobins in the United States. This is a hemoglobin that has its predominance in Southeast Asia, and in middle Tennessee, we have a fairly large Southeast Asian population—we have Cambodians and Vietnamese—and in our center, we have an individual who speaks all of these languages. There is a rural and cultural difference, and you have to be culturally sensitive to talk about taking blood from those individuals. As you may or may not know, individuals from Southeast Asia view blood differently than we do. So we have a person in our center who is aware of that, so when we talk about taking blood, we can use the right ethnic-sensitive approach in helping individuals from Southeast Asia.

So we are involved in a variety of things that I think have expanded our horizons, and those systems that we have developed have allowed other centers to use them, and we are in very close collaboration with many of those centers.

So the support that we have received has been very important for us to expand our horizons, but that did not occur overnight. It took us a while to get to that point, and we are looking forward to continuing to be able to do that with adequate support. I think that is one of the issues that we need to be very careful about in terms of recognizing that there is about $60 million to $70 million coming of the NIH, but hat is not adequate to do the kinds of things that we need to do.

And Dr. Lenfant did not get into it, but I will say it—the moneys that have been coming out have not been adequate. They have been flat. For the last years, we have taken a hit. I get appropriated a line item from NIH in terms of my grant, my P-60, and yet I have had to take from 5 to 8 to 10 percent each year because of the lack of resources that the NIH has.

So I think one of the things that I would like to see come out of this is a recognition that there is ongoing quality, adequate research, but despite our efforts, we are handicapped because many times, we have to put it on the back burner, or we are not able to follow up leads we have in terms of looking at those leads and helping us move toward curing this disease, because of the shortfall that is occurring in Congress.

I know I am not saying anything that you do not know, but what we really need is more support, in a variety of ways, to accomplish some things that many of us have ideas about but have inadequate resources for. Out State institutions many times are not available to provide adequate resources. So it would be very nice if one of the things that happens is a movement to put more money in the pipeline to help us solve some of the problems that many of us have on our burners.

I will stop here and let my other colleagues have the opportunity to speak.

Thank you.

[The prepared statement of Dr. Turner appears at the end of the hearing record.]

The CHAIRMAN. As I said, I am managing the reauthorization of the Elementary and Secondary Education Act on the floor, which deals with disadvantaged students, and I am going to have to go back over to the floor. But I would be interested if the researchers could give us some insight as to the similarities, if any, in terms of sickle cell, Tay-Sachs and Cooley's diseases. Are they basically variations on a theme, or are they pretty disparate?

Dr. TURNER. The biochemical differences are totally different. But when we talk about a chronic illness, whether we are talking about Tay-Sachs or sickle cell disease or hemophilia, we have some common elements that are present. A chronic illness has some things that need to be dealt with. There is the psychological impact. There needs to be research put into those specific diseases. So there are similarities in that respect. But in terms of the biochemistry, the physiology, there are some differences.

Did I understand you?

The CHAIRMAN. Yes, that is helpful.

Dr. MOORE. Both diseases, sickle cell and Tay-Sachs, are genetic in nature. Both seem to afflict different ethnic groups, have a predominance of influence on different ethnic groups. The incidence of sickle cell disease appears to be much higher in the African American community than Tay-Sachs is in the Jewish community.

The CHAIRMAN. And wouldn't Cooley's be basically ethnic as well?

Dr. TURNER. If you are referring to Cooley's anemia, we are talking about the homozygous condition, and the predominance of that disease would be in Italian descent. But we have beta-thalassemia, and we can have the combination beta-thalassemia trait in the Af-

rican American population. So we have the S-beta-thalassemia syndromes that we have to address also, which can be just as severe in many instances as the homozygous SS condition in individuals with sickle cell disease.

Dr. MCMAHON. Putting it very basically, on thalassemia and sickle cell, in sickle cell, hemoglobin that is produced is abnormal, and in thalassemia, there is not sufficient hemoglobin being produced, although biochemically, it is normal.

The CHAIRMAN. Thank you.

Just before calling on Dr. Moore, Shawnita, if I could, I would just like to ask you a couple of questions. As far as your greatest challenge in coping with the disease, what is the most difficult thing about coping with the disease itself for you?

Ms. AGNEW. The pain, really.

The CHAIRMAN. The continuing pain.

Ms. AGNEW. Yes.

The CHAIRMAN. And that just seems to go on and on. Has the Boston City Hospital Center been really helpful to you?

Ms. AGNEW. Yes, a lot.

The CHAIRMAN. And do you remember which programs there have been the most helpful?

Ms. AGNEW. The teen support group.

The CHAIRMAN. The support group. And have you thought about the research a little bit and which areas you would like to see researched, or just the whole thing?

Ms. AGNEW. Everything, the whole thing.

The CHAIRMAN. Everything. OK. Thank you.

The CHAIRMAN. Dr. Moore.

Dr. MOORE. Thank you, Mr. Chairman.

I want to talk about Southern University, but in so doing, I want to allow that to set the tone for what I believe are some of the concerns that have been raised, especially from Senator Simon, a concern that was raised about peer review, and of course, the degree of medical school affiliation and whether that has anything to do with an institution's capability.

I am William E. Moore, vice chancellor for academic affairs at Southern University in Baton Rouge. I am pleased to have the opportunity to speak in behalf of our institution and to seek committed support for the establishment of a national sickle cell research center on the Baton Rouge campus, a major constituent of the Southern University system.

The four entities that constitute the Southern University system are strategically located throughout the State of Louisiana. They include a 2-year campus in Shreveport, a law center in Baton Rouge, an urban commuter campus in New Orleans, and a Level-3 doctoral institution in Baton Rouge.

The Southern University system, with almost 17,000 students, is the only system of higher education within the historically black college community in this country, or in the world, for that matter.

Dr. Delores Spikes, who is here today, is president of the Southern University system, and Dr. Marvin Yates, who is also here, is chairman of the Baton Rouge campus.

I am also joined by Dr. Jonathan Roberts, who is the director of Charity Hospitals of Louisiana. Before assuming that position, Dr.

Roberts served as coordinator of planning of our national sickle cell disease center.

Our appearance here today provides a mechanism for us to share with you, Senator Kennedy, what we believe to be indisputable documentation of the need for the proposed center and why it should be at Southern University in Baton Rouge—for indeed, despite our best efforts, some of the noteworthy accomplishments of our institution remain well-kept secrets, and we sense the tone of that today, and I hope in your allowing me to tell you a little bit about some of them, we will also address the issue of peer review, documentation, and of course, budgetary needs.

I should say that the warm hospitality we have already received has enabled me to dispel the belief that the atmosphere near the Potomac or inside the beltway would be intimidating at best. We thank you for this reception.

By way of experience, I have spent my entire professional career as a university professor and administrator having had the privilege of full-time teaching appointments at four historically black institutions. I have also served as adjunct professor at four majority institutions, the latter representing some of the finer examples of tradition, elitism, research productivity, and academic standards. I have been a visiting lecturer in Italy, Belgium and France, the highlight being an invited lecturer at the Pasteur Institute in Paris in 1978.

I have served as chairman of the general research support review committee of the National Institutes of Health, and I am currently serving a second 3-year term on the board of review of the National League of Nursing.

I mention these affiliations not in the interest of self-indulgence, but because I believe these experiences have given me an opportunity to observe and participate in a spectrum of scientific-related activities, many of which have relevance to your committee, and some of which I will refer to today in regard to sickle cell research and the appropriateness at our university.

Although I am a part of the Southern University system, I will confine my remaining comments to the Baton Rouge campus, the oldest and largest unit within the system. Southern University at Baton Rouge is an 1890 land grant institution, with enrollment on the Baton Rouge campus in excess of 10,000 students. the history of the university is punctuated with the achievements of its graduates.

For example, the university claims among its graduates eight generals in the United States Army; a significant percentage of the minority lawyers in this country—and I should say that in less than 10 years, our nursing program has achieved the status of being one of the leading undergraduate programs in the United States. Our graduates consistently score above 95 percent on board examinations, and our recent self-study and its initial accreditation was selected by the National League of Nursing as a model for other institutions across this country to use as a guide.

Southern University has a long history, Mr. Chairman, and this has some implications of peer review, as one of the leading HBCUs to produce graduates who have earned the Ph.D. in political

science. In fact, we rank at the top of producing black political scientists at the Ph.D. level.

What is little-known, however—and I point this out by underscoring it—is that between 1985 and 1989, 10 percent of all of the blacks in this country who received a Ph.D. in physics were Southern University graduates. This is indeed a major accomplishment given the large number of colleges and universities in this country. Further, Southern University provides a wholesome intellectual and cultural environment for the development of leaders among its graduates. Three former Southern University student government presidents now serve in the Louisiana legislature or have served there, and as I speak to you today, I should remind this distinguished committee that two of those graduates, William Jefferson and Cleo Fields, are the only African Americans represented in the State of Louisiana in the United States Congress. And a third, State Senator Charles Jones, is the architect of the sickle cell anemia bill in Louisiana, and is also present today.

My point in mentioning these few examples is to underscore the fact that our general university environment is geared to support and to sustain excellence in teaching, research, and service.

I will not read to you the details of the background of the need for the sickle cell center, because you have heard about that from several of the scientists and persons who have testified before you today. I would like to point out, though, that the center we are proposing will include a section which will focus on physical-chemical studies, principally on in vitro studies of hemoglobin. We will draw on the faculty in the departments of physics, chemistry, and biology to investigate the effects of physical stress and chemical agents on the solution properties of hemoglobin.

We will also have a division which will focus on anti-sickling agents, which are still important despite the progress that is being made. This division will be devoted to the isolation, characterization, and synthesis of anti-sickling agents, substances which enable patients to lead a normal life by decreasing the chances of blood cells to become sickled.

We will have a clinical division—and this is extremely important, because we have heard questions raised about the need to be associated with a hospital. We will devote primary attention to longitudinal studies of patients who have sickle cell disease, and these investigations will be carried out in conjunction with the Earl K. Long Hospital and with other clinical settings. The physicians providing immediate supervision for these studies will be hospital physicians who will hold adjunct appointments in biomedical sciences at Southern University.

I have other information about the clinical studies in the written text.

We will have a division of molecular biology and genetic engineering, where we hope to do gene therapy research. We will also have a laboratory on ultrastructural studies, in which we will engage in electron microscopy as a major tool for investigating in vitro and in vivo sickling.

Finally, there will be a laboratory on behavioral and epidemiological studies. This division of the sickle cell center will have the role of investigating disease patterns similar to what you have already

raised, Senator Kennedy, with a view toward using the knowledge gained therefrom for education and prevention.

The CHAIRMAN. Dr. Moore, I am going to have to interrupt you here. We have present Dr. Ohene-Frempong, who will be testifying as well. I have been called over to the floor by the Majority Leader, and Senator Wellstone will be here momentarily to chair.

Let me just ask you this. There is no question that the university has been an extraordinary educational center. I suppose the question is the reason why it is necessary to have a new center, or whether the scarce resources should not be further targeted on the existing research centers which have been working in these areas. How would you respond to that?

Dr. MOORE. I will try to answer that, Senator, by giving four bullets, which was going to be my concluding statement, if I may, because I think that shows you where we are different from——

The CHAIRMAN. If you can do it; I must leave in a couple of minutes because I am required to be on the floor of the Senate. We could make it part of the record, and if you want to summarize in a couple of minutes, I would be glad to hear you. If you need a longer period of time, we can put it in the record.

Dr. MOORE. Sure. It will not take 2 minutes to do it.

The CHAIRMAN. Fine. Go ahead.

Dr. MOORE. First of all, the State of Louisiana has already committed substantial financial support to this effort. The proposal has received the categorical endorsement of both State and Congressional Black Caucuses.

We have a peer review at the Board of Regents in Louisiana, and that board relies heavily on outside scientists to evaluate what we have done.

We have the full endorsement of the hospital systems of Louisiana, the two medical schools, Tulane University and Louisiana State University, and as I said, we have the director of Charity Hospital, who is providing support.

So when you look at the track record combined with the support that has emanated from within our State, we believe that it is unmatched in any State in this Nation, and for that reason, we are seeking your support for the momentum that we have already generated to be carried out.

The CHAIRMAN. Thank you. I saw some references to those points in the testimony, which I will study further at another time. We appreciate very much your presence here.

[The prepared statement of Dr. Moore follows:]

PREPARED STATEMENT OF WILLIAM E. MOORE

Mr. Chairman and members of this committee, I am William E. Moore , Vice Chancellor for Academic Affairs at Southern University in Baton Rouge. I am pleased to have the opportunity to speak in behalf of our institution and to seek the committee's support for the establishment of a National Sickle Cell Disease Research Center on the Baton Rouge Campus a major constituent of the Southern University System. The four entities which constitute the Southern University System are strategically located throughout the state of Louisiana. They include a two-year campus in Shreveport, a Law Center in Baton Rouge, an urban commuter campus in New Orleans, and a Level III Doctoral institution in Baton Rouge. The Southern University System, with almost 17,000 students, is the only system of higher education within the Historically Black College and University (HBCU) Community.

Dr. Dolores Spikes is President of the Southern University System and Dr. Marvin Yates is Chancellor of the Baton Rouge campus. I am joined today by Chan-

cellor Yates and by Dr. Jonathan Roberts, Director of Charity Hospitals of Louisiana. Before assuming his present position Dr. Roberts served as coordinator of planning for the National Sickle Cell Disease Center.

Our appearance here today provides a mechanism for us to share with you what we believe to be indisputable documentation for the need for this proposed center and why it should be at Southern University at Baton Rouge. For indeed, despite our best efforts, some of the noteworthy accomplishments of our university have remained well kept secrets, and it is through a hearing such as this that we are able to tell you why this modest investment would serve the Nation well in scientific research and improving human health.

The warm hospitality we have already received has enabled me to dispel the belief that the atmosphere near the Potomac or inside the Beltway would be intimidating at best. We thank you for this reception.

By way of experience, I have spent my entire professional career as a university professor and administrator, having had the privilege of holding full-time teaching or administrative appointments at four historically black institutions. I have also served as visiting or adjunct professor at four other majority institutions—the latter representing some of the finer examples of tradition, elitism, research productivity, and academic standards. I have been a visiting lecturer in Italy, Belgium, and France—the highlight being an invited lecturer to The Pasteur Institute in Paris in 1978. I have served as chairman of the General Research Support Review Committee of the National Institutes of Health and I am current serving a second three-year term an the Board of Review of the National League of Nursing. I have written for The New York Times, Saturday Review, The Houston Chronicle and Change Magazine. In the case of Change, I was one of four essayists selected in 1977 to publish articles on how the educational needs of Blacks are being met.

I mention these things, not in the interest of self indulgence, but because I believe these experiences have given me the opportunity to observe and participate in a spectrum of scientific and health related programs, many of which have relevance to the concerns of your committee, and some to which I will refer today in regard to Sickle Cell Disease research and its appropriateness at our institution.

Although I am a part of the Southern University system I will confine most of my comments to the Baton Rouge campus, the largest and oldest unit within the system. Southern University Baton Rouge is an 1890 Land Grant institution with an enrollment in excess of 10,000 students. The history of Southern University is punctuated with achievement of its graduates. For example, the university claims among its graduates eight generals in the United States Army which is more than 25 percent of all generals produced by 1890 Land Grant institutions. The prominent role the University has played in graduating a significant percentage of minority lawyers is no doubt well known to this committee. In less than ten years, we have produced one of the leading undergraduate nursing Programs In the United States. Our graduates consistently score above the 95 percent level on national Board examinations, and when our program achieved its initial accreditation, our self-study was selected by the National League of Nursing as a model for others schools across the nation to use as a guide.

Southern University also has a long and distinguished history as one of the leading HBCU's to produce graduates who have earned Ph.D. degrees in political science, chemistry, and biological sciences. In fact the University has traditionally led all schools in producing black political scientists and ranks among the top four HBCU's in producing graduates who have obtained the Ph. D. in chemistry. What is little known is that during the period of 1985 through 1989, 10 percent of all blacks in the United States who received the Ph. D. In physics were Southern University graduates. This is indeed a major accomplishment, given the large number of colleges and universities in this country. Further, Southern University provides a wholesome intellectual and cultural environment for the development of leaders among its graduates. In 1990, three former student government presidents from Southern University served in the Louisiana Legislature, and today as I speak to you, I should remind this distinguished committee that two of those graduates (Representatives William Jefferson and Cleo Fields) are the only African Americans representing the State of Louisiana in the the United States Congress, and a third former SGA president (the Honorable State Senator Charles Jones) is the architect of the Bill to establish a Sickle Cell Disease Center at Southern university. My point for mentioning these few examples is to underscore the fact that our general university environment is geared to support and sustain excellence in teaching, research and service.

Background and Focus of The Center

Sickle Cell Disease is a devastating, multifaceted blood disorder which has a high incidence in African Americans. This hereditary disease can only be cured by a complete bone marrow transplant or by some yet to be discovered method of DNA manipulation. The former approach has drawbacks in the difficulty of the procedure, the problem of finding suitable marrow for transplantation, and the inability of the patient receiving a transplant to produce non-sickle cell offspring. The genetic solution to the sickle cell problem must await further understanding of the human gnome and the development of DNA procedures which can shut down the synthesis of sickled hemoglobin and activate the manufacture of normal adult hemoglobin.

Because sickled blood cells do not bind nor transport oxygen effectively, the symptoms of the disease are numerous. These may include stroke, ulcers, heart attacks and a variety of internal disorders. Until very recently most patients died before the age of 25 and those who managed to survive experienced intense suffering. Hence during the past 20 years much of the research has focused on developing methods to alleviate pain, to minimize crises, and to enable patients to function without much discomfort or suffering. Success in this area has come through the synthesis and isolation of a variety of antisickling agents—drugs which when taken properly will cause the blood cells to retain a normal shape and will minimize the likelihood of a patient experiencing a crisis.

Southern University at Baton Rouge proposes to establish a comprehensive sickle cell research center—one which will offer a unique opportunity for clinical research affiliation with Earl K. Long Hospital and other medical centers. The Southern University facility will focus on five or six major research thrusts which will include the following:

Physicochemical Studies

This facet of the program will focus principally on in vitro studies of hemoglobins. Faculty members in the departments of physics, chemistry and biology will investigate the effects of physical stress and chemical agents on the solution properties of hemoglobins. This program will provide further knowledge regarding conditions under which sickling is most likely to occur. Such information will have national significance and will prove particularly beneficial to other investigators in the Southern University Center;

Anti-Sickling Agents

This division will be devoted to the isolation, characterization, and synthesis of antisickling agents, substances which enable patients to lead a normal life by decreasing the chances for blood cells to become deformed.

Clinical Studies Division

In this section of the proposed center, We will devote primary attention to longitudinal studies of patients who have sickle cell disease. These investigations will be carried out in conjunction with the Earl K. Long Hospital and other clinical settings. The physicians providing immediate supervision for these studies will be hospital physicians who will hold adjunct appointments in biomedical sciences at Southern University. It is expected that some members of the nursing faculty at Southern University will be involved in this program.

The clinical studies unit will have a strong interdisciplinary focus which will bring together chemists, biologists, biophysicist, nurses and physicians. Results from from the basic disciplines will be tested within the boundaries of FDA guidelines and other provisions which protect human subjects.

Division of Molecular Biology and Genetic Engineering

This phase of the program will focus on various genetic approaches to investigating sickle cell disease. In this regard we will devote particular attention to DNA manipulation and various techniques of modern biology which could cause a patient to begin synthesizing normal adult hemoglobin.

Laboratory of Ultrastructural Studies

This section of the center will use electron microscopy as a major tool for investigating in vitro and in vivo sickling. Although many research studies will originate in this laboratory, this facility will provide an important service function to several other parts of the center. This use of the electron microscope will provide an impor-

tant bridge between the basic physicochemical and biological studies and hospital related clinical investigations.

Laboratory of Behavioral and Epidemiological Studies

This division of the Sickle Center will have the role of investigating disease patterns, with a view toward using the knowledge gained therefrom for education and prevention. This facet of the program will also investigate psychological and social manifestations of sickle cell disease. In this regard, the new knowledge produced will contribute to improved counseling approaches and better behavioral methods for managing the disease.

Summary

By way of summary I wish to call the committee's attention to two evaluative statements recently made about our institution. In the first case we were recently evaluated by two different panels of the National Institutes of Health for the establishment of a center of Cellular and Molecular Biology at Southern University. At both levels of review the panels rated our scientific leadership and administrative capability as outstanding. For this review, we achieved a priority score of the highest order.

In the second instance, our university was invited to be featured in the fall 1994 Education, a 118 year old scholarly journal of which I have the privilege to be guest editor. We were recently informed by the publisher that the Southern University issue promises to be the best ever produced. And this is in the face of some of the most prestigious universities and educational agencies in the country having been featured in previous issues. Mr. Chairman, That is the standard of quality we continuously set at Southern University and that same spirit of competence and achievement would carry over into the sickle cell disease center.

I wish to further summarize further by reminding the committee of the following elements of uniqueness to the Southern University proposal:

The state of Louisiana has already committed substantial financial support to this effort.

The proposal has received the categorical endorsement of both the state and congressional black caucuses.

The university's track record in research and academic excellence are well documented.

Our outreach activities are well established. We have one of the more comprehensive wellness programs you will find anywhere, and we are a national leader in service learning at public institutions in the United States.

The uniqueness of the Southern University System makes it an appropriate setting for the sickle cell disease research center.

Southern University is prepared to establish a first rate National Sickle Cell Disease Research Center. The disease itself is one that afflicts African Americans, and it is fitting that a university which is predominantly African American has the vision, track record, technical capability and willingness to provide leadership in this area. Through the collective efforts of the Health Research Center, the School of Nursing, the Center for Social Research, and Center for Rehabilitation Counseling, the University stands poised to make this Center become a reality—one for which the Nation will be proud.

We appreciate this opportunity and would be pleased to answer any questions the committee might have.

Southern University and A&M College

INSTITUTIUONAL SETTING AND RESEARCH CAPABILITY

During the past thirty years, Southern University has achieved an exemplary record in science teaching and research—two activities which compliment one another in the preparation of well qualified graduates. The following examples are representative accomplishments in the college of Sciences and health related areas.

Student Achievements

-From 1967 through 1972 an average of three chemistry graduates per year obtained the Ph. D. degree in chemistry.

From 1972 to 1985 the University was one of the leading producers of minority undergraduates to obtain M. D. degrees.

From 1985 to 1989 the university produced 10 percent of all African Americans in the United States who went on to obtain the Ph. D. degree in physics.

Although the School of Nursing is a relatively new academic unit it has gained a nation reputation for the quality of its graduates as judged by performance on board examinations and overall program quality revealed through the accreditation process.

Success in graduate and professional school is matched by the accomplishments of other science graduates who have risen to prominent positions in government and the corporate world.

Faculty Accomplishments

In addition to a noteworthy record of general scholarship, the Southern University Science faculty has been recognized for its accomplishments in the following ways:

In 1992–93, Dr. Fitzgerald Spencer of the Biology department was appointed a Fulbright lecturer.

Dr. Gary Ross, a long-time biology faculty member who recently retired was recognized as a world authority on butterflies.

During the past ten years two Southern University faculty member have appointed to NIH Study sections at the National Institutes of Health. Dr. William Moore chaired the General Research Support Review committee in 1982 and Dr. Earl Doomes is presently in the second year of a four year term.

Faculty in the computer science department have developed software that is used in major universities in the United States.

Dr. William Moore was invited lecturer at the Pasteur Institute in Paris, France in 1978. His pioneering work on plasma albumins is closely related to a variety of physicochemical studies of sickle cell hemoglobin.

In 1991 Dr. William Moore was elected to the Board of Review of the National League of Nursing. He is one of two public members serving on the Board which accredits all nursing programs in the United States.

In the applied sciences, Dr. James McNitt has become a leading authority on rabbitry and several investigators in the Center for Energy and environmental Studies are becoming increasingly recognized for their work on pollution of the Mississippi River.

PERSONNEL

The basic personnel in a sickle cell disease center will consist of a director, associate director, clerical staff, and faculty who will hold tenure or tenure track appointments in an appropriate department. A second level of personnel would include research associates and assistants who may be employed on specific funded projects. Some personnel will hold adjunct appointments in the biomedical sciences. This group will consist largely of physicians (pediatricians and hematologists) affiliated with one of the local hospitals or health care agencies.

Faculty members holding joint appointments in the sickle cell research center will obtain these positions through released time. This mechanism will enable department chairs to find suitable replacements to meet departmental needs.

Faculty Research investigators will be hired initially through support from external funding. Each investigator employed will therefore come through an appropriate departmental screening process. These persons would move into funded positions over the next five years as such vacancies become available through anticipated retirement or other forms of attrition. Hence by 1997, there should be at least one faculty member in each section of the center.

The administrative staff and other core personnel would be supported through special funding. However, our long-range plan would call for the raising of a five million dollar endowment which would cover much of the basic operational costs.

Research assistants and associates would be employed mainly through special grants. It is projected that by 1998 there would be at least one funded project in each division of the center.

Southern University and A & M College

RESARCH PROGRAMS AND CENTERS

The University's demonstrated ability to develop and sustain research centers over a long period of time provides the most compelling argument that Southern University can develop and implement a successful sickle cell disease center. The following three examples provide evidence of that success.

The NASA Industrial Applications Center

In 1987 Southern University was one of eleven Universities selected by the National Aeronautics and Space Administration (NASA) to house an industrial application center. When the agency discontinued this program, Southern University maintained its industrial applications initiatives through funding from the Department of Defense and from other NASA programs. The continuation of this program without State support underscores the University's commitment to industrial applications and to identifying funding sources to sustain this effort.

The Health Research Center

This center was constructed with funds form the Public Health Service in 1961 and expanded by funding from the National Institutes of Health in 1985. Although the center has attracted limited external support since its inception, the health Research Center as been an area of pivotal research activity at Southern University since 1972. During the ensuing 20 years the University has attracted Federal support from the National Institutes of Health, Eli Lily Foundation, and the United States Department of Agriculture. Only nominal state support has been required for two staff positions and modest supplies and travel.

During its twenty-year history of substantial funding, the Health Research Center has provided salaries, assistantships, equipment for teaching and research, and indirect costs. Since many of the faculty have done research on released time, the center, through grant funding, has provided a mechanism for the university to look at a long list of temporary faculty and determine which ones were suitable for probationary appointments.

On numerous occasions, we have learned that the large number of graduates who went on to medical school and graduate school gained considerable advantage by having had positive experiences in the Health Research Center. The point to be emphasized is that for more than 20 years the health research center has become an indispensable component of scholarship and student preparation without reliance on State funding..

The Center for Energy and Environmental Studies

This is the youngest comprehensive research center at Southern University. After its inception in 1986 it has grown to become a thriving unit with a staff of more than forty persons including students and faculty who hold part-time appointments. The center has been designated as one of three minority centers of excellence by the Department of Energy. Recently it completed a meritorious policy study of the Mississippi River Corridor and the center ranks high among top candidates from the McKnight Foundation to conduct a more comprehensive study of the integrity of the Mississippi River. At present the center receive grants and contracts in excess of two million dollars. The total cost of state funding is less than $100,000.

There are other examples of relatively self sufficient research centers at Southern University. This track record over the past two decades indicates that with sufficient start-up funds the proposed sickle cell disease center, within a six year period after completion, would have little reliance on ongoing state support.

William E. Moore is Vice Chancellor for Academic Affairs at Southern University in Baton Rouge, a position he has held since 1989. During his twenty-seven years of work in higher education, Dr. Moore has held a series of professorial and administrative positions at several universities. He has published more than 35 articles as a research chemist, science educator, and more recently in the broad area of testing and education of minorities. In 1976, he served as a NATO Fellow on Computers in Science Education—a conference held in Brussels, Belgium. In 1977, Dr. Moore was selected by Change Magazine as one of four essayists nationally to write on the adequacy of education of minorities. In 1978, he served as invited lecturer at the Pasteur Institute in Paris, France. There he gave talks on his work on the chemistry of blood proteins, with specific reference to the artificially induced aging of plasma albumins and in 1980 he was appointed Chairman of the General Research Support Review Committee of the National Institutes of Health.

During the 1980's, Dr. Moore assumed several administrative positions in higher education and continued to publish in the areas of science education, testing, environmental science, and race relations. In 1985, as a member of the NAFEO Science and Technology Advisory Committee, he became one of the principal contributors to the guidelines for the Research Centers at Minority institutions, known as the RCMI program. Since that time he has been principal investigator of two RCMI projects. In the first instance he led a $3.76 million project aimed at studying diseases which show a high incidence in ethnic minorities, and more recently he as-

sumed the leadership of a $4.8 million NIH project to establish a research center in cellular and molecular biology at Southern University. At the time of this award, Southern was one of two such non-Ph. D. programs in science to be nationally awarded a center by NIH.

In 1991 Dr. Moore was elected to the Board of Review of the National League of Nursing as one of two public members on this 18 member accrediting council. In 1994, he was reelected to a three-year term on this body. During this period, he also introduced several innovative programs aimed at improving the quality of undergraduate education for minorities. These included a wellness program, a multimedia learning environment, a mentoring program, a precollege enrichment project, and a service learning requirement for all undergraduates. In 1991, he was designated as a Commissioned Research Scholar for the NABSE Moody Roundtable and that same year was invited by the NAACP to participate in the Daisy Bates Educational Summit at Little Rock, Arkansas. In 1994, he was invited to serve as guest editor of Education 115 year old International journal. Recently he was informed by the publisher that the forthcoming issue which will feature Southern University is the best issue ever produced. Dr. Moore holds a B. S. degree in Chemistry from Southern University and was the first African American to earn a Ph. O. in Chemistry from Purdue University. He is married to the former Willa Warren, and they are the parents of two children, Deirdra and Marcus.

The CHAIRMAN. We will recess just very briefly, and Senator Wellstone will be here for the completion of the hearing. I want to thank all of you very, very much. Shawnita, we thank you. We know you have made a special effort to be with us. You are a very courageous and brave individual and a real inspiration, and we thank you very, very much for your presence.

We will stand in recess.

[Recess.]

Senator WELLSTONE [presiding]. The committee will come to order.

First of all, let me apologize to the panelists for the delay. We had the service for Hugh Scott, and a good many people on the committee are at that service; and in addition, the Elementary and Secondary Education Act is also up on the floor, and Senator Kennedy had to go to manage that. So I really apologize from all of us.

Dr. Ohene-Frempong, would you proceed, please, and thank you very much for being here.

Dr. OHENE-FREMPONG. And thank you very much, Senator, for the opportunity.

Earlier, my colleagues at Boston Sickle Cell Center and at Meharry Comprehensive Sickle Cell Center gave overviews that I think pretty much describe what the comprehensive sickle cell centers are about. And I will briefly just go over some of the accomplishments of the center at Philadelphia where I am, and also finish with some recommendations that I have for consideration.

Our center serves the greater Philadelphia-Delaware Valley area as a resource for families affected by sickle cell disease. Directly, we care for 520 children up to 19 years of age who are affected by this disease. We also serve as the referral center for all of Louisiana, for the southern part of New Jersey, and also for Delaware, for children with sickle cell disease who suffer very serious consequences.

For the State of Pennsylvania, we also serve as a resource in developing and monitoring the State sickle cell programs. We developed the newborn screening program for the State and actually conducted a pilot project in Philadelphia for 2 years before the State picked up the program and went statewide with it.

Our sickle cell effort started in 1973, and we have had some support from the State to care for sickle cell patients continuously since that time.

We became a comprehensive sickle cell center in the 1988-93 cycle, and we and our colleagues here went through the competitive renewal applications in 1992 and were lucky to get funded from the 1993 to 1998 cycle.

Our research addresses all the major areas that the comprehensive sickle cell centers deal with. We have basic in basic laboratory areas, in clinical areas, in psychosocial areas, and in education, counseling, and testing areas.

In the basic research arena, our attention has been focused on studies that would lead to gene therapy and other treatment for sickle cell disease. A team of our investigators studying the regulation of the synthesis of fetal hemoglobin at the DNA level found two previously undescribed changes in the DNA from Benin and Bantu haplotypes of sickle cell disease. These are separate origins of the sickle cell gene in Africa. The major Benin haplotype was associated with a genetic change which had not been previously described, and another change was also found in the Banto haplotype.

We think that ultimately, this sort of knowledge promises to be useful in developing ways to modify the expression of these fetal hemoglobin genes, and hopefully, this will lead to a way of improving sickle cell disease as patients can be given treatment that will increase the fetal hemoglobin production.

As we all know, sickle cells are abnormally shaped and stiff in comparison with normal red blood cells. Effective treatment or cure for sickle cell disease will have to alter the abnormal morphology and the deformability of sickle cells.

Another team of our investigators has developed an accurate technique to analyze the morphology of sickle cells, using a computerized image analysis system. This technique allows the accurate determination of morphological differences of sickle cells numerically, by calculating several differentiated factors. This system facilitates the investigation of the relationship between the morphology of sickle cells and various environmental and drug conditions. This technique is currently being applied to support the testing of new drugs in sickle cell disease patients.

One of the drawbacks of the development of new treatments for sickle cell disease has been the lack of animal models for this disease. All drug tests are either performed in vitro in the laboratory or directly in humans. A group of our investigators together with others in the country have developed transgenic sickle cell diseased mice which produce sickle cells containing human sickle hemoglobin. These mice offer the opportunity to study sickle cell disease in the model that will permit the testing of a wide range of agents and also for trials of gene therapy.

In clinical research, we have conducted studies aimed at understanding some of the most difficult problems encountered by sickle cell disease patients, as well as to test new drugs for potential use in treating the disease. Stroke is one of the most devastating complications of the disease, affecting about 5 percent of all patients, including children less than 2 years of age. Our studies of the blood circulation of the brain have aimed at discovering children who

may be at high risk for stroke so that preventive therapy can be developed for them. Using magnetic resonance techniques, we and others in the country have shown that as many as 20 percent of children with sickle cell disease suffer silent stroke, and that these children may be at the highest risk for overt strike. We are currently working with our collaborators at the national level to develop methods of intervention to stop the occurrence of the first stroke.

Stroke and sickle cell disease again have a nasty tendency to recur, and when they do recur, they lead to more severe brain damage. The objective of current treatment of stroke, chronic transfusion therapy, is to prevent this recurrence. One of the major hazards of long-term chronic transfusion therapy is iron overload, a problem which is potentially fatal if not aggressively treated. Investigators at our center have successful demonstrated that iron overload in chronically transfused patients can be safely reduced in two ways. First, they demonstrated that in stroke patients who had been transfused aggressively for at least 3 years and who have had no neurological setback, the intensity of the transfusion can be safely reduced without recurrence of stroke.

In addition, they have shown that when this modified transfusion program is coupled with a red cell exchange instead of simple transfusion regimen, further reduction in transfusional iron loading and in body iron stores can be achieved. These findings are expected to have a major impact on management of the problem of iron overload in sickle cell patients who are on chronic transfusion therapy. In combination, these methods have the potential to postpone the need for iron chelation therapy for a number of years.

Hydroxyurea is perhaps the most promising drug ever tested in sickle cell disease. This drug, as we heard earlier, is currently undergoing control trials in adult sickle cell patients in an NIH-funded study. In anticipation of the potential impact of hydroxyurea on sickle cell disease treatment, investigators at our center began preliminary studies of hydroxyurea in children with sickle cell disease 2 years ago. This summer, we and others from three other institutions are beginning a limited trial of hydroxyurea in a larger group of children in an NIH-funded study.

Have we made any progress at all in sickle cell disease? The answer is a qualified yes. Certainly, sickle cell patients today are living longer than they lived before. Thirty years ago, half of sickle cell patients did not live beyond 20 years of age. In a recent publication which came out of the cooperative study of sickle cell disease, where the NIH organized a large group of centers that have been collaborating in clinical studies since 1978, we have been able to show that for patients at least living in the 1980's, at least half of them lived beyond 45 years of age. This is a tremendous improvement from what it was 10 years ago. But that still means that about half of these patients lose at least 30 years of useful life, so we still have a long way to go, and sickle cell disease research needs to be supported.

I have the following recommendations to make. First, that the 10 National Institute of Health approved comprehensive centers, which have not had a real increase in their level of support for the last 15 years, need to be funded at least at their approved levels.

Last year, these centers suffered an average of about 8.5 percent reduction in their funding, and this year, they are operating at 5.6 percent below their recommended and approved budgets. We ask that Federal funding for the centers be increased by at least $4 million to enable the approved research projects to be conducted as recommended in the peer review process.

The centers should be specifically mentioned in the language of any appropriation for increased funding for the National Institutes of Health.

The well-organized cooperative study of sickle cell disease, a network of medical centers established through the National Heart, Lung, and Blood Institute, should be supported as the ideal set-up for testing of new treatments in sickle cell disease. This network demonstrated its value in the 1980's by the rapid conduct of the penicillin prophylaxis study in children with sickle cell disease, and I must say this study was the most important clinical study ever conducted in this disease.

Funding for centers for gene therapy for sickle cell disease should be increased. Many brilliant molecular biologists and gene therapy experts whose talents could be recruited into this area of research are hesitant to join the effort because of concerns about long-term commitment of support. Congress should make a commitment to finding a cure for this genetic disease through major funding for gene therapy for sickle cell disease. And this will be a fitting response to the contributions made to medical science and the understanding of genetic diseases in general by those affected by sickle cell disease and its related disorders.

My final recommendation is that there is a severe under-representation of African Americans and other minority groups in biomedical research. In order to increase the number of African Americans and members of other minority groups in biomedical research, adequate funding should be provided to fully fund the Minority Supplement Program of the National Heart, Lung, and Blood Institute.

In addition, in accord with a report of a National Heart, Lung, and Blood Institute task for on the declining number of investigator-initiated research proposals in sickle cell disease, a Sickle Cell Research Scholars Program should be established within the comprehensive sickle cell centers. Each center should be provided sufficient resources to support at least one scholar drawn from the ranks of young investigators on the medical school and hospital faculties where centers are funded.

I think that sickle cell centers have truly been much more than what we expected from them. they have been worth much more than the funding that they have received. The work that has been done through the Sickle Cell Disease Branch of the NIH has advanced research in this work further than any of us expected. We are very close, we think—and we promise this to our patients—we are very close to a cure for this disease, and this is the time that I think we should pull together all these resources to support the scientists who have been working so hard in this area.

Thank you very much, Senator.

Senator WELLSTONE. Thank you, Doctor.

I think what we will have to do, since I will have to leave in a short period of time, is we will submit written questions to you.

I did want to mention, though—and I really appreciate your testimony—I was a little saddened by what you said—not by what you said, because I was actually inspired by what you said—but when you talked about the budgets, I think back to when my father, who suffered from Parkinson's disease, was in the original L-DOPA pilot group, when that was first used as a drug, at George Washington Hospital here, in the same room was a young African American man who was in a sickle cell crisis period, and I have just never seen such agony, and I will never forget it.

The reason I mention that is I work with people who come here, unfortunately, just in their 40's, with Parkinson's, and they too are trying to see some expansion of the budget, and there is all sorts of promise.

On the NIH budget, there is the Harkin-Hatfield initiative to try to have a set-aside of one percent increase across-the-board. I just do not want to see different people who are struggling with different illnesses pitted against one another, and it does seem to me that we are making such a terrible mistake by not really committing the resources to the research, to save money in the short run, we end up spending more in the long run. It is not just a question of spending less; it is also a question of what you can do for people. So I really appreciate what you say, and I thank you.

Dr. OHENE-FREMPONG. Thank you, Senator.

Senator WELLSTONE. And if it is okay, I would like to get some of these questions to you to get a response in writing.

Dr. OHENE-FREMPONG. That will be fine, Senator.

Senator WELLSTONE. Thank you.

[The prepared statement of Dr. Ohene-Frempong follows:]

PREPARED STATEMENT OF KWAKU OHENE-FREMPONG, M.D.

A. GENERAL COMMENTS

Sickle cell disease is an inherited disease of red blood cells. The red cells of people with the disease have a tendency to become rigid ad abnormally shaped, causing them to break up easily and lead to anemia, and also block the flow of blood through blood vessels and lead to many other complications. The hallmark of the disease is the episodic attack of severe pain in various parts of the body. Most people with sickle cell disease eventually die from it. In the best circumstances, half of all sickle cell patients die by 45 years of age, about 30 years earlier than expected in the general population. There are approximately 60,000 sickle cell disease patients in the United States of America with 2.5 million people with sickle cell trait, the healthy carrier state of the sickle cell condition. Worldwide, hundreds of thousands of babies are born each year with this disease, about 150,000 in Africa alone. Most of these babies die by five years of age without the recognition of sickle cell disease as the underlying cause of their deaths from malaria, respiratory and other diseases. Children with sickle cell trait, not the disease, are protected from severe malaria. While people of African descent are predominantly affected by sickle cell disease, the disease is also found in all the countries in the Mediteranean basin, especially Italy, Turkey, and Greece, all the Middle Eastern countries, and in India. Throughout these areas of the world and where descendants have immigrated, sickle cell conditions are a major health problem.

Sickle cell disease was discovered by modern medical science in 1907 in Chicago. From the early stages of research into the nature and effects of this disease, it was also discovered that the disease in the United States of America affected predominantly Americans of African origin. The fact that the patient through whom the disease was revealed to medical science was a dental student from Grenada and not one of the hundreds of American patients who must have suffered the pain and other complications of the disease may reflect another facet of sickle cell disease.

Since the general public has become aware of the disease, there has been the impression that the disease has not received much attention because it affects primarily a minority African-American community.

The fact is that sickle cell disease has received plenty of attention from basic laboratory research scientists in the U.S. and elsewhere. Sickle cell disease and its related disorders are some of the best studied and best understood diseases of man. Sickle cell disease was the first "molecular disease". It was the first disease whose cause was found to reside in an abnormality in a molecule, hemoglobin. The simple difference between "sickle" hemoglobin and its normal version was determined almost 50 years ago. When the genetic code was discovered, the genetic basis of sickle cell disease was easily established as a simple singular mutation in one gene. The gene for sickle cell disease was discovered in 1977, almost twenty years ago! With all these "firsts", one would expect that research would have made dual progress in the treatment of sickle cell disease. Unfortunately, medical science has gained a lot more from the study of the blood of people affected by sickle cell conditions than the people have received from medical science.

The treatment of sickle cell disease today is largely symptomatic and does not address the fundamental cause of the disease. As the first molecular genetic disease, it has always been expected that sickle cell disease would be one of the first diseases for which gene therapy would be attempted. To date, this has not happened.

However, patients with sickle cell disease are better off today than they were 20 or 30 years ago. Thirty years ago, only half of children with sickle cell disease were expected to live beyond 20 years of age. For patients living in the 1980's this had improved to about 45 years of age. This improvement had come about because of on-going research to understand the effects of sickle cell disease and to develop treatment methods for its many complications.

Much of what we have learnt about sickle cell disease has come out of research sponsored by the National Institutes of Health primarily through the Sickle Cell Disease Branch of the National Heart, Lung and Blood Institute. A large part of this NIH effort on behalf of sickle cell disease has been organized through the Comprehensive Sickle Cell Centers. These Centers, funded on a competitive 5-year cycle, have provided a large body of new information on the basic, clinical and psychosocial aspects of sickle cell disease. The Centers have also provided opportunities for the development of demonstration projects on testing and counseling of individuals for sickle cell conditions. The lessons learnt from the testing and counseling of large numbers of people for sickle cell disease are currently being applied to other genetic disorders such as cystic fibrosis, as the discovery of the genes for other diseases make such testing possible. For the past 15 years, there have been 10 Comprehensive Sickle Centers. Even though the number 10 was established as a minimum there have not been more than 10 Centers since that minimum was established. The Comprehensive Sickle Cell Center at the Children's Hospital of Philadelphia is one of the current cycle of 10 Centers. Our Center and some 22 other Centers have participated in the Cooperative Study of Sickle Cell Disease (CSSCD). Perhaps the greatest achievement of the CSSCD is the studies conducted on the risks and prevention of bacterial infections in young children with sickle cell disease. The famous Penicillin Prophylaxis Study (PROPS) conducted in the mid-1980's by the CSSCD showed that the lives of young children with sickle cell disease could be saved by giving them ordinary penicillin twice a day every day. Infection from strains of the bacterium, pneumococcus, had been well established as the leading cause of death in these children and the first 3 years of life had been found to be their riskiest for death. The eventual outcome of PROPS was the establishment of newborn screening for sickle cell disease. Since young lives could be saved with penicillin prophylaxis, it became important to discover babies with sickle cell disease early so that the penicillin treatment can be started before they died of pneumococcal infection. Today, some 43 states have added testing for sickle cell conditions to their newborn screening programs. Many young lives are being saved and the first three years are no longer the most dangerous for people with sickle cell disease.

While survival beyond childhood may not be as major a problem as it used to and, while their overall life expectancy has improved, the lives of sickle cell disease patients are not without tremendous difficulty. They still lead lives frequently interrupted by painful attacks ("crises "), paralyzing strokes, acute chest syndrome (lung damage), acute splenic sequestration (lifethreatening sudden enlargement of the spleen), aplastic crisis (transient cessation of red cell production), priapism (painful sustained erections), and other acute manifestations of the disease. Over several years, many patients suffer chronic damage to and failure of organs such as the spleen, lungs, kidneys, liver, and heart. In the absence of treatment that prevents the production of sickle cells, much of our efforts has been directed to understanding and management of these acute and chronic complications.

B. RESEARCH AT THE COMPREHENSIVE SICKLE CELL CENTER, THE CHILDREN'S HOSPITAL OF PHILADELPHIA

At the Comprehensive Sickle Cell Center at The Children's Hospital of Philadelphia, we have devoted our research efforts to address all the important aspects of sickle cell disease, basic, clinical and psychosocial. The following is a brief summary of our recent accomplishments, placed in the context of national developments in sickle cell disease research.

1. Basic Research

Our attention has been focused on studies that will lead to gene therapy and other treatments for sickle cell disease. A team of our investigators studying the regulation of the synthesis of fetal hemoglobin at the DNA level found two previously undescribed changes in the Benin and Bantu haplotypes of the sickle gene. The major Benin haplotype was associated with a Gy-309 A to G change and the Central African Republic with an Ay-271 C to G change. Ultimately this knowledge promises to be useful in developing ways to modify the expression of fetal genes and therefore ameliorating the severity of sickle cell disease.

Sickle cells are abnormally shaped and stiff in comparison with normal red blood cells. Effective treatment or cure for sickle cell disease will have to alter the abnormal morphology and deformability of sickle cells. Another team of our investigators has developed an accurate technique to analyze the morphology of sickled cells using a computed image analysis system. This technique allows the accurate determination of morphological differences of sickled cells numerically by calculating several different shape factors. This system facilitates investigation of the relationship between the morphology of sickled cells and various environmental and drug conditions. It is currently being applied to support the testing of new drugs in sickle cell disease patients.

One of the drawbacks of the development of new treatment in sickle cell disease has been the lack of a natural animal model for the disease. All drug tests are performed either in vitro or directly in humans. A group of our investigators and others in the country have developed transgenic sickle cell disease mice which produce sickle cells containing the human sickle hemoglobin. These mice offer the opportunity to study sickle cell disease in a model that will permit the testing of a wide range of agents and also for trials of gene therapy.

2. Clinical Research

In clinical research, we have conducted studies aimed at understanding some of the most difficult problems encountered by sickle cell disease patients as well as test new drugs for potential use in treating the disease.

Stroke is one of the most devastating complications of the disease, affecting about 5 percent of all patients including children less than 2 years of age. Our studies of the blood circulation of the brain have aimed at discovering children who may be at high risk for stroke so that preventive therapy can be developed for them using magnetic resonance techniques, we and others in the country have shown that as many as 20 percent of children with sickle cell disease suffer "silent" stroke and that these children may be at the highest risk for overt stroke. We are currently working with our collaborators at the national level to develop methods of intervention to stop the occurrence of the first stroke.

Strokes in sickle cell disease have a tendency to recur and lead to more severe brain damage. The objective of current treatment, chronic transfusion therapy, is to prevent this recurrence. One of the major hazards of long term chronic transfusion therapy is iron overload, a problem which is potentially fatal if not aggressively treated. Investigators at our Center have successfully demonstrated that iron overload in chronically transfused patients can be safely reduced in two ways. First, they demonstrated that in stroke patients who had been transfused aggressively for at least three years, without any neurological set-back, the intensity of the transfusion can be reduced without recurrence of stroke. In addition they have shown that when this modified transfusion program is coupled with a red cell exchange instead of simple transfusion regimen, further reduction in transfusional iron loading and in body iron stores can be seen. These findings are expected to have a major impact on the management of the problem of iron overload in sickle cell patients on chronic transfusion therapy. In combination these methods have the potential to postpone the need for iron chelation therapy for a number of years.

Hydroxyurea is perhaps the most promising drug ever tested in sickle cell disease. This drug is currently undergoing a controlled trial in adult sickle cell disease patients in an NIH-funded study. In anticipation of the potential impact of hydroxyurea on sickle cell disease treatment, investigators at our Center began preliminary studies of hydroxyurea in children with sickle cell disease two years ago.

This summer, we and investigators at three other institutions are beginning a limited trial of hydroxyurea in a larger group of children in an NIH-funded study.

C. HAVE WE MADE SIGNIFICANT PROGRESS IN SICKLE CELL DISEASE RESEARCH?

The importance of sickle cell disease research in our understanding of human genetic disease is well recognized. Recent developments finally are bringing some hope of effective treatment and universal cure for this disease. Some of these important developments are summarized below.

1. Treatment to increase the level of fetal hemoglobin in red blood cells

Fetal hemoglobin, Hb F, is the predominant hemoglobin in the red cells of babies during pregnancy. Normally, we switch off the production of Hb F toward the end of pregnancy as we increase the production of Hb A, the normal "adult" hemoglobin. Sickle cell disease is due to an abnormal form (Hb S) of Hb A. The most important fact in sickle cell disease research is that Hb F in appreciable amounts can block the abnormal behavior of Hb S and prevent the formation of sickle cells. Much research attention has been devoted to understanding the natural switch for Hb F production and to find ways to stimulate the production of large amounts of Hb F beyond birth. Currently, two groups of medications hold promise toward this goal. Hydroxyurea, alluded to above, has been the most tested, and Butyratess are beginning intensive testing. This direction of research promises the simplest and most cost effective way in which sickle cell disease can be treated worldwide.

2. Bone marrow transplantation for sickle cell disease

Sickle cell disease can be cured by transplantation of normal bone marrow. The application of this treatment to sickle cell disease was first attempted. in Belgium and has been gaining deliberately slow trial in the U.S. Because of the risks associated with marrow transplantation and the need for tissue matched donors, it is not expected that large numbers of sickle cell disease patients will be treated with this method in the near future. Lessons learnt from the few cases being performed will be very useful in gene therapy for sickle cell disease.

3. Newborn testing for sickle cell disease

In the public health arena, the addition of sickle cell testing to the newborn screening programs of most (43) states is the most important development in the past twenty-five years. In 1986, the Sickle Cell Disease Branch of the National Heart, Lung, and Blood Institute with the CSSCD published the results of the Penicillin Prophylaxis Study. The implementation of newborn testing and penicillin prophylaxis therapy at about two months of age is perhaps the most significant improvement in the care of sickle cell disease patients to date. Implementation of similar programs around the world has the potential to save over a hundred thousand lives a year.

4. Gene Therapy for sickle cell disease

In theory, this has been the expected cure for sickle cell disease ever since the disease was found to be caused by a simple mutation in a single gene. Unfortunately, as gene therapy was being aggressively pursued for other genetic disorders, sickle cell disease, the prototypical genetic disease, was left to wait. Encouraging development came this year as the NIH accepted applications for research projects in gene therapy of sickle cell disease. It is hoped that this area of research will expand into treatment trials in the not too distant future.

D. RESEARCH NEEDS IN SICKLE CELL DISEASE

At a time when there is excitement in sickle cell disease research for effective treatment or universal cure, scientists are being discouraged by diminishing funds for research. Since 1982, investigator initiated applications for funds for sickle cell disease research has been dwindling. One of the reasons must be the perception of unavailability of funding support. Research scientists are spending half of their working hours writing and rewriting grant applications as they search for support. On the patient and community side, there is increasing concern that when funds become short in supply, conditions such as sickle cell disease, which affect a largely minority population, receive even less attention.

Sickle cell disease has been a "natural" attraction for young African Americans and members of other minority groups seeking careers in biomedical research. The Comprehensive Sickle Cell Centers, with their large collection of senior and middle level research scientists, have served as fertile breeding grounds for such budding scientists. However, the Centers are no longer allowed to recruit students and young physicians as part of the Minority Supplement Program of the NIH. Each year, we turn down several applications for research apprenticeship from students because of lack of support.

I would like to make the following specific recommendations:

1. Overall the funding for research projects dealing directly with sickle cell disease has been declining in relationship to other conditions supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health. The 10 National Institutes of Health-approved Comprehensive Sickle Cell Centers have not had a real increase in their level of support for the past 15 years. These Centers are currently funded at 5.6 percent below their recommended and approved budgets; they suffered 8.5 percent reduction in funding for 1993/94. We ask that federal funding for the Centers be increased by $4 million to enable approved research projects to be conducted as recommended in the peer review process. The success of the Centers concept in advancing research in sickle cell disease deserves to be recognized by adequate funding. The Comprehensive Sickle Cell Centers should be specifically mentioned in the language of any appropriation for increased funding for the NIH.

2. The network of medical centers established through the National Heart, Lung, and Blood Institute of the National Institutes of Health for clinical investigations in sickle cell disease should be maintained as the best system for quickly testing new treatments in sickle cell disease. In this regard, the well organized Cooperative Study of Sickle Cell Disease should be supported as the i ideal network for clinical trials in sickle cell disease. This network demonstrated its value in the rapid conduct of the Penicillin Prophylaxis Study.

3. Funding for Centers for Gene Therapy for Sickle Cell Disease and Related Disorders should be increased. At the moment only two such Centers are expected to be established through the National Institutes of Health. Many brilliant molecular biologists and gene therapy experts whose talents can be recruited into this area of research are hesitant to come in because of concerns about long term commitment of support. Congress should place its commitment to finding a cure for this genetic disease through major funding for gene therapy for sickle cell disease. This will be a fitting response to the contributions made to medical science and the understanding of genetic diseases by those affected by sickle cell disease and related disorders.

4. There is severe underrepresentation of African-Americans and other minority groups in biomedical research. In order to increase the number of African Americans and members of other minority groups in biomedical research, adequate funding should be provided to fully fund the Minority Supplement Program of the National Institutes of Health particularly in relationship with the Comprehensive Sickle Cell Centers. In addition, in accord with a report of a National Heart, Lung, and Blood Institute Task Force on the declining number of investigator-initiated research proposals, a Sickle Cell Research Scholars Program should be established within the Comprehensive Sickle Cell Centers. Each Center should be provided sufficient resources to fund at least one such Scholar drawn from the ranks of young investigators on the medical school and hospital faculties where Centers are funded.

Senator WELLSTONE. Mr. Jones.

Mr. JONES. Thank you, Senator Wellstone.

It is indeed an honor and a distinct privilege for me to have an opportunity to address the committee this afternoon on this very important issue.

Southern University in Baton Rouge has, as a result of the 1992 legislative statute, created a vehicle for a national research center for sickle cell anemia. Southern University is the largest predominantly black, historically black college or university in the United States, with approximately 16,000 students in the Southern University system.

This research center not only has the support of our Governor and our legislature, but also has the support of the National Baptist Convention U.S.A., the National Rainbow Coalition, and the 40 members of the Congressional Black Caucus. So this research center that is proposed at Southern University, as a national research center, because there is no national research center—there are comprehensive centers, and the basic difference between this proposal and the comprehensive centers is that this center will be dedicated to research and research only.

The practical effect of the disease was summed up by a young woman with the disease who made this statement during the 23rd Annual Congressional Black Caucus Week: "I have sickle cell ane-

mia, and I am not supposed to be here today. I usually wish that I was not. I wished that I was dead. Sickle cell causes me a lot of pain. The pain is so bad I cannot stand it. Sometimes, I start breathing fast and can hardly catch my breath. I get weak. I start to slur my speech and go in and out of consciousness. Sometimes, I pass out in the street. People step over me or on me. They think I am a drug addict. If I get to the hospital, everybody thinks I am on drugs, too, and they treat me like some kind of criminal. I cannot hold down a job because of the frequency of my crises. I do not have no money, no nothing, because of sickle cell."

The role of the National Sickle Cell Research Center at Southern University, again unlike the 10 comprehensive sickle cell service and counseling centers which presently exist, this center will engage exclusively in research, basic biomedical research and psychosocial research.

Why establish the National Sickle Cell Research Center at Southern University, some have asked. Even if Congress opts to support a National Sickle Cell Research Center, why should it be located at Southern University, and not in some other State or at another institution?

The answer is three-fold. One, Southern University's location in the State of greatest need, in a State that is approximately one-third African American, with 3,248 persons with the disease, 25 percent of whom will have the acute form of the disease which is usually fatal.

The second point is that Southern University is in the State of Louisiana, and the State of Louisiana has made a commitment to this project as evidenced by a $7 million appropriation to the national center for its establishment. No other State in the United States has made such a commitment. In fact, in furtherance of the State's effort, this year, just 2 months ago, the State of Louisiana put an additional $700,000 into the State budget to create clinics for sickle cell patients throughout the State of Louisiana. There is not one urban area in the State of Louisiana that will not have a sickle cell clinic where these patients will be able to receive treatment, with a hematologist on staff.

Senator Wellstone, as I sit here today, a little more than 1 year after the national center's launching meeting at Southern University, in addition to the $7 million committed to the effort by the State of Louisiana, Southern is obtaining financial commitments for the center from alumni, corporations and foundations. Southern has faculty, research staff commitments, and collaboration between LSU and the Earl K. Long Hospital, which are located less than 5 miles from Southern.

I am here today to ask the Federal Government to join us in this collaborative public-private venture, to help us turn the lives of tens of thousands of Americans who are impacted by sickle cell anemia. Join in our partnership to find a cure for sickle cell anemia tomorrow by investing the 3-to-1 match of $21 million today.

The investment will help the State of Louisiana and the region to develop a cure for the United States and for all persons who are affected by sickle cell anemia.

I would like to again thank you for this opportunity of addressing the committee and to say that we are committed to finding a cure

for sickle cell anemia. We need your help, and we would ask you to vote favorably and support this support this initiative.

[The prepared statement of Mr. Jones appears at the end of the hearing record.]

Senator WELLSTONE. Thank you, Mr. Jones.

Certainly, there is no question about the reputation of Southern University, and I think we will probably want to put some questions to you as to what the State commitment might be, not just this year, but the following year and the year after that, what kind of annual appropriation would it be over a period of time. But let us put those questions to you and get a written response.

I thank both of you, and I do apologize for the committee. It is very, very unusual the way this happened today. It is the worst possible timing for everyone. I personally think that all too often, sickle cell and those who suffer and struggle with it are out of sight, out of mind, put in parentheses and put into brackets. There should be, must be, has to be more of a commitment.

I only came in at the very end because of other commitments I made a long time ago, but I think your testimony is very important, and I thank everybody who was here today, and I apologize for my colleagues for the conflicts that they had.

[Additional statements and material submitted for the record follow:]

THE ACCOMPLISHMENTS OF THE COMPREHENSIVE SICKLE CELL CENTER AT MEHARRY MEDICAL COLLEGE

JULY 26, 1994

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INTRODUCTION

Sickle cell disease (SCD) refers to a group of chronic, hereditary blood disorders that primarily affects African-Americans. One in every 400 black babies born in the United States is affected by SCD. The disease is characterized by diverse symptoms, and numerous complications; throughout their lives affected individuals are plagued by recurrent bouts of pain secondary to vaso-occlusion which is the hallmark of the disease. These recurrent episodes of pain and vaso-occlusion often result in incapacitation. Other problems include increased risk of infections aseptic necrosis, increased risk of infections, and delays in growth and development just to name a few of its associated complications.

The Physical Aspects of SCD

Sickle Cell Disease is an autosomal recessive red blood cell disorder characterized by sickling of erythrocytes, obstruction of the microcirculation and a chronic hemolytic anemia. The disease is seen predominantly among the Afericain-

American population in the United States, but is also prevalent among populations of Africa, the Mediterranean, Caribbean, Middle East, and southern India. Thus because the United States is composed of many individuals from all parts of the world its is also diagnosed in other ethnic groups within the US. On the African continent SCD is thought to provide a natural immunity to malaria, but it has no such usefulness to its carriers in the rest of the world.

Pathogenesis

The first documentation of SCD was made in 1910, by a Chicago cardiologist, James Herrick who discovered it in the bloodstream of a West Indian student. Almost four decades later, Pauling and colleagues demonstrated that the sickling phenomenon was due to a structural defect in the hemoglobin molecules and this work resulted in reward of the Nobel prize for medicine.

Hemoglobin is composed of heme, the red-colored substance, and globin, a protein component. The function of hemoglobin is to transport oxygen from the lungs to the tissues. The abnormality in sickle cell disease lies in the globin portion of hemoglobin. Globin consists of two pairs of polypeptide chains which include alpha chains and non-alpha chains. The alpha chain consists of 141 amino acids, while the non-alpha chains consist of 146 amino acids.

A decade after Pauling's discovery, Ingram demonstrated that the abnormality in the hemoglobin molecule was due to a biochemical alteration, which was the result of the substitution of a single amino acid by another. With classic sickle cell disease, sickle cell anemia, (HbSS), valine has been substituted for glutamic acid at the sixth position of the beta chain. Currently over 700 abnormal hemoglobin are known. Some of the more common variants are describe are found in Table 1.

SICKLE SYNDROMES
Table 1

Syndrome	Substitution	Site
HbS	Glu-> Valine	86
HbC	Glu-> Lysine	86
HbD	Glu-> Glna	8121
HbE	Glu-> Lysine	826

Ordinarily, red blood cells with normal hemoglobin are able to maneuver through the microcirculatory system with relative ease. In sickle cell anemia, because of the single amino acid substitution the hemoglobin takes on different properties. It continues to have normal oxygen carrying capacity. Upon deoxygenation, however, there is a change in the solubility of the protein so that the HbS molecules clump together to form tactoid. The cell membrane becomes distorted, and assumes a sickle shape. these cells are inflexible, sticky, and survive about 7-20 days. Sickled cells are often described as having a "log-jamming effect" in the smaller passage ways, which result in a broad range of clinical manifestations. Sickled cells can resume their rounded shape upon re-oxygenation but only for a limited number of times. After a period of time, they become irreversibly sickled and are removed from circulation via the reticuloendothelial system.

Hemoglobin Variants

Currently more than 700 abnormal types of hemoglobin have been identified in man. Three hemoglobin form our total hemoglobin picture: Ha, Ha_2, and HbF. Hemoglobin A is the most abundant of the three. It is composed of two alpha chains and two beta chains. The other two hemoglobin are found in lesser amounts, but must be present for a normal hemoglobin pattern. Ha_2 is composed of two alpha chains and two delta chains. HbF is composed of two alpha chains and two gamma chains. HbF is

also known as fetal hemoglobin and is the major type of hemoglobin produced before birth. After birth, production of gamma chains decreases as production of beta chains begin. Thus one would see a decreased amount of HbF and an increased amount of Ha. Most abnormal hemoglobin result from point mutations in the structural genes that code for the amino acid sequence of the globin chains of the molecule.

Hemoglobin AS is sickle cell trait. Sickle cell trait occurs in one out of every 10 Black Americans. In fact, there are over two million Black Americans with sickle cell trait. Sickle cell trait is not a disease, it is a benign carrier state that rarely produces health problems. The concern of the sickle cell trait carrier is that of prospective parenthood. If both partners have the trait, there is a 25 per cent chance that with each pregnancy the couple will have a child with sickle cell anemia. Except in a few unusual circumstances, individuals with sickle cell trait are asymptomatic.

The carrier state AS is benign because there is a preponderance of hemoglobin A in each red blood cell of the hemoglobin AS type. Usual proportions in each cell are approximately 60 per cent hemoglobin A and 40 per cent hemoglobin S. There is therefore not enough hemoglobin S to cause the symptoms of the homozygous condition, HbSS.

Variants of SCD

After sickle cell anemia, the most common forms of sickle cell disease in decreasing order of frequency are sickle hemoglobin C disease (HbSC), and sickle-beta thalassemia of which there are two subtypes (S-β^0 and S-β^+ disease). In each form of sickle cell disease, at least one β-globin structural gene β^s codes for the synthesis of a sickle hemoglobin. The allelic β-globin gene may code also for a sickle hemoglobin (HbSS), another structural abnormal hemoglobin (HbSC), or may produce either a partial defect in hemoglobin A synthesis (S-β^+ thalassemia), or a complete defect in hemoglobin A synthesis (S-β^0 thalassemia).

Sickle Hemoglobin C Disease

It has been estimated that 2 per cent of the Black population carry the gene for hemoglobin C. The incidence is 1 per 1000 live births. The carrier state as in the case of sickle cell trait is asymptomatic.

Sickle hemoglobin C disease has been described as a milder form of classic sickle cell disease,that is sickle cell anemia. Individuals with the disease have a higher hemoglobin level and less frequent episodes of pain. Growth and development may not be affected to the same degree as in hemoglobin SS disease. As in the case of sickle cell anemia, HbSC patients have an increased risk of developing certain complications that are related to their disease. For example, retinopathy can result in retinal detachment, and necrosis of the femoral head can be seen (Lin-Fu, 1979). Individuals with HbSC have bouts of transient functional hyposplenia. This puts them at risk for not being able to combat infections adequately. Many individuals with the disease are less symptomatic than the homozygous HbSS patient and may not obtain adequate medical supervision.

Hemoglobin Sickle Beta-thalassemia

Sickle beta-thalassemia occurs in about 0.4 per cent of the Black population in the United States. Individuals with sickle beta-thalassemia have symptoms that vary from mild to those as marked as hemoglobin SS. Clinically, there is less anemia, and less sickling was found in vivo. The vaso-occlusive phenomenon that causes painful episodes still occurs.

As was mentioned earlier, there are two types of beta-thalassemia, β^+ and β^0. In sickle beta$^+$-thalassemia some normal hemoglobin A is produced, but far more of the abnormal hemoglobin S is produced. In sickle beta^0-thalassemia, only abnormal beta chains are made, producing hemoglobin S, and no hemoglobin A is found. Often different clinical pictures are seen with these two hemoglobinopathies. Variability is an important factor. Some experts report that Sickle beta-$^+$thalassemia produces milder clinical symptoms than sickle beta^0-thalassemia. Nevertheless, sickle beta-thalassemia is a sickling disorder and must be managed in the same way as other sickling syndromes.

Table 2

Incidence of Sickle Cell Disease
in the United States

Condition	Hb Types	% of Blacks
Sickle Cell Trait	AS	8-14%
Sickle Cell Anemia	SS	0.3-1.3%
Hemoglobin C Trait	AC	2.3%
Homozygous C Disease	CC	.016%
Sickle Hemoglobin C Disease	SC	0.1-0.25%
Hemoglobin D Trait	AD	0.08-0.4%
Homozygous D Trait	DD	NA
Hemoglobin E Trait	AE	NA
Sickle Cell Thalassemia	S-Thal	0.04%
Beta-Thalassemia Trait	Thal Minor	1%

* NA = Not Available

Diagnosis

The diagnosis of sickle cell disease is made by performing a hemoglobin electrophoresis. The basic concept of electrophoresis is that protein molecules are electrically charged and will migrate in an electric field. The way a particular hemoglobin migrates depends upon the pH and allows for identification of different proteins.

Clinical Manifestations

The complications of sickle cell disease are quite varied. In some cases individuals are entirely asymptomatic and are detected only during population screening, whereas others are constantly plagued by painful episodes.

The major complications of sickle cell disease can be placed into three catagories: acute events, chronic events, or health related events that require added medical attention. Acute events include painful episodes, acute chest syndrome, right upper quadrant syndrome, skeletal and joint events, hand-foot syndrome, cerebrovascular accidents, aplastic episodes, sequestration crisis, acute febrile event, and priapism. Chronic events include leg ulcers, renal

complications, aseptic necrosis, and ocular complications. Health related events include delayed growth and development, delayed sexual maturation, pregnancy, surgery, and anesthesia (Walters, 1983).

For the first few months of life there is usually no indication of the disease upon physical examination. Because there is more production of sickle hemoglobin and less HbF, by six months of age, more symptoms begin to develop. These include dactylitis, hepatomegaly, and splenomegaly. In the older child, during non-acute phases varying degrees of pallor, scleral icterus, hepatomegaly and cardiomegaly can be seen. In homozygous HbSS disease, the spleen is enlarged in early childhood as a result of its function in removing sickled cells from circulation. Functional activity is lost, however, in the first few years of life. After about 6-8 years of age, autosplenectomy or the self-destruction of the spleen occurs as a result of repeated splenic infarcts. Delayed growth and delayed sexual maturation, frontal bossing, and sometimes gnatopathy are characteristic of sickle cell disease.

The physical aspects of sickle cell disease constitutes only one facet of the health problem. A number of psychosocial issues, including the psychological concomitant of extended hospitalization and isolation, long term adjustment to survival, and an uncertain disease course have also surfaced. Many care-givers feel that addressing these problems is equally as important as addressing the physical problems that arise as a result of the disease.

Despite the complexities of SCD, the health prognosis has improved over the past decade. Prior to 1974, SCD was considered a terminal illness. Although still considered a chronic disease, SCD is no longer considered a fatal disease prior to adulthood. In fact, individuals with SS have been reported as living well into their 70s. Deaths occurring before adulthood were largely related to severe infections, e.g., pneumonia and organ failure. Fortunately, treatment and management, which include early detection, proper medication, and counseling, have improved the overall physical status.

In summary, SCD is a non-contagious, inherited blood disorder. There are many variants of SCD, the SS, and the SC states are the most prominent in the United States. Although many physical discomforts are associated with the disease, affected individuals can lead useful and productive lives, given proper medical treatment and management.

The improvement in the overall survival of individuals with SCD has occurred since 1972 when President Nixon in 1972 enacted the National Sickle Cell Disease Act. This is directly related to the establishment of Comprehensive Sickle Cell Centers which have provided for:

1. an environment for research
    a. basic
    b. clinical
2. Laboratory diagnosis
3. genetic counseling
4. universal sickle cell education

At the Meharry Comprehensive Sickle Cell Center the development of our center has in addition to the above activities being accomplished the following have also been achieved:

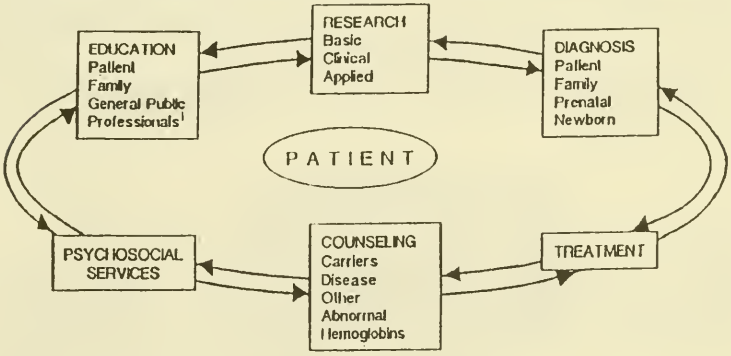
1. the achievement of a referral Center status
2. Stimulation of Research
    a. intramural
    b. extramural
3. becoming a resource center locally and especially for region IV
4. the development of a strong community outreach program

STIMULATION OF RESEARCH

Without the support of the NIH and the sickle cell disease branch it would have been difficult to establish the environment where limited resources, facilities and manpower existed to coordinated and stimulate research. The actual development process took a number of years to develop.This support has also allowed us interact with Vanderbilt University School of Medicine to further develop and apply application of new knowledge in the diagnosis and treatment of sickle cell disease. In the development of these overall activities a multidiscipline team approach from many individuals involved with health care delivery was required. And to maintained the activities requires that this team approach be maintained.

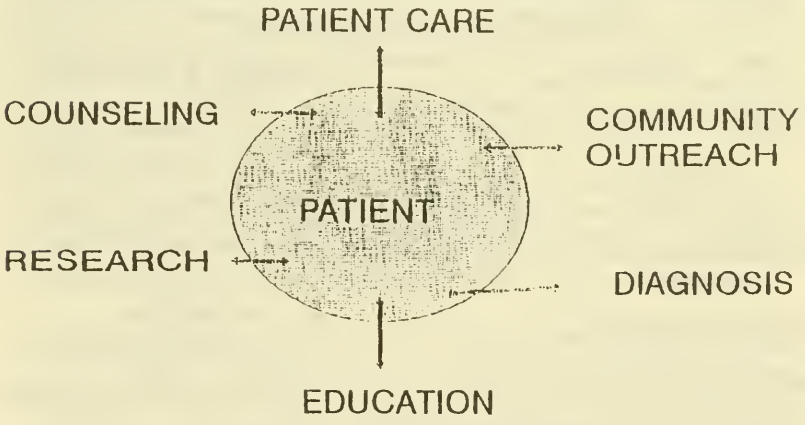
COMPREHENSIVE SICKLE CELL CENTERS

Program Components



COMPREHENSIVE SICKLE CELL CENTER

COMPONENTS



COMPREHENSIVE SICKLE CELL CENTER
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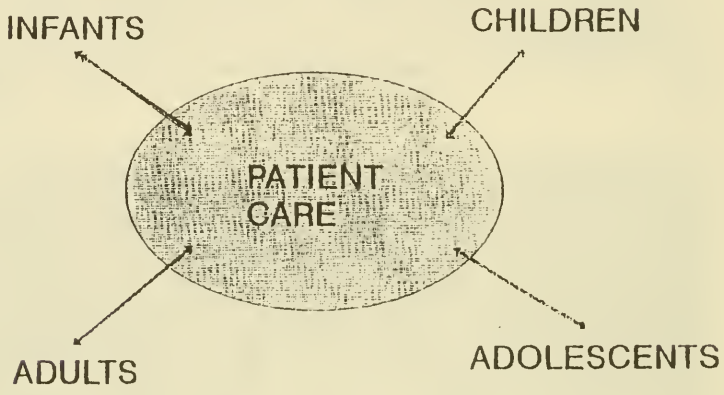
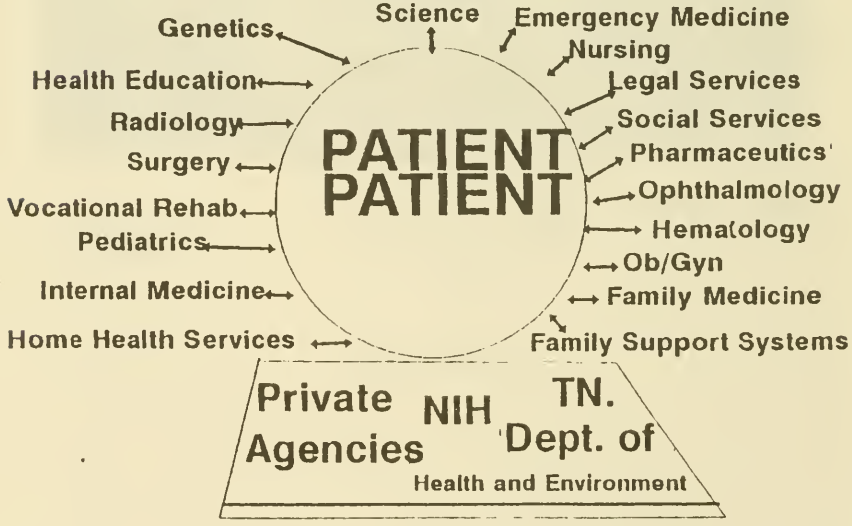


COMPREHENSIVE SICKLE CELL CENTER
CASE MANAGEMENT



TESTIMONY OF CHARLES D. JONES
LOUISIANA STATE LEGISLATOR
CHAIRMAN, LAW & JUSTICE COMMITTEE,
NATIONAL BLACK CAUCUS OF STATE LEGISLATORS
&
CONVENOR.CHAIRMAN, DELTA PILOT ECONOMIC DEVELOPMENT PROJECT
DELTA ECONOMIC ENERGY DISTRICT
BEFORE THE UNITED STATE SENATE
COMMITTEE ON LABOR AND HUMAN RESOURCES
JULY 28, 1994

INTRODUCTION

Chairman Kennedy, Senator Kassenbaum, other distinguished members of the Committee, I am Louisiana State Senator Charles Dean Jones, representing Louisiana's 34th Senatorial District. I also appear before you this morning as Chairman of the Law & Justice Committee of the National Black Caucus of State Legislators (NBCSL) and as the Convener and Chairman of the Delta Pilot Economic Development Project and its Delta Economic Energy District, Inc., (DEED). My remarks before this body today are also embraced by the National Baptist Convention, USA, Inc., and the National Rainbow Coalition.[1]

Before discussing the background of, the need for and the utility of federal support for the National Sickle Cell Research Center at Southern University, I want to thank Senator J. Bennett Johnston for his unstinting support and his championship in the United States Senate of legislation authorizing the Secretary of the Health and Human Services to award a grant for the establishment of the National Center for Sickle Cell Disease Research and Southern. I want to thank Senator Johnston also for his presence here today.

I take this opportunity to extend my gratitude to my long-time friend Congressman William Jefferson (D-2-LA) who is providing the leadership necessary to advance the measure through the United States House of Representatives. Congressman Jefferson also joins us today. Finally, I take this opportunity to acknowledge the efforts of Congressman Cleo Fields (D-4-LA) to garner support for House legislation that wILL establish on the campus of Southern University– located in Congressman Field's District– the National Sickle Cell Research Center. The establishment of this Center is a matter of paramount concern not only to the residents of Congressman Fields' District and to others in the State of Louisiana and the Delta Region, but to African Americans across the nation.

As evidence of the broad national support for the National Sickle Cell Research Center, I note that the unanimous 40-member Congressional Black Caucus of the United States Congress is in support of the National Center. In March of 1993, every member of the Congressional Black Caucus joined in sending a letter to Secretary of Health and Human Services, Donna Shalala, urging her support for the National Research Center at Southern. (Letter attached.)

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[1] The National Baptist Convention, USA, Inc., (NBC, USA) is the nation's oldest and largest association of Black Baptist ministers, representing tens of thousands of active and involved registered voters across America, as well as residents of Africa and the Caribbean. The national president of NBC, USA is Reverend Dr. T.J. Jemison, who hails from the State of Louisiana. Last year at its annual convention in New York City, NBC, USA, adopted by unanimous consent "A Concurrent Resolution" urging and requesting that its members support in any manner of means, the establishment of a national Sickle Cell Disease Research Center at Southern University. (Resolution attached.)

The National Rainbow Coalition is a national multi-racial, multi-cultural political and economic empowerment association, founded and chaired by The Reverend Jesse L. Jackson. Earlier this year, The Rainbow Coalition's Health Task Force recommended to Congressman Louis Stokes (D-OH), Chairman of the Congressional Black Caucus Health Braintrust and Convener of the African American Leadership Health Care Reform Work Group, that the CBC and the Work Group support and urge the appropriation of adequate federal funds to compliment (in a three to one match) the state funds appropriated by the State of Louisiana to establish and maintain at Southern University, the nation's only Sickle Cell Research Center.

The National Black Caucus of State Legislators, too, is in support of the Center. During its 17th Annual Conference in Denver Colorado last year, NBCSL adopted a resolution in support of the National Center for Sickle Cell Research, by unanimous consent. NBCSL is the educational, research and training association of the nation's 540 African American state legislators who primarily represent Africans Americans across the country--some of whom reside and/or work in rural communities, others in urban areas. Some who exist in affluent America, many who exist in poor America. Whether representing urban or rural, affluent or poor Americans, NBCSL members are united in their belief that the continued political, economic and social empowerment of African Americans and the enhancement of their communities and institutions, is central to the continued growth and development of this nation. NBCSL members, too, are united in the belief that true equality in this country can only be achieved when each American is guaranteed equality of life chances; and that a crucial prerequisite for likely achievement of equal life chances is accessibility of affordable, quality health care beginning before birth. This access must include necessary research to find cures for diseases peculiar to either gender; diseases peculiar to infants, children, and seniors; and people of every race and ethnicity, including African Americans. Access must also include necessary research to find cures for those whose diseases are behavioral in origin and those whose diseases are hereditary.

BACKGROUND AND NEED FOR THE NATIONAL SICKLE CELL RESEARCH CENTER

It is axiomatic that accessibility of affordable, quality health care, proper nutrition, safe and sanitary home and employment conditions and a clean environment are necessary components of an overall quality health care system. It is a fact that quality health care, proper nutrition, safe and sanitary home and employment conditions, and a clean environment are necessary to begin to equalize life chances among the haves and the have-nots. As a child who grew up in the poorest region in America, in the nation's poorest city, Lake Providence, Louisiana, where 82% of the population is on public assistance; and as a state legislator for nearly two decades, representing not only Lake Providence, but also the city of Monroe, Louisiana, where I presently reside-- which is the nation's third poorest city-- I see daily and have witnessed firsthand for more than four decades, the fact that children cannot study to capacity and cannot grow to be sturdy, productive members of our communities without sound nutrition, safe housing and health maintenance based on prevention. I have seen firsthand the deleterious and debilitating effect that poverty and the concomitant lack of health and human needs services; absence of proper nutrition; lack of safe and sanitary and employment conditions; and a hazardous environment have, not only on a people, a city, parish or a state, but on an entire region.

It was in part my witnessing these things, that lead me in 1993, to organize the Delta Pilot Economic Development Project, and to launch as its initial project the Rural Community Health Service Project. The Delta Pilot Economic Development Project is an Arkansas/ Louisiana/Mississippi Tri-State regional economic and human development corporation launched at my urging with broad and diverse support from the Tri-State region, including that of the governors of the three states; many members of the congressional delegations of the three states; state and local elected officials from the Tri-state Region; business persons, labor, religious leaders, community leaders and with the support of thousands of the suffering residents of this beleaguered region. Our goal is to formulate and implement collaborative regional solutions to the myriad problems which plague this region, not the least of which are that it has the nation's highest illiteracy rate, highest poverty rate, rural poverty and minority poverty rate, highest infant mortality rate, highest infirmity rate, and lowest educational attainment rate in the nation. The group set as goals, *inter alia*, the establishment of an economic development and health corridor defined by the Mississippi River. In so doing, we were building upon and organizing to implement the recommendations of the Lower Mississippi Delta Commission, chaired by then Governor Bill Clinton.

With regard to the establishment of the Health Corridor, the Delta Pilot Economic Development Project noted that the ArkLaMiss Region has the highest percentage of medically under-served residents in the nation, the highest infant mortality rate in the nation, the highest low birth weight births, the highest incidents of births to teen mothers, among the lowest primary care physician-to-patient and registered nurse-to-patient ratio in the nation. Collective remedial goals were established to bring the Tri-State region at least up to par with the rest of the nation. Each of you has been provided with a copy of the Delta Pilot Economic Development health care findings and goals.

The State of Louisiana took the lead in following up on the Tri-State Health Care recommendations. The Northeast Louisiana Council on Black Economic Development conducted a survey of the rural health care problems in all 45 rural parishes in the state. A copy of the survey and a copy of the recommendations and actions taken pursuant to the survey--including the passage of state legislation to address some of the findings-- have been provided to each of you this morning. While all of the findings are troubling, most were anticipated. We were alarmed, however, by the exceedingly high number of African Americans across the state with the Sickle Cell Anemia disease or trait. We found that Louisiana has the highest number of citizens per capita afflicted with the Sickle Cell disease in the nation. Of Louisiana's 1,299,281 minorities, 3,248 have Sickle Cell Anemia and 129,928 have the trait. In the rural parishes alone, 990 residents have the disease, while 37,838 possess the trait. Nationally, the sickle cell disease is estimated to affect more than 50,000 Americans. Approximately one in every twelve (12) black Americans is born with the Sickle Cell trait, and about one in four hundred (400) has Sickle Cell Anemia.

For those of you who are unfamiliar with the disease, it is not a silent killer, like high blood pressure, it takes its victims kicking and screaming. It causes excruciating pain. It causes diseases, infections, mal-functioning of crucial organs like the spleen, then it kills! It is an inherited disorder of the red blood cells, that disproportionately affects persons of African ancestry. To a far lesser degree, persons of Arabian, Caribbean, Central and South American, East Indian and Mediterranean ancestries are affected by the disease, also. As you know, red blood cells carry oxygen to all parts of the body through a protein called hemoglobin. Normal red blood cells contain normal hemoglobin and are donut shaped. They move easily through blood vessels. For those with sickle cell disease, the red blood cells contain sickle hemoglobin which causes them to have a curved or sickle shape-- much like the end of a tuning fork-- after oxygen is released. Sickled cells become stuck in blood vessels, thus blocking the blood flow and causing damage to the tissue. A major effect of the disease is the sickle cell "crisis" which occurs when sickle cells plug blood vessels and block the flow of blood. The blockage typically lasts several days, usually affecting the arms, legs, hands, feet, abdomen or another local part of the body. Tissue damage, often involving major organs, occurs with each successive episode of oxygen deprivation. The cumulative effects of the disease are debilitating and life threatening. Those afflicted with severe forms of the disease usually do not live through their teens.

The practical effect of the disease was summed up by a young woman in her early twenties, from Senator Mikulski's state, who appeared on a panel Congressman Louis Stokes convened on this deadly disease, last September during the 23rd annual Congressional Black Caucus Week. Said the woman:

> "I have Sickle Cell Anemia and I am not supposed to be here today. I usually wish that I wasn't [sic] here. I wish that I was dead....sickle cell causes me a lot of pain. The pain is so bad I can't stand it.... Sometime I start breathing fast and can't hardly [sic] catch my breath... I get weak, start to slur my speech and go in and out of consciousness. Sometime I pass out in the street. People step over me or on me. They think I'm a drug addict. If I get to the hospital, everybody there think [sic] I'm on drugs, too, and they treat me like some kind of criminal....I can't hold down a job for long because of the frequency of my crises. I don't have no [sic] money, no nothing [sic] because of Sickle Cell."

Despite the fact that the cause of the sickle cell disease has been known for years--the very minor structural variation in the mutant hemoglobin--very little progress has been made toward developing a cure or suitable treatment for the disease. At the present time, the major treatment for the painful crisis is medication for relief of pain, which simply treats the immediate symptoms. It does not cure the malady or enhance the quality of the lives of those who have sickle cell.

In recent years, the federal government has been responsive to this situation. The Department of Health and Human Services has a national program to reduce the morbidity and mortality from sickle cell disease. The Department's National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) has the lead responsibility for carrying out

the government's sickle cell abatement program. There are currently ten (10) Comprehensive Sickle Cell centers across the nation which engage in demonstration education projects, screening, diagnosis, management, counseling and clinical studies. No where is there a national center dedicated exclusively to conducting multi-disciplinary research that will lead to the discovery of a cure for this deadly disease. And, neither the current NIH appropriations nor federal authorization legislation provide for the expenditure of federal funds to erect a state-of-the-art Sickle Cell Research Center. No present monies can be used for structural development. There is a need for such a center, to foster the expeditious discovery of a cure for this disease that affects more than 50,000 Americans.

THE ROLE OF THE NATIONAL SICKLE CELL RESEARCH CENTER AT SOUTHERN

Unlike the ten (10) comprehensive Sickle Cell service and counseling centers which presently exist, the National Sickle Cell Research Center will engage exclusively in research: basic biomedical research, and psychosocial research.

BASIC BIOMEDICAL RESEARCH

The Center will undertake investigations such as gaining a better understanding of the formation of sickle cells, the behavior of sickle cells when they flow through blood vessels, and the characteristics of sickle cells after they sickle. Considerable study will be devoted to the isolation, characterization, and synthesis of anti-sickling agents- substances that enable victims of the disease to lead more normal lives by decreasing the chances of red blood cells becoming deformed. These areas of investigation are required in order to determine the types of drugs that prevent, inhibit, or reverse the sickling process. A search of current literature suggests that this is an area of basic investigation that leaves many questions unanswered.

Collaborative arrangements will be undertaken with other universities in the state that have the interest in and expertise to do basic biomedical research related to anti-sickling agents as well as sickle cell disease and other hemoglobin abnormalities.

The Center will conduct studies as the ultrastructural levels in the areas of molecular biology and genetic engineering. These investigations will focus on various genetic approaches to the sickling process. Specific attention will be given to DNA manipulation and other techniques of modern biology which could cause patients to begin synthesizing normal adult or fetal hemoglobin. Electron microscopy is one of the tools that will be used in investigating *in vitro* and *in vivo* sickling. The concept of genetic engineering is one of the new and rapidly developing disciplines in science. Searches of the literature suggest that not enough attention is being given genetic engineering with sickle cell disease at the target.

PSYCHOSOCIAL RESEARCH

The Center will conduct a wide variety of human behavioral studies designed to shed new knowledge on such issues as the effectiveness of various counseling and education methods, coping skills on the part of patients and families, and counselor education and evaluation. Qualification standards do not currently exist for sickle cell genetics counselors. Research questions need to be answered as to what minimum body of knowledge needs to be mastered in order to become effective in the role.

A broad range of national studies intended to shed new light on public policy issues related to Sickle Cell Anemia will be undertaken. Many of these will be observational studies of which some will be descriptive while others will be analytical in approach, depending on the types of research questions they address. Cross-sectional, group comparison, and longitudinal studies on questions related to mandatory genetic testing of susceptible newborns, premarital testing for the presence of S (sickling) genes and the need for state and national sickle cell registries are all areas of public policy that lack hard data.

Clinical Research Collaborative arrangements will be made with other Louisiana higher education institutions, such as the Shreveport and Tulane University Medical Center to conduct clinical trials on anti-sickling agents, some of which may have been discovered during basic laboratory investigations at this Center and elsewhere. Because of the close proximity of Earl K. Long Memorial Hospital to Southern University, basic biomedical investigators at the Center and LSU faculty at Earl K. Long, will be able to conduct a number of joint studies.

The Center will not engage in sickle cell services to patients except as needed in support of its research objectives. However, the Center will work cooperatively with the Baton Rouge Sickle Cell Foundation and other Sickle Cell service organizations in the state, when asked by these organizations to do so.

WHY ESTABLISH THE NATIONAL SICKLE CELL RESEARCH CENTER AT SOUTHERN UNIVERSITY

Some of you have asked, even if Congress opts to support a National Sickle Cell Research Center, why should it be located at Southern University and not in another state or at another institution. The answer to this question is twofold:

Southern's Location in the State of Greatest Need,
Its Capability and Its Commitment to the National Center; and

The State's Commitment to the Project as Evidenced by its
$7 million Appropriation for the National Center.

SOUTHERN'S LOCATION IN THE STATE OF GREATEST NEED, ITS CAPABILITY & ITS COMMITMENT TO THE NATIONAL CENTER

Southern University is located in Baton Rouge, Louisiana. As noted previously, the state of Louisiana has the highest number of citizens per capita afflicted with the Sickle Cell disease in the nation. Of Louisiana's nearly 1.3 million minorities, more than 133,000 have either the disease or the trait. More than 10% of the state's minority population is directly affected by this killer disease. Nationally, approximately one of every twelve (12) persons of African descent is affected. Southern University, one of the state's premier institutions of higher education, and the nation's largest historically and predominantly black land grant institution, wants to do something immediately to find a cure for this disease. Southern has begun taking steps to identify a remedy for this malady.

Located in Baton Rouge, more than 16,663 students attend Southern University. Southern has been graduating scholars and sending them out into the national and international workforces for 113 years. It has a long track record of graduating students with degrees in basic sciences, some of whom go on to attend medical school. Others receive advanced degrees in research and the sciences, including chemistry and biology.

The National Aeronautics and Space Administration and Department of Energy have acknowledged Southern's research capability and its important role in educating African American scholars. Senator Mikulski, just last year, the National Aerospace and Science Administration and the Department of Energy awarded the institution a five-year, $5 million grant to develop an aerospace engineering undergraduate option in the Department of Engineering. This is just one example of the type of federal support the institution has received and, the type of federal recognition the institution receives for academic excellence.

As the nation's largest HBCU and one that is located in the state with the largest percentage of sickle cell victims, Southern has committed its resources to finding a cure for Sickle Cell disease. Toward this end, the University assembled on its campus for a two-day work session, the foremost experts in the fields of biomedical research, psychosocial research, pediatric hematology, oncology, and related fields. (The attendees and notes from the work sessions are contained in the back of the Rural Community Health Service Project, which you have been provided.) The group developed a proposed curriculum for the Center, a set of goals and a timetable for launching the National Research Center. It was resolved that the National Sickle Cell Research Center at Southern would conduct collaborative research with other Louisiana universities, agencies and medical schools. The group resolved that the Center will later collaborate with other universities and agencies in the region, and across the nation. The work group also discussed the ways and means of building a state-of-the-art Sickle Cell Research Center. Southern alumnae, foundations, corporations, state and federal funds were targeted for support of the project.

Southern is taking affirmative steps to prepare its faculty for the coming of the Center. Faculty internships have been conducted on Southern's campus in the area of Sickle Cell

Anemia. For one week, faculty attend lectures conducted by the nation's foremost experts on the sickle cell disease.

Evidencing its support for the National Center, the Louisiana State Legislature passed a bill which I authored, committing $7 million to the effort: an initial $1.5 million in start up funds; and $5.5 million for capitol outlay to be used toward building a research center. This latter appropriation is contingent upon Southern's receiving a three-to-one match from the federal government.

CONCLUSION

Mr. Chairman, as I sit here today, a little more than one year after the National Center's launching meeting at Southern, in addition to the $7 million committed to the effort by the state of Louisiana, Southern is obtaining financial commitments for the Center from alumnae, corporations and foundations. Southern has faculty, research staff commitments and collaboration agreements with LSU and Earl K. Long Hospital, which are located less than five miles from Southern. I'm here today to ask the federal government to join us in the collaborative public/private venture...to help us turn the lives around of the tens of thousands of Americans who are impacted by Sickle Cell Anemia. Join in our partnership to find a cure for Sickle Cell Anemia tomorrow, by investing $21 million today.

This investment will help the State of Louisiana and the Delta Region take the first step toward launching its regional health and economic development corridor-both of which are sorely needed to bring relief to this beleaguered region. For, as long as the Delta is suffering, America will suffer. As long as there is poverty in the Delta, the region of New England won't be rich. As long as disease is rampant and thousands of people in the Delta cannot expect to live to be twenty or thirty years, the people of Minneapolis can never be totally healthy even if they get a good check up at the Mayo Clinic. Senator Durenburger. For we can never be what we ought to be until the "least of these" are what they ought to be. We are interdependent. No man or woman stands alone. Senator Kennedy, Members of this Committee, please stand with Southern University, the State of Louisiana, the Delta Economic Energy District, the Congressional Black Caucus, the National Black Caucus of State Legislators, the National Baptist Convention, USA, the National Rainbow Coalition and the 50,000 Americans whose lives are adversely affected by Sickle cell Anemia, on the issue of funding a National Sickle Cell Research Center at Southern University.

I thank you; and I will be happy to entertain any questions you may have.

Louisiana State Senate
Committee on Revenue and Fiscal Affairs
P.O. Box 94183
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Secretary

March 30, 1993

The Honorable Donna Shalala
Secretary, Department of Health
and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

Dear Secretary Shalala:

During the 1992 Louisiana Legislative Regular Session, 1.5 million was appropriated for start-up funding, planning and designing the first National Research Center for Sickle Cell Anemia in the United States.

As Chairman of the Revenue and Fiscal Affairs Committee for the Louisiana State Senate, please know that we plan to amend the Capital Outlay bill this session to include 5.5 million dollars for the First National Sickle Cell Anemia Research Center at Southern University - Baton Rouge, Louisiana.

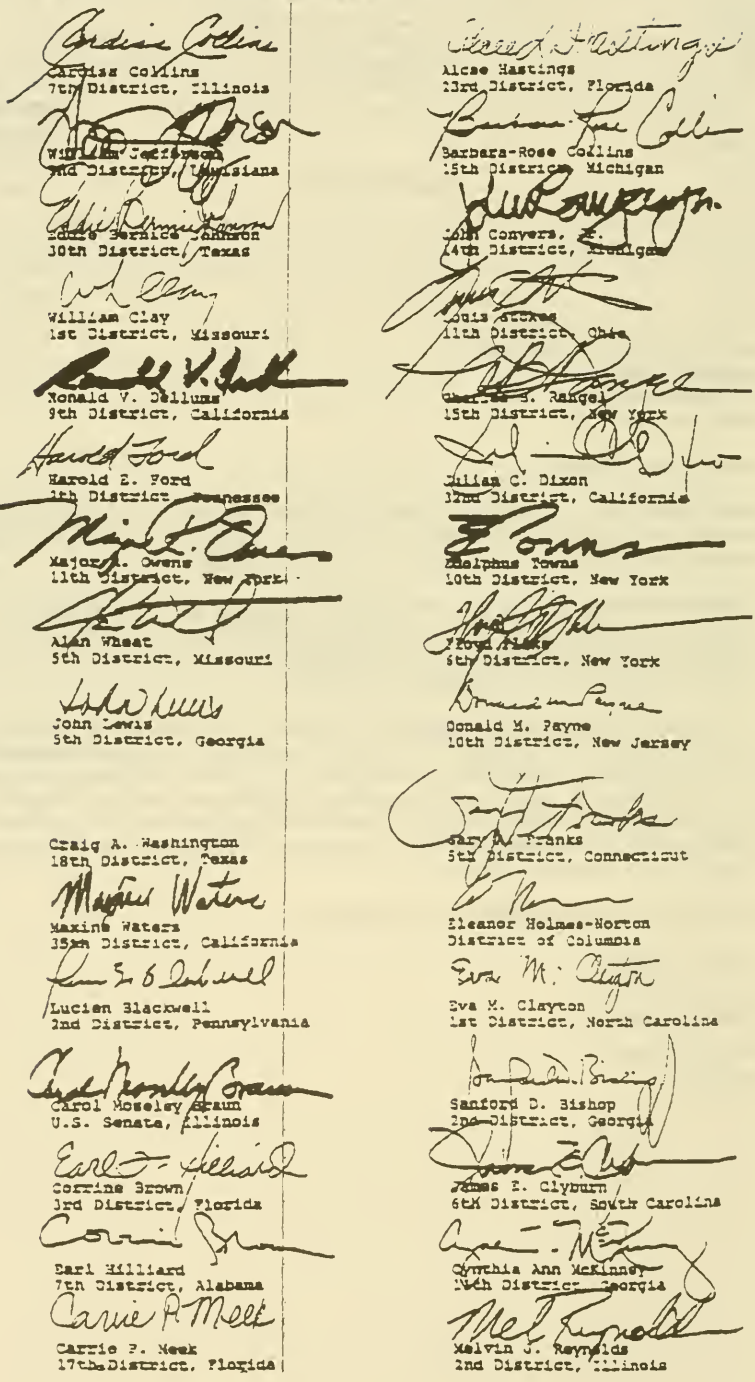
As you know, there is national support for the Research Center and its purpose, which is to research, to develop and to conduct a nationally recognized short and long range program that will delve into the causes of Sickle cell disease and its cure. The Research Center will be domiciled at Southern University in Baton Rouge and establish a cooperative relationship with the Department of Health and Hospitals, other Universities, National and International Associations and Agencies interested in the Research Center.

Thank you for your consideration of this matter.

Very Truly Yours,

Jon D. Johnson
Chairman

Southern University, Baton Rouge, Louisiana
National Sickle Cell Anemia Research Center



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A CONCURRENT RESOLUTION

To urge and request the members of the National Baptist Convention, U.S.A., Inc. to take the necessary steps to support the National Sickle Cell Disease Research Center located at Southern University and Agricultural and Mechanical College in Baton Rouge, Louisiana.

FURTHER, to set aside one Sunday annually for all churches belonging to the National Baptist Convention, U.S.A., Inc. to recognize and financially contribute to the research program of the "National Sickle Cell Disease Research Center." On this Sunday, member churches will take part in a "One Great Hour of Sharing" special offering to be donated to the Research Center in its work toward eradicating sickle cell disease.

WHEREAS, there is no national center exclusively devoted to sickle cell disease research currently existing in the United States; and

WHEREAS, the Congressional Black Caucus, consisting of 40 members of the United States Congress unanimously is in support of establishing a national sickle cell disease research center on the campus of Southern University; and

WHEREAS, during its 1992 Legislative Session, the Louisiana Legislature created a National Sickle Cell Anemia Research Center under the leadership of Senator Charles D. Jones, and funded it with $1.5 million for planning and development and a $5.5 million outlay commitment to begin construction; and

WHEREAS, President-elect Bill Clinton has committed his support for the establishment of a national sickle cell research center on the campus of Southern University and has committed to appropriate a three to one match of the State of Louisiana's $7 million, in the amount of $21 million; and

WHEREAS, the National Black Caucus of State Legislators has commended the Louisiana Legislative Black Caucus, the State of Louisiana and Senator Charles D. Jones, lead author, for passing legislation and for funding the creation of the nation's first National Sickle Cell Anemia Research Center; and

WHEREAS, the National Black Caucus of State Legislators supports the efforts of the Louisiana State Black Caucus to establish this research center at Southern University at Baton Rouge, Louisiana; and

WHEREAS, only the small amount of $15 million is contributed annually by the federal government to research sickle cell disease; and

WHEREAS, one in ten African Americans carries a gene for sickle hemoglobin, and one in every five hundred black newborns in the United States has sickle cell; and

WHEREAS, all newborns at risk should be screened for sickle cell disease to permit earlier diagnosis and treatment and to significantly reduce illness and the death rate among those children with the disease; and

WHEREAS, there exists a need to emphasize the importance of early detection and educate the primary medical care providers, parents and community on the importance of timely medical management of those patients with this inherited disease; and

WHEREAS, sickle cell disease is one of the least understood diseases of our time, which presently has no cure and continued research into its causes and cure is vital; and

WHEREAS, the establishment of a research center for such purposes would certainly enhance the programs currently in place by broadening the resource base for research using those experts committed to finding relief for the unfortunate victims who suffer the consequences of this serious and life-threatening disease.

THEREFORE, BE IT RESOLVED that the National Baptist Convention, U.S.A., Inc. hereby urges and requests its members to take the necessary steps to support the national sickle cell disease research center at Southern University and Agricultural and Mechanical College in Baton Rouge, Louisiana.

BE IT RESOLVED that a copy of this Resolution be transmitted to each member church, each member of the Congressional Black Caucus of the United States Congress, each member of the National Association of Black State Legislators and the President of the United States.

L. J. Johnson

Amos C. Brown

Senator WELLSTONE. Thank you very much. The committee is adjourned.

[Whereupon, at 3:36 p.m., the committee was adjourned.]

82-553 (68)

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