AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

S. Hrg. 106–304

CONQUERING DIABETES: ARE WE TAKING FULL ADVANTAGE OF THE SCIENTIFIC OPPORTUNITIES FOR RESEARCH?

HEARING

BEFORE THE

PERMANENT
SUBCOMMITTEE ON INVESTIGATIONS

OF THE

COMMITTEE ON
GOVERNMENTAL AFFAIRS
UNITED STATES SENATE

ONE HUNDRED SIXTH CONGRESS

FIRST SESSION

OCTOBER 14, 1999

Printed for the use of the Committee on Governmental Affairs

U.S. GOVERNMENT PRINTING OFFICE
61–160 cc WASHINGTON : 2000

For sale by the Superintendent of Documents, Congressional Sales Office
U.S. Government Printing Office, Washington, DC 20402

COMMITTEE ON GOVERNMENTAL AFFAIRS

FRED THOMPSON, Tennessee, *Chairman*

WILLIAM V. ROTH, Jr., Delaware
TED STEVENS, Alaska
SUSAN M. COLLINS, Maine
GEORGE V. VOINOVICH, Ohio
PETE V. DOMENICI, New Mexico
THAD COCHRAN, Mississippi
ARLEN SPECTER, Pennsylvania
JUDD GREGG, New Hampshire

JOSEPH I. LIEBERMAN, Connecticut
CARL LEVIN, Michigan
DANIEL K. AKAKA, Hawaii
RICHARD J. DURBIN, Illinois
ROBERT G. TORRICELLI, New Jersey
MAX CLELAND, Georgia
JOHN EDWARDS, North Carolina

HANNAH S. SISTARE, *Staff Director and Counsel*
JOYCE A. RECHTSCHAFFEN, *Minority Staff Director and Counsel*
DARLA D. CASSELL, *Administrative Clerk*

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

SUSAN M. COLLINS, Maine, *Chairman*

WILLIAM V. ROTH, JR., Delaware
TED STEVENS, Alaska
GEORGE V. VOINOVICH, Ohio
PETE V. DOMENICI, New Mexico
THAD COCHRAN, Mississippi
ARLEN SPECTER, Pennsylvania

CARL LEVIN, Michigan
DANIEL K. AKAKA, Hawaii
RICHARD J. DURBIN, Illinois
MAX CLELAND, Georgia
JOHN EDWARDS, North Carolina

K. LEE BLALACK, II, *Chief Counsel and Staff Director*
LINDA J. GUSTITUS, *Minority Chief Counsel and Staff Director*
MARY D. ROBERTSON, *Chief Clerk*

CONTENTS

	Page
Opening statements:	
Senator Collins	1
Senator Edwards	10
Senator Levin	14

WITNESSES

THURSDAY, OCTOBER 14, 1999

Phillip Gorden, M.D., Director, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health	5
Ryan Dinkgrave, Livonia, Michigan, on behalf of the Juvenile Diabetes Foundation	17
Pam Fernandes, Needham, Massachusetts	18
Gordon Jump, Coto de Caza, California	20
William H. Fuller, Jr., Virginia Beach, Virginia	23
C. Ronald Kahn, M.D., Executive Vice President and Director, Joslin Diabetes Center, Boston, Massachusetts, and Former Chairman, Diabetes Research Working Group	26
Edward H. Leiter, Ph.D., Senior Staff Scientist, The Jackson Laboratory, Bar Harbor, Maine	30
Senator Spencer Abraham, a U.S. Senator from the State of Michigan	33
Jeffrey A. Bluestone, Ph.D., Director, Ben May Institute for Cancer Research, University of Chicago, Chicago, Illinois	34

ALPHABETICAL LIST OF WITNESSES

Abraham, Hon. Spencer:	
Testimony	33
Prepared statement	33
Bluestone, Jeffrey A. Ph.D.:	
Testimony	34
Prepared statement	89
Dinkgrave, Ryan:	
Testimony	17
Prepared statement	62
Fernandes, Pam:	
Testimony	18
Prepared statement	65
Fuller, William H. Jr.:	
Testimony	23
Prepared statement	73
Gorden, Phillip, M.D.:	
Testimony	5
Prepared statement	45
Jump, Gordon:	
Testimony	20
Prepared statement	68
Kahn, C. Ronald, M.D.:	
Testimony	23
Prepared statement with attached charts	75
Leiter, Edward H., Ph.D.:	
Testimony	30
Prepared statement	86

Page

EXHIBITS

*May Be Found In The Files of the Subcommittee

1. Chart: "Increasing Deaths Due to Diabetes" 93
2. Chart: "Diabetes: Research Investment vs. Medicare Costs" 94
3. Chart: "Diabetes Research as Fraction of NIH Total" 95
4. Chart: "Rising Prevalence of Diabetes in the U.S." 96
5. "The Family's Guide To Diabetes," Web site of Ryan Dinkgrave, Livonia, Michigan 97
6. a. *Conquering Diabetes—A Strategic Plan for the 21st Century*, A Report of the Congressional-Established Diabetes Research Working Group, 1999 ..... *
6. b. *Summary of the Report and Recommendations of the Congressionally-Established Diabetes Research Working Group* 100
7. Charts presented by Dr. C. Ronald Kahn:
   a. "Increasing Deaths Due To Diabetes" 115
   b. "The Economic Impact of Diabetes is Staggering" 116
   c. "The Economics of Diabetes" 117
   d. "Goals of the DRWG Plan" 118
   e. "Components of the DRWG Strategic Plan" 119
   f. "Budget Recommendations" 120
8. Statement for the Record of the American Diabetes Association 121
9. Statement for the Record of the American Association of Diabetes Educators 130
10. Statement for the Record of Arnauld E. Nicogossian, M.D., Associate Administrator, Office of Life and Microgravity Sciences and Applications, National Aeronautics and Space Administration 134
11. *Diabetes Overview*, National Diabetes Information Clearinghouse (NIDDK) 137
12. *The Vision of Pam Fernandes*, Diabetes Forecast, September 1999 153

CONQUERING DIABETES: ARE WE TAKING FULL ADVANTAGE OF THE SCIENTIFIC OPPORTUNITIES FOR RESEARCH?

THURSDAY, OCTOBER 14, 1999

U.S. SENATE,
PERMANENT SUBCOMMITTEE ON INVESTIGATIONS,
OF THE COMMITTEE ON GOVERNMENTAL AFFAIRS,
Washington, DC.

The Subcommittee met, pursuant to notice, at 9:30 a.m., in room SD–628, Dirksen Senate Office Building, Hon. Susan M. Collins, Chairman of the Subcommittee, presiding.

Present: Senators Collins, Levin, and Edwards.

Also attending: Senator Abraham.

Staff present: K. Lee Blalack, Chief Counsel and Staff Director; Mary D. Robertson, Chief Clerk; Kirk E. Walder, Investigator; Elizabeth Hays, Staff Assistant; Ryan Blalack, Intern; Leslie Bell, Minority Congressional Fellow; Priscilla Hanley and Felicia Knight (Senator Susan M. Collins); Butch Burke (Senator Ted Stevens); Anne Bradford (Senator Fred Thompson); Laurie Armstrong (Senator John Edwards); Allison Dehosky and Erin Quay (Senator Arlen Specter); and Natacha Blain (Senator Richard Durbin).

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS. The Subcommittee will please come to order.

Good morning. Today the Permanent Subcommittee on Investigations is holding an oversight hearing to examine the impact that diabetes has on Americans, and to determine whether Federal funding for diabetes research is sufficient to take advantage of the unprecedented opportunities for progress toward better treatments, prevention and ultimately a cure.

Diabetes is a devastating condition that affects people of every age, race and nationality. Sixteen million Americans suffer from diabetes, and about 800,000 new cases are diagnosed each year. Moreover, diabetes frequently goes undiagnosed. Of the 16 million Americans with diabetes, an estimated 5.4 million do not realize that they have the disease, with the result that its serious consequences go untreated.

Diabetes is one of our Nation's most costly diseases, both in human and economic terms. It is the fifth deadliest disease in the United States, and kills almost 200,000 Americans annually. As this chart illustrates,[1] while the death rate for other common life-threatening diseases, like cardiovascular disease and stroke, has

[1] See Exhibit No. 1, which appears in the Appendix on page 93.

declined in recent years, the death rate due to diabetes has actually increased by 30 percent since 1980.

Diabetes is also the leading cause of kidney failure; blindness in adults; and amputations not related to injury. It is a major risk factor for heart disease, stroke, birth defects, and shortens life expectancy by up to 15 years.

In addition to the human toll of diabetes, this disease costs the Nation in excess of $105 billion annually in health-related expenditures. At present, more than one out of every ten health care dollars and about one out of every four Medicare dollars are spent each year treating people with diabetes.

Indeed, taxpayers spend more than $40 billion a year treating people with diabetes through various programs such as Medicare, Medicaid, Veterans and Federal employees health programs. In stark contrast, only about 3 percent of the budget of the National Institutes of Health is devoted to research on diabetes and its complications.

This second chart illustrates the huge disparity between the cost of treating just Medicare patients and the amount of the Federal investment in diabetes research.[1] If we looked at all Federal programs, the disparity would be even greater.

What is particularly alarming to me is that the inadequate investment in research has occurred at a time when the percentage of Americans with known diabetes has increased dramatically. The number of diagnosed cases of diabetes has almost doubled since 1970. This trend is only expected to accelerate in the 21st Century as our population ages. Unless dramatic changes occur and occur soon, the number of Americans with diabetes will climb to 23 million over the next 10 years.

There currently is no way to prevent or cure diabetes, and available treatments have had only limited success in controlling its devastating consequences. The problem is made all the more complex because diabetes is not a single disease. Rather, it occurs in several forms and has complications that affect virtually every system of the body.

Children with type 1 diabetes face a lifetime of daily finger pricks to check their blood sugar levels, daily insulin shots, and the possibility of complications such as kidney failure and blindness which can be disabling and even deadly. Older Americans with type 2 diabetes can also be disabled by the multiple complications of this serious disease.

Recently I had the opportunity to meet a courageous 8-year-old boy from North Yarmouth, Maine. His name is Nathan Reynolds, and he epitomizes for me why it is so important to accelerate our fight against diabetes.

Nathan is an active young child. He enjoys school, biking, swimming, baseball, and collecting old coins. He was diagnosed with diabetes in December 1997, a diagnosis that has forever changed his life and the life of his family.

He has had to learn how to draw his blood, something his 4-year-old brother reminds him to do before every meal. He has to check his blood sugar level and give himself an insulin shot. What to me

[1] See Exhibit No. 2, which appears in the Appendix on page 94.

is saddest of all, is that Nathan can never take a day off from his diabetes. It does not matter if it is his birthday, it does not matter if it is Christmas, he still has to take those shots every single day.

The fact that diabetes, once diagnosed, is a lifelong condition, was underscored by a 65-year-old man who recently wrote to me that he estimated he had given himself 76,000 insulin shots since he was first diagnosed with diabetes at age 15; 76,000 shots.

The good news for children like Nathan and our witnesses today is that promising research is underway that may lead to medical breakthroughs for those with both type 1 and type 2 diabetes. The next decade holds tremendous promise for diabetes research. Improvements in technology and the general growth in scientific knowledge have created unprecedented opportunities for medical advances that should lead to better treatments, prevention, and ultimately a cure for children like Nathan.

Earlier this year, the congressionally sponsored Diabetes Research Working Group issued its report entitled "Conquering Diabetes: A Strategic Plan for the 21st Century."[1] The report details the magnitude of the problem and provides a comprehensive plan for NIH-funded diabetes research.

In the report, the Working Group finds that many scientific opportunities are not being pursued due to insufficient funding, lack of appropriate mechanisms, and a shortage of trained researchers. The report also concludes that the current funding, level of effort, and scope of diabetes research falls far short of what is needed to capitalize on these opportunities; and, further, that the funding level is far short of what is required to make progress on this complex and difficult problem. The report recommends funding of $827 million for diabetes research at NIH in fiscal year 2000.

Last week, I am pleased to report, the Senate approved a Labor-HHS appropriations bill increasing funding for NIH by $2 billion, a very positive development. Senator Breaux, who serves as co-chair with me of the Diabetes Caucus in the Senate, helped me win passage of an amendment to that bill calling for increased support for diabetes research in accordance with the recommendations of the Diabetes Research Working Group. The unanimous Senate vote for this amendment sends a strong and clear signal that diabetes research is a high priority for the U.S. Senate.

Diabetes has been underfunded in the past, and it is imperative that we ensure that sufficient resources are available to take full advantage of the extraordinary opportunities we have to better understand and ultimately conquer this devastating disease.

This morning's hearing is intended to examine the effects that diabetes and its resulting complications have had on Americans of all ages in both human and economic terms. We will also hear from researchers who will talk about the scientific opportunities available in diabetes research and the work that they are doing to find better treatments, a means of prevention, and ultimately a cure.

I would note that I am particularly proud that The Jackson Laboratory in Bar Harbor, Maine, have been leaders in this research.

Finally, we will discuss future funding levels for diabetes research, and how we can be helpful in ensuring that NIH does com-

[1] Exhibit No. 6.a. is retained in the files of the Subcommittee.

plete the commitment that the Senate has underscored must be kept. I very much look forward to the testimony of our witnesses today, and to learning more about this critically important issue of public health.

Due to the time constraints of this hearing, the Subcommittee was unable to invite everyone affected by this issue to present oral testimony. We have already received two written statements, one from the American Diabetes Association and the other from NASA, making the Subcommittee aware of NASA's ongoing contributions to biomedical research and in particular diabetes research. I must say that I personally was unaware of NASA's contributions in this area, and I appreciated their providing us with this testimony.

Without objection, these statements and any others that the Subcommittee receives in the next 10 days will be included in our printed hearing record.[1]

Before proceeding to our first witness, I want to take the opportunity to say that the order of witnesses for this morning's hearing is not what I had originally planned. We had originally planned to have the administration's representative testify on the last panel, so that he would have the opportunity to hear and to respond to the concerns raised by diabetes patients, their families, and by some of the leading scientists in the field of diabetes research.

The Department of Health and Human Services liaison, however, informed the Subcommittee that they would "not allow" Dr. Gorden to testify unless he testified first and on a panel of his own. I want to make very clear that I realize this was not Dr. Gorden's decision and I certainly do not hold him personally accountable for the ill-advised policy by the Department of Health and Human Services, but I want to say for the record that I think HHS's policy in this regard is both unfortunate and very arrogant.

It seems to me that it suggests that the Clinton Administration does not want to be held accountable for its decisions. And, moreover, I would think that NIH would be concerned and HHS would be concerned that this policy only serves to reinforce criticisms voiced by the Institute of Medicine and others, that NIH is not sufficiently involving patients and their families, the ones who have the most at stake, in the process of setting research priorities. I understand that research allocation decisions should be made on the basis of sound science, but also it clearly should take into account the human toll of the disease.

I do want to again say I realize this is not Dr. Gorden's fault and it is not his policy, but I did want to express for the record my strong disagreement with HHS's decision and its policy in this matter. I also understand that Dr. Gorden is going to try to remain for the duration of the hearing so that he can do what our intention was, and that is hear the testimony of the other witnesses, and I want to express my personal appreciation for his willingness to do so.

Having said that, our first witness this morning is Dr. Phillip Gorden. He serves as the Director of the National Institute of Diabetes and Digestive and Kidney Diseases, which is part of the National Institutes of Health. Dr. Gorden began his career at NIH in

[1] See Exhibits No. 8–10, which appears in the Appendix on page 121–134.

1966 as a senior investigator in the Clinical Endocrinology Branch of the NIDDK. Dr. Gorden became the Director of the National Institute of Diabetes and Digestive and Kidney Diseases in 1986. We very much look forward to hearing his testimony.

Dr. Gorden, under our Subcommittee rules, we have to swear in each and every witness, so I am going to ask that you stand, pursuant to Rule 6.

[Witness sworn.]

Senator COLLINS. Thank you very much. You may proceed.

TESTIMONY OF PHILLIP GORDEN, M.D.,[1] DIRECTOR, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES, NATIONAL INSTITUTES OF HEALTH

Dr. GORDEN. Senator Collins, I would like to first assure you that I will be available to you throughout the entire course of your hearing.

With your permission I would like to add just one brief personal note to express, on behalf of the Department and the NIH, our sincere appreciation to Dr. Kahn for his work in chairing the Diabetes Research Working Group, and to all the members of that committee who worked so hard to put their report together. In addition, I would appreciate if you would let the record of this Subcommittee show that we extend our congratulations to him on the marriage of his daughter, Stacy Anne, which took place only 4 days ago.

Thank you very much for that.

Senator COLLINS. He does indeed have a lot to be proud of. Thank you.

Dr. GORDEN. Madam Chairman, I am very pleased to have the opportunity to testify this morning as the Director of the National Institute of Diabetes and Digestive and Kidney Disease, which has lead responsibility for diabetes research at the National Institutes of Health and within the Department of Health and Human Services. I very much appreciate the opportunity to tell you about the Department's efforts to combat diabetes, with emphasis on our biomedical research program.

As you have mentioned, in both human and economic terms, diabetes is an extremely costly disease. It is widely recognized as one of the leading causes of death and disability in the United States and throughout the world. Diabetes affects an estimated 16 million Americans, about half of whom do not know they have the disease and are not being appropriately treated for it. Approximately 800,000 people are diagnosed with diabetes each year, including both genders, the young, the old, all races and ethnic groups, the rich and the poor.

Although diabetes occurs most often in older individuals, it is one of the most common chronic disorders in children in the United States. About 120,000 children and teenagers younger than age 19 have diabetes. Both type 1 and type 2 diabetes are associated with the eye, kidney and peripheral nerve complications, as well as heart attack and stroke.

---

[1] The prepared statement of Dr. Gorden appears in the Appendix on page 45.

According to the American Diabetes Association, diabetes and its complications cost an estimated $98 billion annually. Though there are several interventions currently available to help reduce the burden of this disease, there are no methods to cure it or to prevent its onset.

The Department has a multifaceted agenda to combat diabetes. Diabetes is an important trans-NIH research area because the disease and its complications affect multiple organ systems. The scientific direction of the broad NIH diabetes research program has been recently augmented by recommendations we have received from a special trans-NIH symposium on diabetes scientific opportunities and challenges, as well as by the identification of scientific opportunities and needs in the strategic plan developed by the congressionally established Diabetes Research Working Group.

NIH diabetes research is complemented by programs of the Centers for Disease Control and Prevention, the Indian Health Service, and other parts of the Department. We have also established productive collaborations with the American Diabetes Association and the Juvenile Diabetes Foundation International, as well as the biotechnology and pharmaceutical industries.

Remarkable advances in both fundamental and clinical science are having an enormous positive effect on diabetes research and treatment. These include rapid advances in genetics and genomics, new discoveries of mechanisms to manipulate the immune system, a major new understanding of cell communication, and key advances in clinical science, such as blood pressure and lipid control, which are crucial to the treatment of diabetes.

Two major clinical trials have demonstrated that the complications of diabetes can be ameliorated or prevented through close control of blood glucose levels. These important clinical results, coupled with the demonstrated efficacy of laser photocoagulation in treating diabetic eye disease, and the use of drugs such as ACE inhibitors in ameliorating the kidney disease of diabetes, all represent major steps forward in our continued quest for more effective treatment, and ultimately, prevention and cure of the disease.

In type 1 diabetes, we are pursuing multiple research avenues in the search for underlying causes of this disease, together with new treatment and prevention strategies. We are searching for clues to what causes the body to attack and destroy its insulin-producing cells, the hallmark of type 1 diabetes.

We are also embarking on a new and exciting initiative to restore insulin-producing capacity through islet cell transplantation. This research is propelled by a remarkable study in primates, showing that both insulin-producing islet cells and kidneys can be transplanted using a highly selective method to control for immune rejection of the transplant.

We have also a major clinical trial aimed at preventing or delaying the onset of type 1 diabetes in individuals at risk, and we are seeking to develop more effective ways to achieve good glucose control.

In type 2 diabetes, we are gaining new insights into the mechanism of insulin action, which provides new therapeutic options to combat the body's resistance to insulin, a characteristic abnor-

mality of this disease. We also have a major research initiative on obesity, a serious risk factor for type 2 diabetes.

In fundamental research, the discovery of the obesity gene and its protein product, leptin, in mice have provided new insight into mechanisms of obesity and both the control of eating disorders and energy regulation. The fundamental observations underlying this discovery were made at The Jackson Laboratory years ago. These findings have now spearheaded the discovery of at least five different genetic defects in humans that lead to obesity, and may provide new insight into the interrelationship between obesity and type 2 diabetes.

We have also launched a major clinical trial in which drug and lifestyle interventions are being studied to see whether they can delay or prevent the onset of type 2 diabetes. Over 50 percent of the patients in the trial are from minority populations who suffer disproportionately from the high burden of this disease. A second multicenter clinical trial is designed to study the health benefits of long-term weight loss in type 2 diabetic patients. Furthermore, the National Heart, Lung and Blood Institute has inaugurated a major clinical trial to determine whether glucose control can augment the beneficial effects of blood pressure and cholesterol control in ameliorating the vascular disease of diabetes that leads to heart attack and stroke.

Madam Chairman, I am grateful for the opportunity to share with you some examples of our efforts and progress in combating diabetes. I have tried to underscore today that we understand the great burden that diabetes places on families, patients and communities. A number of those individuals are here with us today to demonstrate that even further.

At the same time, I want to share my feeling of encouragement and hope. I believe that our strong national programs hold the essential key to curing this disease. We have important programs under way, but much more remains to be done. I am very pleased to answer any questions that you may have.

Senator COLLINS. Thank you very much, Dr. Gorden. I am going to direct your attention to Exhibit 3.[1] And if I could have Exhibit 3 put up, also, I believe it is in the notebook before you if it is not clear from the chart.

Dr. Gorden, as I mentioned in my opening statement, I am concerned that only about 3 percent of NIH's budget has been devoted to research on diabetes and its complications. Moreover, if you look at this chart, you can see that the percentage has actually declined over the past 20 years, at the same time that the death rate from diabetes has actually increased by 30 percent.

Now, I understand that there is no universally agreed-upon method for determining the appropriate level of research funding, but it seems to me that this is an awfully small investment when you consider that this is a disease that affects about 6 to 7 percent of the population, accounts for 10 percent of all health care expenditures and about 25 percent of our Medicare budget.

Your institute is the lead institute for diabetes research. What percentage of your budget is dedicated to diabetes research? I real-

[1] See Exhibit No. 3, which appears in the Appendix on page 95.

ize there is diabetes research going on in other institutes, as well, but you are the primary one.

Dr. GORDEN. In NIDDK, we fund approximately 60 to 65 percent of what is coded as diabetes research across the National Institutes of Health. Those funds constitutes about 27 percent of the total budget for NIDDK.

Senator COLLINS. Overall in NIH it is about 3 percent of the research dollars; is that correct?

Dr. GORDEN. If you were to express the entire NIH budget, which is a very large figure, as a denominator against almost anything else as a numerator, you will come out with a relatively small figure in terms of a specific disease.

What I would like to emphasize, and what I think is by far and away the most important, is the part that starts in fiscal year 1997, when we began to see the increased appropriations for NIH, for which we are enormously grateful to the Congress. I believe that what you are seeing now is the benefit of that being translated into research on diabetes. From 1997 there is an upward trend and I think that is what we are really focused on this morning.

Senator COLLINS. Did you request an increase in your budget as part of the budget process going through OMB that the administration presented to Congress?

Dr. GORDEN. We basically request what the OMB permits us to request, which turns out to be the administration's budget. That request was at a level of approximately a 2.1 percent increase over fiscal year 1998. And this was the budget that NIH presented, as well as the one my individual institute, as well as all the other institutes, presented in our testimony to the Congress this past spring.

Senator COLLINS. So essentially the administration tells you what you are to request for a budget, as opposed to your putting forth what you believe would be the ideal budget to meet the needs and to take advantage of the scientific opportunities?

Dr. GORDEN. It is a rather complex process. At some point in time we may be asked to present a professional judgment budget, as we were by Senator Specter last year. The formal process then goes through a number of iterations, and in the end we present the administration's consolidated budget.

Senator COLLINS. Did you agree with the administration's proposal to request a budget that would provide an increase for NIH of only 2.5 percent?

Dr. GORDEN. I think that it is important that we adhere to some common format in terms of our budgetary presentation. In the context of adhering to that format, I agree with the process. I would obviously prefer, on a personal level, to see our level go higher.

Senator COLLINS. Let me ask you what may be an easier question for you to answer, and one that puts you less on the spot. Do you agree with the findings of the Diabetes Research Working Group that diabetes research has been underfunded, and thus we have not been able to take advantage of scientific opportunities? Maybe it is not an easier question, I do not know.

Dr. GORDEN. I think we need to put in context the fact that the Working Group points out the enormous opportunities in diabetes

research that are open to us. They were dealing with a specific disease and making recommendations on a specific disease.

Both at NIDDK and across NIH, we must take those recommendations and put them in the context of everything that we do, which is also reflective of language that we receive from the Senate and from the House which underscores the multiplicity of diseases that our research combats. We have to place the recommendation of the Diabetes Research Working Group in context across NIH based on all of the considerations and recommendations that are coming to us.

I think that in each disease area we may have concerns about underfunding, and it is difficult to know exactly how one places one of these relative to another. This is really the issue that we face in terms of implementation strategies. I think in terms of recommendations, that this is the way it should be.

Senator COLLINS. The Senate has increased funding for NIH by 13 percent, a far stronger investment than that proposed by the administration. If the 13 percent figure goes through, what funding level would you envision would be provided for diabetes research? Would we be able to approach the $827 million recommended by the Working Group?

Dr. GORDEN. In the example that you gave, the NIH would receive a 13 percent increase for all the diseases within its mission, but the Working Group calls for over an 80 percent increase for diabetes research alone. We have to deal in some way with the difference between a 13 percent increase and an 80 percent increase.

Another issue that I think is a little complicated, when one strictly talks in budget terms rather than scientific terms, is that we were involved with the Working Group's recommendations from its very outset. Because the Congress provided us with a very generous budget in fiscal year 1999, we were able to jump-start some initiatives and lay some of the footprints for many of the Working Group's recommendations across the highest priority areas.

When we talk about science, we can talk in logical terms about what is started and what needs to be completed. When we try to translate that into total dollar terms, it becomes a little bit more complicated in terms of how we express it.

Senator COLLINS. I guess my concern, Dr. Gorden, is the Senate has gone on record very strongly in favor of the Working Group's recommendations. The report language in the appropriations bill is equally strong. We provided a 13 percent increase, which I hope will survive in conference. The Senate's goal is to double NIH spending over the next 5 years. There are many of us who have cosponsored a resolution in support of that.

I want to know how we are going to get there. I want to know what NIH thinks, whether you are committed to implementing the recommendations of the Working Group, whether NIH shares the commitment of the Senate to providing the necessary research dollars to conquer this devastating disease.

I am pleased that we are on the up-tick, but when you look at the impact of this disease versus the resources that we are now putting in it, it is just a huge disparity. And when I visit with scientists, I am so excited about the research that is underway. When I talk to children and adults who have this disease and I see the

impact on their lives, I want a breakthrough, and I am convinced we have got to be willing to invest to get there.

So I guess what I want to hear from you is, what is the extent of NIH's commitment? Do you agree with the Working Group? Do you have a plan for following the Working Group's recommendations? Are you going to put in the resources that Congress clearly wants you to put in, that this eminent group of scientists and patients have come up with an excellent plan for achieving? What are your intentions? What is your plan?

Dr. GORDEN. Senator, I want to emphasize what has happened with this up-tick, and I am absolutely confident that it is going to continue. We very much support the recommendations. They are scientifically very sound and solid. We are actively involved in implementation strategies, and implementation strategies are mechanisms to actually place these recommendations into operation.

We receive a broad recommendation. We have to translate that into an implementation strategy. We are in the process of making those translations now, as we anticipate over the next possibly 2 weeks to receive an appropriation. At that time I think we will be prepared to move forward in implementing many of the recommendations from the Diabetes Research Working Group.

Plans are afoot, certainly within NIDDK. NIDDK is involved in working with the other institutes to canvass their plans and also to stimulate the efforts that have been proposed by the Working Group so that they can be translated across NIH. There is no question that the momentum is there, and we are very excited about moving forward. We share this feeling of excitement about the research opportunities that exist.

Senator COLLINS. From my perspective, it has been Congress that keeps pushing NIH in this direction. It was Congress that established the Diabetes Research Working Group. It was Congress that has given the increases to NIH, despite the administration requesting increases this year that wouldn't even have kept pace with inflation.

And I want to yield to my colleague for some questions before I wrap up a couple more areas I want to talk to you about, but I want to send a very strong message that we need you as partners in this fight and we admire NIH. I respect the incredible caliber of scientists and research that you are doing. But we need to make a commitment to getting this job done, and it can't be just the Congress pushing, pushing, pushing. We need a commitment from NIH that puts diabetes research as a priority.

Senator Edwards, welcome.

OPENING STATEMENT OF SENATOR EDWARDS

Senator EDWARDS. Thank you, Madam Chairwoman.

Good morning, Dr. Gorden.

Dr. GORDEN. Good morning, sir.

Senator EDWARDS. And I apologize, I missed the beginning of your testimony and I listened to just your answers to the most recent series of questions, and I may be being repetitive but I am not sure I understood your answer.

Are you saying that NIH is committed to following the Working Group's recommendations?

Dr. GORDEN. I am saying that the scientific opportunities that are being proposed by the Working Group are opportunities that the NIH is pursuing to implement.

Senator EDWARDS. So the answer is, you are committed to following the recommendations; is that what you are saying?

Dr. GORDEN. We are committed to following the scientific recommendations of the Working Group.

Senator EDWARDS. One of the issues that has been raised by some of my folks back in North Carolina, for example, Dr. John Busey, who you may know is a diabetes researcher there, has to do with the number of proposals that are made for conducting research in the area of diabetes and the percentage of those proposals that are accepted by NIH.

First of all, in the area of diabetes, do you have any idea about what percentage of the proposals that are made to do research in that area are in fact accepted by NIH?

Dr. GORDEN. In general, we talk about the number of awards for grants, which is the largest expenditure that NIH makes across the board. With the very generous support that we have received from the Congress in the last 2 fiscal years, we now have an award rate of about 33 percent across NIH. That is the proportion of eligible grant applications that are actually awarded.

The same is generally true for diabetes. In other words, our award rate for diabetes-related grants would be in the same range as they would be in our institute for digestive disease or kidney-related grants or nutrition-related grants, and that is generally the same across NIH. We fund about one-third of the grant applications we receive, and that is driven by the peer review system. That system evaluates the scientific quality of each individual grant, which is really the bedrock of NIH support of fundamental science.

Senator EDWARDS. Well, my concern is the anecdotal stories I hear, and I hear what you are saying about the percentages, indicate that some of the young researchers become very discouraged in this area because they do a lot of work, they make these proposals, their proposals are rejected.

And I guess ultimately what you and I both need to be concerned about is making sure that we are able to attract and retain good researchers, particularly, since we are here talking about diabetes today, in the area of diabetes. Do you have any ideas or thoughts about how to deal with that?

Dr. GORDEN. Yes. I have been watching this for some time now, and I believe there is nothing more positive to the community and to young investigators or people who are contemplating biomedical science as a career, as what has been provided to NIH over the last 2 fiscal years. These investigators are encouraged by the commitment on the part of the Congress to double the NIH budget.

Those are very powerful statements to young investigators who are looking for the interest and the importance of a biomedical research career. They now are seeing that this may be really a viable and secure future for them to pursue, in the sense that resources are going to be available. In my view, nothing has been a more powerful statement for young investigators.

In addition to that, we have got to ensure that the young investigators, in diabetes research in particular, have the human infrastructure in place to actually reach the full implementation of all of these recommendations that have been made. That will require furthering the human infrastructure, a goal that we have set. We have set out to establish new kinds of research career mechanisms; to enhance clinical investigation, which is an area that is particularly put upon in the last few years. But, the increased resources that are actually flowing into biomedical research in general have had an enormously positive effect on young people.

Senator EDWARDS. Well, I think I just will point out, and I think you recognize it is critically important that we attract and retain talented people to do research in these areas.

Dr. GORDEN. I agree completely, Senator.

Senator EDWARDS. In terms of the importance of diabetes research, do you agree with the basic premise that although stroke and heart disease at least superficially appear to cause more deaths, more premature deaths than diabetes, that diabetes is often an underlying cause of both stroke and heart disease?

Dr. GORDEN. Yes, that is true.

Senator EDWARDS. And so sometimes the importance of diabetes, at least if you only look at the superficial information, is underestimated.

Dr. GORDEN. That is absolutely true.

Senator EDWARDS. So whatever we can do in the way of diabetes research and prevention of diabetes also has a direct impact on premature deaths caused by stroke and heart disease?

Dr. GORDEN. Absolutely. I would like to add that, for instance, we met recently with the American Heart Association, which has decided to make diabetes one of its major risk factors. If you recall, hypertension, cholesterol and smoking have been key risk factors for their public relations campaign. Now diabetes is added to that.

Although diabetics have benefited tremendously from the same interventions that have decreased mortality in heart disease and stroke, quantitatively they have not benefited as much, and we have got to find the reason for that. What is that additional increment of risk that diabetics have, that is related to diabetes *per se* in some way? We are not certain what that risk is.

Now, if you are a diabetic and you smoke, this is really bad. If you are anybody and you smoke, it is really bad. But if you are a diabetic and you are hypertensive, that is a very bad situation. These things all are additive and are synergistic, really, as risk factors.

In our prevention studies, we are trying very hard to reduce this other layer of risk, and trying to find what it is about diabetes that creates this additional risk for cardiovascular disease, which as you point out are heart attack and stroke. This is a very important objective in this whole enterprise.

Senator EDWARDS. Thank you, Dr. Gorden. We appreciate very much the work you do at NIH. I think it is critically important.

I would just emphasize what Senator Collins said just a few moments ago, which is, we believe it is so important that the diabetes research that needs to be done is focused on, that the Working Group's recommendations are in fact implemented. In my State of

North Carolina diabetes is an enormous problem, and for a variety of reasons. So we would just like to see you continue the up-tick that you show on your chart, and would like very much to see the recommendations of the Working Group followed.

Dr. GORDEN. Thank you, sir.

Senator EDWARDS. Thank you, Dr. Gorden.

Senator COLLINS. Thank you, Senator.

Dr. Gorden, I just have a couple more questions for you. Since diabetes has complications that affect virtually every system in the body, it is not surprising that other institutes at NIH are also involved in diabetes research. One concern that I have heard from scientists and from advocates for the diabetes community is that there is insufficient collaboration among the institutes in planning diabetes research.

What are your plans to improve collaborative efforts so that you do have the most bang for the buck, you do have a synergistic effect of your research?

Dr. GORDEN. I think this is a very important issue. I think that this new emphasis on both collaboration with other institutes and trans-NIH support is fueled by several things.

We created one model in the special appropriation of the Balanced Budget Act of 1997, which was a special appropriation for type 1 diabetes. Though NIDDK is the principal administrator of that initiative at NIH, it is clearly a trans-NIH effort. We have achieved that by working through the Diabetes Mellitus Coordinating Committee. We have also done it by working directly with the institute directors in planning the initiatives to go forward.

We have taken that model now and have used the increased appropriations that you see in fiscal year 1998 and 1999 to propel the momentum in other institutes. When we take the Working Group's plan and their recommendations, we now can look at a spreadsheet and see which recommendations apply most directly to which institutes. We now can communicate directly with those institutes and work with them.

For instance, within the last several weeks we had a workshop with the National Institute of Neurological Diseases and Stroke. Neuropathy of diabetes has been recognized as an area that has been underfunded and under-researched. Therefore, we are prepared to join with them to create a major initiative in fiscal year 2000 to address this problem.

Similar initiatives are under way with the National Heart, Lung and Blood Institute on macrovascular heart attack and stroke. We have a program that we have inaugurated with them. They have joined with us in our major effort to combat obesity in a clinical trial.

These are just a few of the examples of things that are moving forward, and at a much greater rate and momentum than in the past. I feel very comfortable and confident about the collaborative trans-NIH effort for all of these important initiatives, because the essence is that each institute has both resources and expertise, and we need both of those. We need the resources and the expertise that they bring to the table. That is what we are trying to maximally take advantage of in our program development.

Senator COLLINS. The final issue I want to discuss with you concerns reports, very disturbing reports that we are starting to see more type 2 diabetes in teenagers. In fact, just last week when I was in Maine, a dietician came up to me and told me that she is seeing an increase in her practice of diabetic teenagers who are type 2 rather than type 1.

What is NIH doing to combat that disturbing trend, and do you have any research underway, perhaps related to life style issues, that you could share with us?

Dr. GORDEN. This is a very important issue, and we plan to move forward with an initiative in fiscal year 2000 to address this. We want to both define the magnitude of this problem and to define the issues involved in this. We believe that they are similar issues to those occurring in adults with diabetes, but we think that there may be other issues as well.

There are issues of obesity in children, which has been an increasing issue in the last 10 years. The increases in obesity and diabetes are interrelated. These cases of obesity are occurring primarily in minority populations, particularly Native Americans and Hispanic populations. There are obviously reasons.

Our basic research in genetics and other areas will continue in an attempt to define this in a more fundamental way, but we must address this as a public health emergency quickly, and try to do those things that are going to help ameliorate the problem. That is what we plan to do, initially working through the more basic scientific avenues in terms of the broad area of fundamental science, which is going to ultimately address this problem. We have got to do something about it quickly as a public health issue. It is a major problem. We are very concerned about it.

Senator COLLINS. That development to me shows how complex this issue is. We not only need to be doing research focused on a cure which I feel so strongly about, we also need education efforts to help people manage their diabetes better. We need to work on treatment, prevention, and the cure, and I hope that your research will pay attention to all three of those goals.

I want to thank you very much for being with us today, and again I appreciate your willingness to stay and hear from our witnesses. I think we will all learn a great deal from them. Thank you, Dr. Gorden.

Dr. GORDEN. Thank you very much, Senator Collins.

Senator COLLINS. I am now going to call on Senator Levin, who is our Ranking Minority Member of the Subcommittee, who has a great deal of commitment to this issue. We also have one of his constituents with us today to help us better understand this devastating disease. And I would like to, before we call on our next panel of witnesses, call on Senator Levin for his opening statement and any comments he might want to make in introducing his constituent.

OPENING STATEMENT OF SENATOR LEVIN

Senator LEVIN. Madam Chairman, let me thank you first of all for holding this hearing. It is a very important hearing in the battle against diabetes. You have taken a leadership role here which is critically important to the health of the Nation, and I commend

you for doing it. It is a really important cause that you have taken the leadership of here. Thank you, for all of us, for doing so.

As we all know, diabetes is a pernicious disease that affects people of all ages, and in addition to the ill effects that it creates on its own, it causes a variety of other debilitating medical problems such as heart attack, stroke, kidney failure, blindness, and circulatory failure which can lead to amputation. And all of these complications makes diabetes the sixth deadliest disease in the United States. It annually affects 16 million people, about a third of whom are undiagnosed. It kills about 200,000 people a year.

Diabetes afflicts 120 million people worldwide, and the World Health Organization estimates that this number will skyrocket to 300 million within the next 25 years. A new case of diabetes is diagnosed every 40 seconds. It is the leading cause of kidney failure, adult blindness, and nontraumatic amputations. People with diabetes are two to four times more likely to have a heart attack or stroke. Life expectancy of people with diabetes averages 15 years less than that of people without diabetes.

Those are the facts that we have to contend with and try to change. In my home State of Michigan, almost 400,000 people have been diagnosed with diabetes. Medical experts believe another 204,000 have the disease but don't yet know it. We have the fifth highest rate of incidence of diabetes in the country, in my State of Michigan.

The financial cost can be overwhelming. Until recently, Medicare would not pay for one of the basic management tools, an insulin pump, and I want to commend our Chairman for her efforts in getting that policy changed.

We have many witnesses today. One of them is a constituent of mine that we are very proud of, Ryan Dinkgrave from Livonia, Michigan, Stevenson High School, 16 years old. At his young age he has already made a major contribution in the fight against diabetes. He has raised public awareness of this disease, and now wears an insulin pump.

He has told us, first, that the emergency medical personnel in his home city were not trained or authorized in the use of advanced life support methods relative to diabetes. Today, advanced life support is part of the training of their emergency medical personnel, and this life support includes the use of an injectable hormone which stimulates the liver to release glucose.

Ryan has been very active in educating the people about diabetes in other ways. He has created a Web site called "The Family's Guide to Diabetes." He has been interviewed on national television. He has helped raise funds for diabetes research, and we are very proud of the effort and accomplishments of this young man. We are very delighted that he is here with us today, with his dad, I understand. I want to welcome you, Ryan. I wish I could stay for your testimony. I have read your statement, however, and it is a very eloquent and moving statement.

I have to return to another hearing, and the Chairman understands the kind of complications that we have in our senatorial lives. And I thank her again for her leadership, for allowing me to make my opening statement at this time, and to introduce Ryan to the Subcommittee.

And finally, Madam Chairwoman, I would ask unanimous consent that a hard copy of Ryan's Web site be inserted in the record. It is a very clever Web site. It will be particularly attractive to young people. Web sites do that generally, but specifically this Web site is designed in a very creative way which will be specifically attractive to young people. So I would ask, Madam Chairman, that we make a hard copy of this Web site as part of our record.[1]

Senator COLLINS. Without objection.

Senator LEVIN. And, again, my thanks to you for your leadership.

Senator COLLINS. Thank you, Senator Levin.

I am delighted to join Senator Levin in welcoming our next panel of witnesses this morning. He has already introduced Ryan, so I will proceed to introduce the other witnesses.

Pam Fernandes is from Needham, Massachusetts; Gordon Jump from Coto de Caza, California; and William Fuller, Jr., of Virginia Beach, Virginia.

Ms. Fernandes was diagnosed with type 1 diabetes at an early age but did not realize the profound effect that diabetes would have on her life until she had a physical shortly before starting college. Despite her efforts to control her diabetes for the last 20 years, she unfortunately has lost her sight. In spite of the hardships that diabetes has imposed on her life, Ms. Fernandes has become an international tandem cycling champion and a recognized para-olympic athlete. We are very pleased to have her with us today.

We will then hear from Gordon Jump, who most of you probably recognize from his role on the television series "WKRP in Cincinnati." You might also, however, recognize him as the lonely but ever-ready Maytag repairman. In real life, however, Mr. Jump has type 2 diabetes, and he will give us his perspective of living with this disease.

Now, the sports fans out there will undoubtedly recognize our next witness, William Fuller, who played in four pro bowls during his 13 years as an NFL defensive lineman. Mr. Fuller is a former board member of the Juvenile Diabetes Foundation, who first got involved with this cause after his father unfortunately died from diabetes-related illness. Mr. Fuller hosts several fund-raising events sponsored by the Juvenile Diabetes Foundation, including the "Sack the Quarterback" promotion.

So we are very delighted to have all four of our witnesses here with us today. They span different ages, obviously. They have different experiences. And we really appreciate their willingness to come forward and help better educate the Subcommittee, and indeed the entire Senate, on the implications of living with diabetes.

Now, as I explained to Dr. Gorden, pursuant to the Subcommittee rules, we do need to swear you in. At this point I would ask that you all stand and raise your right hands.

[Witnesses sworn.]

Senator COLLINS. Thank you. Ryan, since you are the youngest, you get to go first, so we will ask that you proceed with your testimony.

---

[1] See Exhibit No. 5, which appears in the Appendix on page 97.

TESTIMONY OF RYAN DINKGRAVE,[1] LIVONIA, MICHIGAN, ON BEHALF OF THE JUVENILE DIABETES FOUNDATION

Mr. DINKGRAVE. Madam Chairman and Members of the Subcommittee, thank you for giving me the opportunity to testify this morning on behalf of the Juvenile Diabetes Foundation International. As is already stated, my name is Ryan Dinkgrave. I am 16 years old and a student at Stevenson High School. I hope to attend college at the University of Michigan and eventually find success in a career field which I enjoy.

I was diagnosed with juvenile or type 1 diabetes when I was in the fifth grade, just over 6 years ago. It was one of the scariest things that has ever happened to me. My pediatrician said that my constant thirst and exhaustion were because I had diabetes. I also lost weight, experienced frequent sluggishness and other common symptoms of diabetes. I had no clue what diabetes was, and I really didn't want to know, but we proceeded directly to the hospital. That day was the first of my 6-year experience of trying to live with diabetes.

I was in the hospital for almost a week, and I left with no idea what to expect. It turned out that having diabetes meant my whole life was to be turned upside down and changed in every way. No longer could I just eat what I would like or when I would like, no longer could I really do anything without planning for so many possible situations related to having diabetes, such as low blood sugar that could lead to an insulin reaction or high blood sugar that could lead to severe health complications.

I began trying to manage my diabetes with two shots a day, which eventually became three shots a day and then four. Along with the shots came blood glucose tests four, five, sometimes six times a day. These tests involve pricking my finger to draw a drop of blood.

Along with these daily efforts came worries about what could happen if my blood sugars were not kept in good control: Heart problems, kidney problems, nerve damage, vision problems, blindness, amputations—the list seemed like an impossible thing to avoid. My life would certainly never be the same.

Last November, after doing insulin injections for over 5 years, I switched to a more advanced type of insulin therapy called the insulin pump. This is a device that is about the size of a pager, which administers insulin through a tube that goes into my body and has to be moved to a new location every 2 days. While it has allowed me more freedom, better blood sugar control, and possibly a longer life, it is still not perfect and living with diabetes is still, at best, very difficult. Until there is a cure, nothing will satisfy those who struggle to live daily with this disease.

A common misperception about diabetes is that one with diabetes is healthy. This is because people with diabetes often have no outwardly visible characteristics of the disease, especially teens and children with diabetes. There is no physical evidence of the organ damage and future health concerns of somebody who has diabetes.

Look at any teenager or child with diabetes. They look just like anyone else their age. Put 100 kids in a line, and you cannot pos-

[1] The prepared statement of Mr. Dinkgrave appears in the Appendix on page 62.

sibly pick out who has diabetes or who does not. It is because of this that many people do not realize the severity of diabetes and the urgency for a cure, until it is too late and complications of the disease have set in.

I personally have had to struggle a lot with diabetes, both emotionally and physically. I have to worry about future health concerns, and every moment of every day I must be aware of my condition and treat it. I have had three seizures due to low blood sugar. I know that this scared me and my parents like never before with how serious and trying these events have been.

I have done a lot to help spread out information and awareness on diabetes, and work with others, diabetics and doctors and what not, like myself. About 3½ years ago I started a Web site called "The Family's Guide to Diabetes" at diabetes.cbyc.com for children and teens with diabetes. It was created basically to fill what I thought was a need for a way for people with common situations to exchange information and experiences.

Through the site, and through my speaking to doctors, families and others about diabetes, I have been able to exchange a lot of this information and learn about how others live with diabetes. Also, I have participated in JDF's Walk to Cure Diabetes for each of the past 5 years. In fact, this year my group, Team Ryan, raised a new high of $4,000 which will go to support curing diabetes through JDF's $75 million research budget.

This past summer I was the Michigan representative for the JDF Children's Congress here in Washington, D.C. The JDF Children's Congress allowed 100 children and teens with diabetes to explain to Congress and the Nation how diabetes impacts us and the need for increased research funding for a cure.

I learned at the Children's Congress about the Diabetes Research Working Group report that indicated there are many high-quality diabetes research projects that are not being conducted solely due to a lack of funding. On behalf of all the children and teens with diabetes, I urge you to ensure that this funding be made available so we can find a cure as quickly as possible.

Thank you very much for allowing me the opportunity to testify, and I would be pleased to answer any questions.

Senator COLLINS. Thank you very much, Ryan.

Ms. Fernandes.

TESTIMONY OF PAM FERNANDES,[1] NEEDHAM, MASSACHUSETTS

Ms. FERNANDES. Good morning. My name is Pam Fernandes. I am from Needham, Massachusetts. Thank you for the opportunity to speak with you today about diabetes, a disease which plagues our Nation. Today some people will give you statistics relating to diabetes. These numbers will give you a sense of the overwhelming breadth of the problem. Through my story, I hope to give you a sense of the tragic depth of the problem.

Thirty-four years ago I was diagnosed with type 1 diabetes. At the age of 4, my understanding was quite simplistic: Two painful injections a day, urine tests, and no treats. Through my childhood

[1] The prepared statement of Ms. Fernandes appears in the Appendix on page 65.

and early adolescence I tried desperately to understand the disease that made me different from every other kid.

When I was 18, at the very time in my life when options should have been endless, diabetes threw me a curve. I went to visit my eye doctor 2 weeks before leaving for college. He told me I had a few small hemorrhages, nothing to be worried about, but that I should see a specialist when I arrived in Boston.

Two weeks after arriving in Boston, I got the news that I was going blind. The day I walked into that doctor's office began 8 of the most painful and difficult years of my life. After laser surgery and five eye operations, I was declared legally blind. I was just 21 years old.

One week before my 22nd birthday, I started dialysis treatments. You see, diabetes had also affected my kidneys. I lived on a machine for 5 years, and although everyone said I was doing remarkably well with the treatments, I never felt worse in my life. I couldn't really imagine any kind of future with each day being so emotionally and physically painful.

After more than 30 operations and two episodes of respiratory arrest, I made a life-changing decision. In 1987 I received a kidney transplant. The first year was difficult, but soon I rediscovered the Pam that was vibrant, alive and tenacious.

About the time life began looking up for me, my family was hit with an unthinkable tragedy. My oldest brother, Mark, died from complications of his diabetes. He also had kidney disease, which led to his failing health. One of the most difficult things about Mark's death was watching my parents cope with the loss of a child. Diabetes had taken the life of a 32-year-old man who had a wife and a young girl.

In 1992 I was invited to ride on the back of a tandem bicycle. Little did I realize that that would both change my life and open doors that I never dreamed imaginable. I rode recreationally for about a year to stay fit and have fun. I got involved with American Diabetes Association Tour de Cures, bike rides designed to raise money to support diabetes education and research. I am very happy to have been invited to be the national spokesperson for the American Diabetes Association Tour de Cures for the next 2 years.

Bike racing entered my life in 1993. I attended a camp for cyclists with disabilities held at the U.S. Olympic Training Center. This was one of the most empowering weeks of my life, and I decided to give bike racing a try. In 1994 I won a silver medal at the World Championships for Disabled Cyclists in Belgium. At the 1996 Atlanta Paralympic Games I won a bronze medal. I have earned over 12 national championship titles.

I was surprised to find out that I was the only diabetic athlete on the disabled cycling team. I also learned that I was the only transplant recipient to ever have competed at the Paralympic Games. As if these recognitions were not enough, I have also been recognized through many awards, including being named U.S. Olympic Committee Athlete of the Year.

I am, in many regards, a very lucky girl. This disease hasn't been kind to me, but so far I have come out ahead. I am a living example of how far we have come with research, by the mere fact that I am here talking with you today and that I am doing what I am

doing. I am also a very sad reminder of how far we have yet to go. My story speaks well to the power of the human spirit, but how many setbacks can one spirit endure?

Unfortunately, I am not the rule but the exception. Many people with diabetes don't have the determination, the desire, the knowledge, the opportunity or the family support to succeed as I have. That is why it is so important for you as our Congressmen to understand our disease and to help us by supporting the research that will help us find better treatment options and ultimately the cure.

I learned some very poignant lessons my first few trips to Washington. I learned the enormous responsibility that our Congress has as it relates to our Nation's health. I also learned that there is nothing between me and the cure to my disease but money. We have no lack of researchers. We have no lack of desire. What we have is a lack of money.

Diabetes must become a national priority. Right now there are over 16 million people in the United States with diabetes. In the coming years that number will go up because diabetes isn't going away.

With the diligence of the Diabetes Research Working Group, we have identified extraordinary scientific opportunities. We must find the means to support this research. We must find that $827 million. Diabetes and its complications are a financial drain on our country, not to mention the human toll that it takes.

My mom and I made a pact when my brother Mark died. I told her that I would never give up. She knew that I was a fighter and a survivor. But the sad fact is that I probably will succumb to this disease, because like it or not, it has got a pretty good track record of shortening people's lives.

For as long as I am able, I promise that I will do what I can to stop diabetes. Please make that same commitment today. We need your support, your understanding and your wisdom. Together we can fight this disease, diabetes. Together we can win the battle, but it will take all of us to do what we can.

Thank you for your time and interest in our disease.

Senator COLLINS. Thank you very much for your testimony.

Mr. Jump.

TESTIMONY OF GORDON JUMP,[1] COTO DE CAZA, CALIFORNIA

Mr. JUMP. Madam Chairman, Members of your Subcommittee, my thanks for the opportunity to address you.

About 20 years ago I found that I am a type 2 diabetic. For 5 years I lived in a state of denial. Sooner or later, though, you have to come to grips with the fact that you have a chronic illness. When you finally acquire the gumption to take advantage of the educational programs offered by many of the hospitals, you will encounter a term that you do not usually associate with disease, and the term is "manage." You must learn to manage your disease.

Managing diabetes, a disease with few overt signs and symptoms, is not really an easy task. Self-discipline, almost a dirty word today, is the most important part of disease management for the

[1] The prepared statement of Mr. Jump appears in the Appendix on page 68.

diabetic. Carefully monitoring diet, exercise, body changes, medication, requires a diligence that most of us just simply do not possess. In order to simply survive we have to spend money, and lots of it, to keep the disease under control.

We discover that diabetes is not just a single disease to be treated. Diabetes affects the cardiovascular system, the nervous system, neuropathy, affects your feet, your legs, and ultimately other parts of your body. Your eyes can be affected to the point of blindness. Lack of circulation in your limbs can cause you to require amputation. You are in a constant struggle with life and death, actually.

In the case of type 2 diabetes, onset is usually at the time of life when the person is most productive. This is also the time when you are under the most stress: Climbing the corporate ladder, struggling with teenagers at home, and going through divorce or being downsized, maybe even going through a midlife crisis, whatever that is. It is rather like the chicken and the egg thing: Which comes first, the stress or the diabetes?

The American Diabetes Association has done a tremendous job in bringing the standard of awareness to a much higher level, but I am sure they would agree that the standard of awareness is not nearly high enough. The ADA has also provided tremendous support to physicians in providing educational services on the disease and its management to their patients.

In the 20 years since I was diagnosed, I have suffered a number of health problems, several of which can be directly attributed to diabetes. For the first 8 years or 10 years of my condition, I simply had to take pills, watch my diet, and saw my endocrinologist when I felt I should, which in the case of most diabetics was never enough.

By the time I had acquired enough sense to seriously consider doing something to maintain my health, my health was already all bad. I had high blood pressure, four-digit triglycerides, cholesterol numbers that would scare even an actor. Not only did I go on insulin, but I needed a lot of other medications: Pills for my heart, high blood pressure, triglycerides, cholesterol, digestion, and it goes on and on.

Sometimes a severe and sudden change in someone's eyes gives a physician a clue that diabetes may be the ultimate diagnosis for an individual. I have worn glasses for many years and often had to have my prescription changed. It wasn't too long ago I woke one morning and I realized that I was seeing double; was not anything that I had had to drink or eat.

After a number of tests had been made to assess the situation, I was finally fitted with glasses that made it possible for me to function. It was a frightening time for me, not knowing whether my sight would ever be restored to single vision again. Vision problems, including blindness, is another of the complications of diabetes.

This past June, I underwent angioplasty. The triglycerides and the cholesterol, all spoken of as being part of diabetes, had finally spoken. My blocked artery was discovered much the same way my diabetes was discovered, during a physical exam administered during the month of May. It was not the best time for me to have a procedure that could turn into a situation that might incapacitate

me for several days, because my daughter was about to get married in the month of June.

The angiogram disclosed an artery that was approximately 95 percent occluded. At the very least it would require a stint or angioplasty, and at the worst, bypass surgery. Fortunately, while the artery's shape and placement did not allow for the emplacement of a stint, an angioplasty seems to have been successful.

Being afflicted with diabetes is not something that I would wish on my worst enemy. How much money will be needed for basic research to conquer this insidious disease, I really do not know. How much is the disease itself costing the country in the form of Medicare, Medicaid, disability and other county, State and Federal programs? I really do not know.

I calculated what I thought would be the cost of the most basic diabetic supplies for an insulin-dependent type 2 diabetic for 1 month. Assuming checking the blood sugar only twice a day, using one test strip each time, it would run about $1.34 per day. Two sterile alcohol swabs to help you with that, 16 cents a day. And 20 units per day of insulin, and that is very, very minimal, $4.20 daily. The cost of 1 month's basic supplies would be somewhere around $184.20. Now, this figure also assumes that no other medications are required, and it does not account for doctor's visits, transportation, or the other things, the miscellaneous things, that are involved with the disease.

I calculated that the cost of my medications—that is not including doctor, hospital, extra glasses, or other devices—if I had no insurance, the cost for 1 month would be around $733.20. Even with insurance, I manage to pay more than $200 per month. The standard co-pay for a prescription is $10. However, because of the price of some medications, the co-pay can be as much as eight times that amount. For example, one medication without insurance help would cost $149.50 a month, and another is $111.82 for 1 month's supply.

I think about the monetary cost of this disease and wonder how people who are struggling to live on Social Security can possibly do an adequate job of caring for themselves, even with Medicare. I know there are other programs that help some, but the gap is still way too wide. If it was one disease that remained as one, perhaps it would be sufficient to allow the drug companies to take their time to seek out a cure.

Diabetes takes its toll in the day-to-day wear and tear that it afflicts on the human body in the form of heart disease, amputations caused by wounds that won't heal, eyes that lose their sight, financial burdens, and sundry other complications. The final blow it administers is the worst of all: A parent with type 2 diabetes finds out that his or her child has been diagnosed with the disease, and the cycle begins all over again.

I say let us break that cycle. Let us put type 2 diabetes out to pasture with smallpox, polio, whooping cough, and dyptheria. And let us find the research necessary and fund the research necessary to find a cure. And I ask Congress to make that money available so that can be accomplished.

My thanks to you, Senator, and to those other members of the Senate who see the insidiousness of the disease, know the impor-

tance of its cure for the financial well-being of our Nation, and are willing to do something about it. Thank you.

Senator COLLINS. Thank you, Mr. Jump. Mr. Fuller.

TESTIMONY OF WILLIAM H. FULLER, JR.,[1] VIRGINIA BEACH, VIRGINIA

Mr. FULLER. Chairman Collins and Members of the Subcommittee, thank you for inviting me to testify today regarding diabetes research, an issue I care deeply about.

In 1991, I was in my fourth year of NFL football as a defensive lineman with the Houston Oilers. After playing spot duty for the first years, I was finally getting my long overdue chance at being a starter. Having played 2 years in the old U.S. Football League and 3 years with the Oilers, I had already made more money than I could ever imagine.

This success had enabled me to buy my mother and father their first house, complete with a satellite dish so that they could watch me play anywhere in the United States, this after living in apartments our entire life. I was the first person in the Fuller family lineage to graduate from college. I had been married for 5 years, and had a beautiful wife and two young daughters.

It should have been one of the better periods in my football career, or life for that matter, but that was not the case, for I was seriously considering retirement. You see, back in my home town of Chesapeake, Virginia, a totally different story was unfolding. The people I owed the most gratitude for my success were suffering, suffering because of diabetes.

My father had type 2 diabetes. His diabetes had already caused him to have a leg amputated while I was in college. It also caused his kidneys to fail, and he had to be hooked to a dialysis machine 3 days a week for 3 hours each visit. And now, to make matters worse, he was losing his eyesight.

At 6 feet 3 and 260 pounds, I knew it was getting harder and harder for my mother to take care of him. She also took care of my sister, who cannot hear as the result of a bout with spinal meningitis when she was a baby. Until I left for college on a football scholarship, it had always just been the four of us.

My wife suggested I get a nurse to help my mother take care of him, but mom kept saying they were fine and no need for me to worry. She promised to let me know if things got too tough, but on a recent trip home a neighbor informed me that my father had fallen down in the bathroom and my mother had to call the neighbor to help get him up.

I told my father my thoughts of quitting football so I could return home and help out. If he could have gotten up and punched me, I think he would have. I remember it as being one of the few times I had ever seen my father cry. He told me how proud he was of the man I had become, and no matter what happened, to promise not to quit because of his situation. He said that my quitting football would do more harm to him than diabetes ever could. I did not believe that, but we decided to get some help for my mother, and I promised not to quit, a promise that was made even tougher be-

[1] The prepared statement of Mr. Fuller appears in the Appendix on page 73.

cause of the Oilers' insistence that players live and train in Houston year round.

It was during that same time that I met a gentleman named Milton Slocum at a charity event. He informed me of his business as a publicist and marketing agent for several of the Houston Rockets. We agreed to meet the next day. We met, and basically I told him the story I just told you. When he asked me specific questions about diabetes, I honestly could not answer them. All I knew, that it was a horrible disease that was wreaking havoc on my father, and it had something to do with the fact that his body was not producing enough insulin.

The next week Milton scheduled a meeting with the Juvenile Diabetes Foundation. It was a meeting that would forever change my life. I later served 6 years on JDF's International Board of Directors, and currently serve on its Board of Chancellors. I walked into JDF's office as a helpless and hopeless young man with a lot of questions. I walked out with many answers to my basic questions, but more importantly, I walked out with hope, hope that research would lead to a cure.

Through my annual celebrity golf classic and the "Sack the Quarterback" promotion, we have raised over $1 million toward this important research. I have learned a lot about this disease. I now know that there are over 60 million people with diabetes, and that many of them are children. To watch my father, my hero, suffer and eventually succumb to diabetes was very tough, but I cannot imagine the pain if this disease were to attack one of my four daughters.

However, over the years I have met many parents that are dealing with this nightmare on a daily basis. I cannot imagine having to give my 2-year-old daughter an insulin injection, or having to realize the possibilities of blindness, amputation, or diabetic comas that she or any of my daughters could face for the rest of their lives.

In almost 20 years of playing college and pro football, I have learned a lot about teamwork. I sincerely believe that the team of researchers at the National Institutes of Health, JDF and other organizations are on the right track to find a cure. I am proud to be part of that team.

Every team needs leaders, and Congress, and the NIH, if they provide the funding to support all diabetes research opportunities, have the capability of leading the way to a cure. We are ever so close to our Super Bowl—that is a cure for diabetes.

I thank you for your time, and may God bless you all.

Senator COLLINS. Thank you very much, Mr. Fuller.

I must say I had a series of questions to ask each of you, but I think your testimony speaks for itself. You have put the human face on this devastating disease. Your testimony is so eloquent and so moving that anything I could ask you would be superfluous. It is why I wanted Dr. Gorden to stay. It is why this report is so critical, because it says "conquering diabetes." It is why the increased research is just so vital. Your stories are so moving, your courage so inspirational, that I just want to pledge to you that I accept Ms. Fernandes' challenge to fight for a cure for this disease and to keep fighting until we have achieved that goal.

Ryan, I want to say to you how much I appreciate the efforts that you are making to reach out to other kids and to teens with diabetes through your Web site. You are absolutely right that most people do not understand how serious this disease is.

And that is why all of your testimony is so important, because you have each eloquently described either your own struggle, or in the case of Mr. Fuller, his father's struggle with this devastating disease. You have put the human face on it. We can talk about the statistics, we can look at the charts, but until we hear from you first-hand and what it has meant to your lives and your family's lives, that is what we need to provide the momentum for the cure.

I just want to thank each of you for your eloquence, for speaking out, for caring enough, for your involvement, and for being here today. You are why we are here, and I just want to assure you of my personal commitment to keep up the fight. So I accept your challenge, Ms. Fernandes, and again, thank you for your courage and thank you for speaking out. Thank you for your good work.

I would now like to call our final panel of witnesses this morning, and I am sure our final panel, which are distinguished scientists, have also been moved by what they have just heard, and if anything will redouble their efforts. They are all such leaders in their fields.

Dr. Ronald Kahn is the former chairman of the congressionally mandated Diabetes Research Working Group. He was the chairman of the group that produced this very important report. He is also executive vice president and director at the world-renowned Joslin Diabetes Center in Boston.

Dr. Edward Leiter is the senior staff scientist at The Jackson Laboratory in Bar Harbor, Maine. Dr. Leiter took me around the lab a few months ago and told me of the very exciting research. I became aware of Jackson Lab's role when I was visiting the Juvenile Diabetes Center, Research Center, at Harvard Medical School earlier this year, and all the mice they were using of course came from Jackson Lab.

Finally, we have Dr. Jeffrey A. Bluestone, who is the director of the Ben May Institute for Cancer Research at the University of Chicago in Chicago, Illinois.

I am very pleased to have three such distinguished researchers and scientists who really are on the cutting edge of diabetes research with us today. As I have explained previously, our rules do require that everybody be sworn in. Makes more sense when we are having an investigative Subcommittee, where we are worried that people won't tell the truth, but we do have to apply it across the board, so if you would, please stand.

[Witnesses sworn.]

Senator COLLINS. Thank you. Dr. Kahn, I would like to start with you, and again I want to welcome all of you to the Subcommittee.

TESTIMONY OF C. RONALD KAHN, M.D.,[1] EXECUTIVE VICE PRESIDENT AND DIRECTOR, JOSLIN DIABETES CENTER, BOSTON, MASSACHUSETTS, AND FORMER CHAIRMAN, DIABETES RESEARCH WORKING GROUP

Dr. KAHN. Thank you, Chairman Collins, and I also want to thank you personally and this Senate Subcommittee for giving me a chance to present this report of the Diabetes Research Working Group to you today. As you are aware, the Diabetes Research Working Group or DRWG, as we came to call it, was created in response to a request by the House and the Senate to evaluate the current state of diabetes research in the United States and to develop a strategic plan for the Nation as to how best to proceed making progress against this disease.

The DRWG consisted of 16 members representing the scientific and medical community, the JDF, the ADA, minority populations that are disproportionately affected, and others who have interest in this disease. We had tremendous support from the NIH, in particular from NIDDK, from Dr. Gorden's office and Carol Feld, who is here at these hearings, and from a number of other individuals that all deserve a lot of credit and thanks.

Now, what is diabetes, and why was it so important that this Diabetes Research Working Group was deemed necessary? As you have already stated, diabetes is a very complex disease. Furthermore, it is not a single disease but rather a group of diseases which affect a large number of people.

The two major forms of diabetes, type 1, the insulin-dependent form of diabetes, which used to be called the juvenile-onset form and type 2, the adult onset form, often called non-insulin-dependent diabetes, although it too may require insulin therapy. These two forms affect 16 million Americans, as has been mentioned already.

It is estimated that over 700,000 people, mostly children and young adults, have type 1 diabetes. And as individuals age, diabetes becomes even more common. In fact, if we all live to be 80—and we all hope to live to be 80—17 percent of the people in this room will have diabetes. As a result of these two forces, the type 1 and the type 2, about 800,000 new cases of diabetes are diagnosed each year.

In addition, there are many other forms of diabetes. Some are rare, but some are quite common. For example, gestational diabetes is a form of diabetes that occurs during pregnancy and affects over 5 percent of all women in the United States who become pregnant.

As we have already also heard, diabetes spares no one. We have heard from Ryan, and my neighbor Avi Robbins who is about the same age. We have heard in the House and in the Congress from Nicole Johnson, last year's Miss America. We know it from our parents and our grandparents and our grandchildren, from one coast to the other. Everyone is at risk.

The risk is particularly high in minority populations of the United States. African Americans, Hispanics, Native Americans

[1] The prepared statement of Dr. Kahn with attached charts appears in the Appendix on page 75.

and Asian Americans not only represent some of the fastest growing segments of our population, but they are particularly vulnerable to diabetes and its complications. Among these groups, the Pima Indians of Arizona have the highest incidence of diabetes in the world. Over 50 percent of the adults have diabetes in that indian tribe.

Not only does living with diabetes present many day-to-day challenges, but as has already been said, affects virtually every tissue of the body with long-term and severe damage.

Diabetic eye disease is the most common cause of blindness in working age adults. Diabetic kidney disease accounts for 42 percent of end-stage renal disease, that is, patients requiring dialysis or transplantation. It is the fastest growing cause of end-stage renal disease. Stroke and heart disease are increased two to four times, as you have already said yourself, and this is especially increased in women who normally are protected from these vascular problems, at least in the premenopausal age group.

Diabetes affects the nervous system, leading to impaired sensation, pain, and slow digestion, impotence and many other problems. The rate of congenital malformations in offspring of diabetic women is increased three- to four-fold, and more than half of the lower limb amputations in the United States are secondary to diabetes.

As has already been said also, diabetes is the sixth leading cause of death in the United States, but in fact in some of these minority populations it is the third leading cause of death.

Now, as you have already shown, and one of the surprising findings even to the members of the DRWG is that despite all of our knowledge and despite all of our efforts, since 1980 the age-adjusted death rate due to diabetes has increased by 30 percent, while the death rate from other common diseases such as stroke and cardiovascular disease has fallen.

Of course these are only statistics. We have already heard from a number of individuals today about the very personal impact of this disease. In our report we had five personal profiles, including one from Pam Fernandes, who presented today. I am sad to tell you that one of the individuals who was discussed in our report, Jerrold Weinberg of Detroit, actually passed away from the time the report was being prepared to the time we were able to present. He died at the age of 39 from complications of this disease.

The economic impact of diabetes is also staggering. The cost of diabetes to the Nation has been estimated at $105 billion annually, and some estimates have gone as high as $130 billion. Somewhere between 10 and 14 percent of all U.S. health care dollars are spent for people with diabetes. One of every four Medicare dollars pays for health care of people with diabetes.

Next chart, please. Another striking finding of the DRWG was that while health care costs for each person in the United States affected with diabetes average $6,560 annually, the current investment in diabetes research is only about $30 per person affected per year. That is, less than one-half of 1 percent of the cost of the disease is invested in R&D in an attempt to reduce the burden caused by diabetes. This is a very small investment for a disease that affects 6 to 7 percent of the population and accounts for 10 to 14 percent of all health care dollars.

With these facts in mind, the strategic plan created by the Diabetes Research Working Group had multiple goals. We felt that it was important to understand the causes of diabetes and the causes of its complications; to develop methods to prevent and treat diabetes, and to prevent and treat diabetic complications, methods to reduce the impact of diabetes in minority populations; and to develop the research infrastructure and to train investigators to do the necessary research to achieve these goals; and of course, very importantly, to translate these research findings into clinical practice.

In developing an approach to this plan, I took some advice that was given to me by Lee Iacocca, who is a strong supporter of diabetes research through his own foundation and supports diabetes research at the Joslin as well. And he said, ''Just imagine you are in the year 2010, and you would like to look back and see what you have accomplished in the area of diabetes. Then, given these goals, what would you have to do over the next decade to at least have some chance of accomplishing them?''

And so this was the challenge to the committee, and this is what led to this 140-page Research Strategic Plan that you have before you today.

There are three major components of the DRWG's strategic plan:

Extraordinary opportunities, these were areas that we viewed as rapidly expanding and important areas of research, where increased investment or development of new approaches would significantly speed research.

Special needs for special problems was an area that we felt was equally important, but these were more focused areas of research, usually targeted to specific populations or specific complications or some cases specific methodological approaches.

And then, finally, resources and infrastructural needs. This was, of course, the plan for increasing research manpower and technology, as well as the infrastructural elements required for diabetes research.

In this plan, all in all, there are 88 recommendations in 16 different categories, and I would just like to briefly talk about a couple of these today.

Perhaps one of the most exciting areas in all of research today is in the area of genetics, and the genetics of diabetes and its complications. If we identify the genes for diabetes and its complications, we may someday be able to predict and prevent the disease. Understanding the genetics will also give us the opportunity to develop new therapies that are directed at the true, central problem of the disease.

The DRWG proposes several initiatives in the area of genetics, including the creation of a national consortium for the study of the genetics of diabetes. One of the goals of this consortium would be to develop a diabetes DNA chip. In fact, I brought this actual DNA chip to show you. The little square in the center of this black holder is the DNA chip that we are using in my laboratory and is being used in other laboratories to try to identify some of the genes that might be altered in diabetes.

We believe that with the proper investment in research, within a decade a diabetes-specific chip could be developed, that when exposed to DNA from a few drops of blood, would tell us who is likely

to develop diabetes, which of the diabetic patients are most likely to develop which complications, and perhaps even who would respond best to each specific treatment approach.

A second area that we will hear I am sure more about from Dr. Bluestone is the area of autoimmunity and the beta cell. This holds the key to type 1 diabetes, since type 1 diabetes is an autoimmune disease that destroys the insulin-producing beta cells. Important progress has been made in this area over the past several years, including identifying some of the genes involved in predisposing to type 1 diabetes, some of the components of the beta cell that are attacked; developing markers for detection of pre-diabetes; and demonstrating the critical importance of tight glucose control for reducing diabetes complications.

But there remain many challenges which are critical if we are to conquer this disease, and in the DRWG report we describe a program to intensify research to understand the immunologic basis of type 1 diabetes; to develop optimal strategies for blocking the immune destruction; for expanding research in the area of transplantation as therapy, which will require solving critical issues such as, where do we get enough islet cells to treat the hundreds of thousands, or perhaps eventually millions, of people who could benefit from this treatment; and how do we protect these transplanted cells from immunologic rejection?

Other extraordinary opportunities that are listed in the report include an area of basic research called cell signaling and cell communication. This is a very important area, because we believe that in this area will be the keys for understanding type 2 diabetes; and type 2 diabetes, after all, does account for 90 percent of all of the patients with this disease.

Obesity, another critical area of extraordinary opportunities. Research in animal models, such as has been done at The Jackson Laboratory and in other laboratories, has pointed the way to the great opportunities here that need to be approached in our studies for humans with this disease.

And, finally, the area of clinical research and clinical trials which must be applied to develop evidence-based medicine to approach this disease.

The DRWG has also made special recommendations, in our special needs for special problems area, regarding the eye, kidney and nerve complications as well as the cardiovascular complications, which is the major killer of people with diabetes.

In these areas we must define exactly how and why does diabetes enhance the atherosclerotic process or these other vascular problems. Why do women with diabetes tend to be at special risk and lose their vascular protection? What are the factors that occur in diabetic patients, that lead them to be at increased risk of dying after a heart attack, and how can we develop therapies to enhance their survival? And can we develop better specific, noninvasive techniques to identify the presence of diabetic complications, predict their progression, and assess their response to therapy?

We also describe basic and clinical research programs to better understand the impact of diabetes in the young, in the old, in women, and in minority populations.

As I have already indicated, the current investment in diabetes research is small, and indeed far too small to provide the resources needed to begin to address the research plan. As requested by Congress, therefore, the DRWG has developed budgetary recommendations to accompany this plan. You will see that the recommendations call for a 5-year step-up in the research budget for diabetes, from the current level of about $443 million to, as you have pointed out, $827 million for the year 2000, and actually rising to $1.6 billion by the year 2004.

Let me point out to this Subcommittee and to this group that these numbers were not arbitrarily chosen. They were based on a planning process, a detailed planning process that took 15 months, and we believe describe what is realistically needed to bring diabetes research to a point where there would be at least a reasonable chance that we could accomplish a number of the goals that we have set forth over the next 10 years. In the full report, this detailed budget is outlined in a project-by-project and institute-by-institute manner.

Finally, I would like to point out that the members of the Diabetes Research Working Group do not believe that diabetes research should necessarily be funded by taking resources from other important biomedical research needs. We understand the problems that NIH faces. We are very supportive of NIH, the Director of NIH, Dr. Varmus, the Director of NIDDK, Dr. Gorden, and we recognize the many challenges that must be faced in utilizing their precious resources.

But we would like to use the analogy that like the military, which must be prepared to fight a battle on at least two fronts, the NIH and the biomedical research community must be prepared to fight a battle of human disease, not just on two fronts, but on many fronts at once, and this will require a significant investment both immediately and in the long term.

The DRWG is convinced that there is both great urgency and unprecedented opportunities in diabetes research. We are convinced that taking action now will save thousands of men and women and children from severe consequences of diabetes. We have done the first part of the job by developing the report, and we applaud and are delighted by the support of the Senate and its recommendation to support this. We now ask the U.S. Government and the NIH to give its continuing support to allow us to do the research that will be required to conquer this dread disease. Thank you.

Senator COLLINS. Thank you, Dr. Kahn. Dr. Leiter.

TESTIMONY OF EDWARD H. LEITER, PH.D.,[1] SENIOR STAFF SCIENTIST, THE JACKSON LABORATORY, BAR HARBOR, MAINE

Mr. LEITER. Madam Chairman, I wish to begin by commending you and the other Senator co-sponsors of the recently passed sense of the Senate resolution calling to the attention of the American people the impact that diabetes has on our population and urging increased support for diabetes research, education and early treatment.

[1] The prepared statement of Mr. Leiter appears in the Appendix on page 86.

I am a senior staff scientist at The Jackson Laboratory, a world center for mammalian genetics, and my research focus has been mouse genetic models of both type 1, insulin dependent, and type 2, non-insulin dependent, diabetes. Now, the fact that there are different forms of diabetes underscores the genetic complexity of the diseases, but there is something in common, and unfortunately we have heard about that commonality. Those are the complications of kidney failure, blindness, heart disease and stroke, and amputations.

I have a personal family reason for being interested in both type 1 and type 2 diabetes. My grandfather had type 2 diabetes and my uncle, Frank Black of Los Angeles, California, has been struggling valiantly with his type 1 diabetes since first diagnosis in 1942. So it is concern for my uncle, for the millions of Americans who now fight with their diabetes, and for those Americans that will develop diabetes, that leads me to give you my comments.

We now know that most cases of type 1 diabetes in humans represents an autoimmune disease, wherein a rogue immune system turns against the body in which it resides. We have an excellent mouse model, the NOD mouse, for autoimmune insulin dependent diabetes. One of the most important lessons we have learned from the NOD mouse is that autoimmune diabetes is a preventable disease. This finding, along with similar findings in another animal model, provided the impetus for NIH to initiate clinical trials to prevent type 1 diabetes from developing in young adults deemed at high risk.

One of the most exciting recent developments in my laboratory comes from the close relative of the NOD mouse. Like the NOD mouse, this relative seems to have just the right genetic program to develop type 1 diabetes. It doesn't. Why?

It seems that the insulin-producing beta cells of this mouse are unusually resistant to immune-mediated injury. With support from the American Diabetes Association and the Juvenile Diabetes Foundation, we are working very hard to try and decipher or understand the factor that is protecting these beta cells. We hope that these findings can be extrapolated to make human islets more resistant to damage by a rogue immune system.

Of equal importance in my research are the mouse models of obesity in type 2 diabetes that I am developing. Such new models are of tremendous importance in the testing of pharmaceutical compounds to be used in the treatment of human type 2 diabetes. For example, these mice are helping us identify genetic targets that respond favorably to a given pharmaceutical compound, as well as identifying the genetic makeup of individuals that would suffer adverse side effects if they were treated with a comparable anti-diabetes drug.

I would like to add some thoughts about the recommendations made to Congress by the Diabetes Research Working Group. Obviously, as a recipient of NIH funding to do my own diabetes research, and having participated in the development of the DRWG recommendations, I am biased in my hope that the recommendations could be implemented by the NIH.

Although considerably more NIH funds have been designated for diabetes-related research in the past year or two than ever before,

research dollars that are allocated are still inadequate to fund all the meritorious investigator-proposed grant applications in the areas identified by the Diabetes Research Working Group. I have personally served in NIH peer review panels evaluating diabetes research, and have observed that the competition for grant funding today is so stringent that many scientific avenues that could be explored are not being explored.

Indeed, if the discoverers of insulin, Drs. Frederick Banting and Charles Best, were to apply for an NIH grant today, providing only their interesting hypothesis that the pancreas made a substance that might control blood sugar, I am fairly convinced that their application would be turned down. Why? The answer is that with NIH's rather limited resources devoted to diabetes research, only those investigators receive funding who can demonstrate with preliminary studies that the hypothesis they are proposing to test is correct.

This review process assures the Congress and the American taxpayers that their monies are being wisely spent by the NIH. However, it also means that the process of scientific discovery, which often moves by trial and error, and sometimes even serendipity, on the road to getting an "eureka," is not being promoted to its fullest extent. Thus, progress on the path to better therapies and an eventual prevention of diabetes is not as rapid as it might be if all the Diabetes Research Working Group recommendations could be implemented.

So, in closing, let me thank the Subcommittee and especially the Senator from my own State of Maine, Senator Collins, for inviting my comments. We are now in an unparalleled age of discovery in molecular genetics in both mice and in humans.

The Human Genome Project, which the Congress has so wisely supported, will provide a genetic blueprint on which a massive structure of new knowledge will be built. This new knowledge will certainly contain the key to new therapies not only to control diabetes but more importantly, as Dr. Kahn has suggested, to identify individuals at risk to develop this devastating disease, and thereby permit interventions to prevent diabetes from happening. This is a reality now in my mouse models. Let us work to make it a reality in the human family as well.

Senator COLLINS. Thank you very much, Dr. Leiter.

I notice that the other Senator from Michigan, Senator Abraham, who has been a leader in the fight against diabetes, has also arrived, and I wanted to give the Senator the chance to either join us at the dias or to make any statement if he would like.

Senator ABRAHAM. I don't think it would hurt to sit here.

Senator COLLINS. That would be great. Senator Abraham was a cosponsor of an amendment that I offered last week to the Labor-HHS bill, supporting the recommendations for $827 million in funding by the Working Group, and we have worked very closely on diabetes research issues. So I asked him if he would like to join us today, and I appreciate the fact that you have been able to stop by.

OPENING STATEMENT OF SENATOR SPENCER ABRAHAM, A U.S SENATOR FROM THE STATE OF MICHIGAN

Senator ABRAHAM. Senator Collins, thank you very much, both for inviting me and for giving me a moment. I will not detract too long from the panel's efforts because we really want to hear from experts at these events.

We had a hearing in my committee, or actually a markup on a bill, downstairs in the Judiciary Committee, so I couldn't be here as early as I had wanted and I have to head on back, but I did want to just congratulate you and thank you for the leadership you have demonstrated on these issues in our State as well as the other States.

We have obviously a lot of folks who are in various ways incapacitated by diabetes. In our own family, both my wife's mother and father are diabetics who take regular insulin injection, so it is not an issue that doesn't have its impact even on us here in the Senate.

And so I just want to thank you for the leadership. I fully support the efforts you have engaged in to try to both draw more attention to this disease, as well as to try to focus more of the Federal Government's efforts on trying to combat it. We appreciate all who have been part of this.

Of course, we have a Michigan witness. I missed his testimony, but I had a chance to say "hi" to Ryan, and I want to welcome him and his family to the Senate. We appreciate having our constituents down to participate, but in particular when they bring important messages like he has today.

So I just thank you very much, and I will let you return to the hearing, but I really appreciate very much an opportunity to speak out in support of your efforts.

The prepared statement of Senator Abraham follows:

PREPARED STATEMENT OF SENATOR ABRAHAM

Madam Chair, I am proud to speak today on the importance of funding for diabetes research.

Diabetes affects the lives of 15.7 million Americans, with approximately 2,200 newly diagnosed cases a day. High levels of funding are vital in developing a cure for this disease, which is why I strongly support an increase of 45 percent in funding within the Fiscal Year 2000 NIH budget for diabetes research, bringing funding levels to a total of $827 million.

Diabetes affects almost every aspect of daily life. Imagine having your schedule being dictated by a regime of specialized diet, blood sugar checks, and insulin shots. Now, imagine being a kid and having to endure the countless doctors visits, injections, and tests. Or, not being able to attend a sleep-over, play a sport, or even enjoy the Halloween candies passed out during class. Imagine, instead of enjoying the freedom and spontaneity of being a kid, having your life revolve around a disease.

This year, I was proud to be a Honorary Co-Chair for the JDF Children's Congress. The JDF is dedicated to discovering a cure for diabetes and the accompanying complications through the support of medical research. The Children's Congress provided a way for kids with diabetes to come to Washington and not only get an opportunity to meet their peers, but to educate their Senators and Representatives about coping with this disease.

Our children face this disease with a courage beyond their years, but it is our responsibility to make sure that someday they won't have to. Today we have the privilege of hearing the testimony of a young constituent of mine, and one of this year's delegates of the Children's Congress. Ryan Dinkgrave is only 16 years old but has lived with diabetes since the fifth garde. I would like to take this opportunity to commend Ryan for his achievements in promoting diabetes awareness. He has created a Web site called the "Families Guide to Diabetes" for families to learn about

coping with the disease. In addition, during this year's Juvenile Diabetes Foundation's (JDF) Walk to Cure Diabetes, Ryan's group, "Team Ryan" raised an event-record $4,000. All of us can learn from Ryan's courage and dedication.

It is vital that we continue to fund diabetes research so we can someday find a way to cure this debilitating disease. I want to commend Senator Collins for her work to educate government and the public about this disease and the need for increased funding. I was proud to vote for her amendment to the Labor, Health and Human Services, Education appropriations bill, which calls upon Congress to raise awareness of the devastating impact of diabetes and instructs NIH to increase funding levels to that which has been recommended by the Congressionally-mandated Diabetes Research Working Group. Her amendment, which passed overwhelmingly, demonstrates, beyond a shadow of a doubt, the strong commitment in the Senate to finding a cure for diabetes and improving the lives of those affected by this disease.

Senator COLLINS. Thank you, and thank you for your support in this area. I want to let you know that Ryan did a terrific job. You can be very proud of him and the efforts that he is making.

Senator ABRAHAM. Thank you.

Senator COLLINS. Thank you. Dr. Bluestone, if you would proceed.

TESTIMONY OF JEFFREY A. BLUESTONE, PH.D.,[1] DIRECTOR, BEN MAY INSTITUTE FOR CANCER RESEARCH, UNIVERSITY OF CHICAGO, CHICAGO, ILLINOIS

Mr. BLUESTONE. Good morning, Chairman Collins. My name is Jeffrey Bluestone. I am the Chairman of the Committee on Immunology at the University of Chicago, and also the Director of the Juvenile Diabetes Foundation Islet Transplant Center at the University of Chicago and University of Minnesota.

But I am addressing you today mostly as a Ph.D. basic scientist at the University of Chicago, on behalf of myself and other scientists, both basic and clinical colleagues of mine, all of us in continued pursuit for the cure for diabetes and other debilitating autoimmune diseases. All of these diseases depend very much on the Federal Government's support and your efforts and others for the basic and clinical research funds that we use.

In my short presentation, I hope to impart to you my personal sense of optimism. I believe we are really on the precipice of making dramatic changes in the way we treat autoimmune diseases and diabetes, and with your help I feel that we have a chance of turning the corner quickly to fight these autoimmune diseases such as type 1 diabetes.

I thought I might share with you some of my own research and why I think that we are indeed at a time to be very optimistic. My laboratory has focused for a number of years on the basic processes that determine why immune cells respond or don't respond to tissues, self tissues, foreign bacteria, or viruses. We have used organ transplantation as a model to try to understand how to reeducate, train the immune system not to recognize self tissue and not to recognize transplants of kidneys, livers, and most prominently in our recent research, islet cells from other individuals.

What we have learned in the last 10 years, quite dramatically actually, is that type 1 diabetes is indeed an autoimmune disease, a disease caused by the T cells in the body's ability to recognize and target and kill the very beta cells that are critical for insulin pro-

[1] The prepared statement of Mr. Bluestone appears in the Appendix on page 89.

duction. And, as Dr. Leiter pointed out, the animal models that have been developed and exploited at The Jackson Laboratory has made our work very easy in trying to understand better the basic processes of this disease.

And perhaps the most dramatic observations that we have made in the last 10 years is that the T cells, the cells that are most prominently involved in the destruction of the islet cell of the pancreas, are very much regulatable. We have learned that the T cell works like a lock-and-key mechanism, where each T cell recognizes a protein uniquely, and the T cells that recognize the insulin-producing beta cells are not the same as the T cells that recognize a virus or a bacteria.

We have also learned that the process of T reactivity is a multistep process, in which not only is there recognition of the tissue but then subsequent exposure to other signals that determine whether the T cell gets turned on or turned off. These fundamental observations have changed the way we have thought about how we are going to manipulate or alter the T cells responsible for generating immune responses against autoimmune diseases in self tissue.

What we have learned is that our basic processes of immune intervention that we have used over the past 2 decades, which have had extraordinary success in treating autoimmune disease to some extent, but more often kidney transplants and liver transplants, that these are sledgehammers. These are drugs that suppress the whole immune response. They have worked very well, but they lead to many complications and toxicities. They require treatment for the whole life of the individual who has the transplant or the disease, and although they have been very successful, they beg for more sophisticated and targeted approaches.

And what we have learned is that we can now develop drugs against these lock-and-key mechanisms on the T cells, the drugs against the receptor itself that recognizes the islet cell, as well as drugs against these other molecules that are necessary for signaling a competent immune response. I think there is a tremendous amount of excitement and enthusiasm in the community that some of these drugs, when combined in appropriate ways, will lead to what we call immune tolerance, the ability to treat with drugs for a short period of time and reeducate or train the immune system so it does not recognize any more its self tissues, like in the pancreas, and that we can subsequently do islet transplantation in a setting in which the islet cells will not be rejected.

It is these exciting new approaches to the treatment of immune disorders that actually led the NIH and the JDF and, as you mentioned earlier on, a very concerted effort among different institutes to put together what I think is an exciting, bold new initiative. It is called the Immune Tolerance Network.

It is a 7-year project funded, as I said, by the NIH and the JDF—I have been fortunate to be asked to lead this effort—in which over 70 investigators from around the world will be putting their energies towards trying to study not just diabetes, a very important area in islet transplantation, but other autoimmune diseases like lupus and multiple sclerosis and rheumatoid arthritis, to work with kidney transplantation as well, and even allergy and asthma, to try and understand common mechanisms in regulating all of these dis-

eases and common approaches, as I say, redefine and reeducate the immune system, such that we can now avoid the attack of these terrible T cells.

This effort, which has just begun—yesterday I closed a meeting of the 70 investigators, our first—is supported by $140 million from the NIH and the JDF over the next 7 years. It is a tremendous opportunity. I feel a tremendous amount of pressure, in fact, to make a difference in this thing.

It is a testament to the confidence of you in the Senate, to the research community, that we really are now putting these kinds of dollars in, and I truly believe that we need to continue to do that, and we need to do that because the basic research underpinnings that have gotten us here today don't just stop, that we need to keep moving on, to come up with new ideas and new opportunities. Genetic research is going to have tremendous impact, as well.

So there is no doubt that the recent scientific developments represent remarkable progress in our understanding of human disease. We have new tools now, those little chips that Dr. Kahn brought today—which may now give us a fresh approach to the treatment of diabetes and related diseases.

I urge the Congress and the NIH to implement the recommendations of the Diabetes Research Working Group. I sit before you today full of enthusiasm and optimism. I am confident that 50 years from now, when we look back at the turn of the century, it will not be remembered as a time when we argued over managed care and how to redefine our public health system. It will be regarded as a golden age of biology that marked the beginning of the end for so many diseases. And like the industrial revolution at the end of the last century, the biological revolution will be remembered as a time of innovation and discovery, when diseases like diabetes are only a memory. Thank you.

Senator COLLINS. Thank you very much, doctor.

Dr. Leiter, first I want to again commend you and the other two scientists here today for your excellent work and commitment in this area. I was struck by your testimony that if the two inventors of insulin, Dr. Banting and Dr. Best, I believe the names were, were to apply today for an NIH grant to support their theory, that you do not believe they would be funded based on what they would be going to NIH with.

That suggests to me the magnitude of the problem, and that there are many meritorious projects out there that we are just not funding, and that we may be missing the chance for a tremendous breakthrough. Is that what you are trying to tell us by using that example? That is a startling statement.

Mr. LEITER. Things have improved dramatically over the last 2 years, as your diagram and the testimony of Dr. Gorden have indicated, so with the funding of one in three applications now, that really is a very positive step. But still, within the one out of three that gets funded, there is probably one out of three in there that is deemed excellent but not outstanding.

The peer review panel, just to ensure that NIH is going to get what it hopes to get, which is a real positive outcome, will send the investigator back a message, "Get us some more preliminary data and come back, and let's then reevaluate your hypothesis to see

how close to the scientific truth it really is." And if we can just get that second out of three grants funded, progress will be moved forward because the scientist will not be frustrated, will not be scraping.

Thank goodness for the Juvenile Diabetes Foundation and the American Diabetes Foundation. If you are from Maine or Michigan or some other cold weather State, jump starting in winter time is a very common concept. Well, these two private organizations have jump started scientific research in diabetes in this country, and it is through their efforts that many of these one out of three grants are not lying fallow but actually some of that preliminary data is being obtained.

I know Director Varmus is aware of the problem, I know NIDDK is trying to remedy the problem, how to fund innovation at the same time as NIH is putting its money on sure things. So it is certainly a problem that is being tackled at the governmental levels. They are aware of it, they are trying to deal with it, but certainly it will be helped out if the Diabetes Research Working Group recommendations, at the funding level you and your co-sponsors have supported in the Senate, were to become reality.

Senator COLLINS. I appreciate your mentioning the terrific support provided by the Juvenile Diabetes Foundation and the American Diabetes Association. I am so impressed with their advocacy and their commitment to research, and I know that Dr. Bluestone, also the project that you described involved some funding, some private funding, as well.

I guess that leads me to a question for Dr. Bluestone, which is, how well does it work to have private funding in addition to NIH funding? Are there problems with merging the funding streams, or are you able to handle the combination of private and public dollars without any problems?

Mr. BLUESTONE. I can speak about the JDF Foundation, which I have had the most experience with, which may actually be a pioneer in this area, I believe. What they have done is, they have actually partnered very effectively with the NIH. They have taken advantage of tremendous talent in the NIH and the review process identifying outstanding research opportunities, and helped to support research.

One of our grants is basically an NIH-funded grant that at the time in the early 1990's had to be cut because of administrative cuts due to budget restrictions. The JDF came in and restored that cut so we could do all the research that we had hoped to do. So it has been an exceptional partnership, I believe.

More recently, the ability of the JDF to actually help in getting the tolerance network going, contributing 10 percent of the money actually that is going towards this network, was actually an extraordinary opportunity. Again, they did it in an incredibly productive way, by not trying to fund separately or fund independently, solely, but here to partner with the NIH and put the money together. So if the JDF could be used as a role model in this, it would be very good for all of us.

Senator COLLINS. Thank you.

Dr. Kahn, I want to get back to one of the key issues that has been before us, and again I want to salute you for excellent work.

You made a very important point, which is, the budget numbers recommended by the Working Group are not plucked out of a hat. They are not arbitrary. They are tied to a planning process and to achieving specific goals, and that to me is the strength of your report.

What has been NIH's reaction to your good work, to the funding levels? Are you satisfied with the reaction? And I realize I may be putting you in a little bit of a difficult spot. Maybe, though I am very pleased that Dr. Gorden has stayed for the hearing, I should have him go away for this part.

Dr. KAHN. No, that is fine. But yes, I think that as you gathered from Dr. Gorden's testimony, they are caught in a bind in a sense that they have many initiatives brought to them and a limited budget.

I think that NIDDK actually should be commended for, as Dr. Gorden pointed out, jump starting a number of things in this report. NIAID, the National Institute on Allergy and Infectious Disease, in this program that is partly through that institute and partly through NIDDK, and the JDF has also jump started some of the initiatives related to the autoimmunity. So there has been actually some very positive response by a number of institutes and institute directors, and attempts to use some of the existing funding to pick, if you will cherry pick some of the ideas from this report to see if they could not be jump started.

Clearly, however, with the existing levels of funding that are available, the type of effort that we hoped could be achieved cannot be achieved. It will take a significant increase in diabetes research funding to achieve this, in part because these efforts really require a multidisciplinary, multifaceted approach. You heard from Dr. Bluestone that this immunology initiative alone is going to be $140 million over 7 years, and we believe that our genetics initiative could be in the range of $100 million over 7 or 8 years, or maybe even more.

So each of these initiatives, if we really want to concentrate and maximize the scientific opportunity, will take a very significant investment. Of course, we can do something with half that amount or a third that amount, but it will be half as much or a third as much. You cannot get the whole process for part of the price.

So I think that NIH has made some efforts to actually use its resources to do this, but I think that they will be greatly enabled by, hopefully by the legislation or the recommendations that you have made and that have been passed by the Senate. And I think that that would allow the full magnitude of the report to really have its maximal impact.

Senator COLLINS. I think that is a very important point, because given the state of the research, we really do need this infusion of funds and we need it now, if we are going to achieve the goals. And that is one reason I want to hold this hearing today, to try to give momentum and try to frankly put some pressure on NIH to keep pushing forward in this area, since I think it is very clear there is very strong congressional support for doing so.

Dr. Bluestone, you gave a very lucid explanation of how the type 1 diabetes autoimmune—of the fact that it is an autoimmune disease. As I have read more about type 1 diabetes, it seems to me

that islet cell transplantation has tremendous promise, but I do not understand how we are going to prevent the body from attacking the transplanted cells. Or at one point I thought, "Why don't we just transplant pancreases? Why don't we?"

I mean, maybe that is an option, but it seems to me you always have the problem of turning off whatever is causing the host body to attack the islet cells all over again. Is that part of your work? It sounds like that is part of the focus, is to figure out how, without using the kinds of powerful anti-immune system drugs that cause so many other problems, we can tackle that issue.

Mr. BLUESTONE. Yes. It is actually worse than that. The transplant has two problems. The first problem is what you said, which is, the autoimmune response which was ongoing in the patient before you put in the islets is still ongoing. The second problem is, you have now taken islet cells from another individual, like when you take a kidney, and you have that so-called allo response, the foreign response, as well. So there are two responses you have to deal with. In kidney transplantation we only have to deal with one; in liver transplantation, only one.

So you are right, it is a tremendous challenge, but the things that I was talking about, the ability to understand the basic mechanism by which the T cell recognizes both the autoimmune and the alloimmune response, is exactly what we are targeting right now. And what is very exciting is the fact that the transplant gives you is an opportunity to intervene just at the point when the T cell is just about to recognize the tissue.

In an autoimmune patient, there is now data that at 6 months of age there are already signs in the type 1 diabetic of an immune response against the pancreas, and it is progressive, so that by 6, 7, 8, and 10 years old it is to late, the patient is diabetic. With the transplant, we know when the transplant is going in, and we can now try to manipulate the immune response precisely at that time, which I think will give us a tremendous advantage.

Finally, the only other point that I would make is that we do do pancreas transplants right now, and in fact they are rather successful. But one of the great opportunities in islet transplantation is the opportunity to be able to not only manipulate the islet cells so that when they go in they are less likely to be rejected, which is difficult in pancreas to do, but also the cost and morbidity associated with surgery and clinical care will be avoided.

And then, finally, of course, are great opportunities led by places like the Joslin to try to create the ability to grow these cells, so that even though there are only about 4,000 pancreases a year, that we might be able to treat the millions of people who are going to be able to take advantage of the technology.

Senator COLLINS. And, as you pointed out in your testimony, the work you are doing also has implications for other autoimmune diseases like multiple sclerosis, I think you said.

Mr. BLUESTONE. Yes. It is actually true that there is great opportunities. When I talk about this in public, I talk about Teflon and the space program. I truly believe that the outcomes of these kinds of research are often serendipity and unanticipated, and there is, from cancer to AIDS to the various autoimmune diseases, these are

processes that are dealt with by the immune system over and over and over again.

And what we have learned is that immune disorders really affect many diseases and dozens of diseases now, so I am optimistic that the basic research done in the area of diabetes will almost certainly have implications for many of these other diseases.

Senator COLLINS. Dr. Leiter, you mentioned in your testimony that you are working with the NOD mouse to try to identify predictors, I believe, so that we could identify young people who are at risk for type 1 diabetes. Could you explain more about that research? That very much interests me, because perhaps if we can intervene at an earlier age, we can prevent some of the devastating consequences of diabetes, or figure out eventually how to switch off the cell that is causing the problem.

Mr. LEITER. The basic approach that we have to predicting what the genetic makeup is for a program to get diabetes is marriage. We heard Dr. Kahn has just had a daughter married, and let us see, Mr. Jump I think just had his daughter married. Well, we choose different husbands and wives for NOD.

The NOD mouse is really a replicate of just one single human being at risk to get insulin-dependent diabetes. So depending who we call in as a marriage partner, we come up with different genetic combinations that will lead us toward diabetes or away from diabetes. And sometimes, to our amazement, if we choose a certain marriage partner, the kind of diabetes that ensues may not be the same kind of autoimmune diabetes that the NOD has.

So we see all kinds of complex intermixtures, telling us once again that genetically there are all kinds of ways to get diabetes. But with regard to pre-diagnosis, there is one major factor that tells us that the mouse really could get diabetes if the genetic program would allow it, and those are genes which tell the teachers of the T cells that Dr. Bluestone was talking about. There is a certain genetic component that tells these teachers of the T cells how to teach.

And in humans at high risk for insulin-dependent diabetes, we can see that there are certain similarities between their instructional genes or T cell education and what the NOD mouse has. So genetically that is the first thing we look for, for an autoimmune genetic bad education, and that is true in humans as well. So there is a major genetic component in the mouse and in humans for type 1, and they are in the same place genetically.

But after that, you really are limited to some of the immunologists' and the clinicians' tools, and that is, you look in the blood. You could either do what Dr. Bluestone might do, and pull out some T cells and show them something that the beta cell makes and ask, "Do you recognize this, and if so, would you attack it or will you let it go?" And if that recognition is there without letting it go, then you already know that mouse is on the road to developing type 1 diabetes and you darn well better think about doing something early if you want to stop that, and that is what Dr. Bluestone and his 70 other scientists are working on doing.

The other thing you can do is measure antibodies. If the beta cell is being attacked by the T cells, then signs of the destruction are antibodies against beta cell components like insulin and other com-

ponents. So if you see this combination of a major genetic component that leads to a bad education of the T cells, so they do not tolerate the way they should, so teaching tolerance is missing; if you see that the Beta cells are being attacked, as reflected by these immune signposts, and you could also do a glucose tolerance test, those would be signs in a mouse or a human that it is time for some sort of intervention.

And that, of course, is what NIH is working with the JDFI and the ADA to develop, just the right kinds of interventions.

Senator COLLINS. Thank you. I am fast reaching the end of my scientific knowledge. Once I get past the T cells and the beta cells and the islets, I am really on thin ice, but fortunately we can rely on the experts.

Dr. Kahn, I had one other area that I wanted to raise with you. I think we heard from our panel of people coping with diabetes a very important point. Ryan mentioned it. In fact, all of them mentioned it, one way or the other.

And that is that there is a common misperception about how serious diabetes is, and that the public does not understand how serious the disease is and how devastating the consequences can be. Ryan points out that if you take a classroom of students, you cannot tell who has diabetes and who does not by looking at them. Mr. Fuller talked about when he first learned his father had diabetes, he knew it had something to do with insulin and that was about it. Mr. Jump talked about that he was in denial at first about his own diabetes. Ms. Fernandes did not realize the risks of going blind at first.

I think that part of the challenge that we face is the lack of public awareness about the severity of diabetes. Do you think that that lack of public understanding has contributed to the fact that diabetes research has been so severely underfunded?

Dr. KAHN. That is a very tough question. I definitely would start off by agreeing with your perception, and by the perception that has been stated, that too many people believe that diabetes is not a serious disease, and it obviously is a very serious disease.

I would actually say that the problem in a certain way is greater in the area of type 2 diabetes than type 1 diabetes. In type 1 diabetes, we are more sensitive to the fact that these are young children, that their life styles and their growing up period of their life is very disrupted with management of this disease. Their parents are obviously distraught, and they have to help manage this disease. And of course we talk about a lifetime of disease.

We are perhaps a little less sympathetic to the older person who has diabetes, but who is equally devastated, and who may have in fact many more complications because of their age. They may already have heart disease or have kidney disease or have other chronic, debilitating diseases that only make the situation for them that much more complex. And Mr. Jump gave us some idea of even for an individual like himself, how many different medications and how many different monitorings he has to do.

And both of these, even type 2 more than type 1, seem to be so silent. The type 2 diabetic individual, we have heard that as many as a third to a half of them don't even know they have the disease. And yet they are, during this period of silence, actually at risk for

developing complications. Many times they present first with some of the complications, the neuropathy, the retinopathy, and so forth.

I don't know if public awareness is the rate-limiting step in our research funding, because I think that obviously the ADA and the JDF have both done a lot to increase public awareness about this disease. But I think that it is perhaps one factor that has given somewhat less pressure or tension on this disease than on AIDS or cancer, which are such rapid devastating diseases. Here we have a slow and devastating disease.

And I think that we need to be aware that because it is slow and because it looks like not much is going on, does not mean that not a lot is going on. And so I think that we do have to be cognizant of the fact that more people die of diabetes each year, by a factor of several fold, than die of AIDS, and more people will have diabetes complications of various sorts than many other diseases which are much more high profile.

So I think that there is a need to realize how important this is. The economic impact I think also speaks to this. It tells you that there is a very big public health burden as well as a personal health burden. So I think that there are plenty of reasons that we should be more attentive to this disease. I think that Congress' initiatives, both on the House and the Senate side, have been tremendously helpful.

And I hope that with this and with more funding for NIH, that institute directors like Dr. Gorden will have more resources to put into this disease, because I know that they would like to. He cannot say that but we can say that. He would like to do it, we would like him to do it, and I think that what he needs is a green light from you to go ahead.

Senator COLLINS. And that he has.

I want to thank you very much for your testimony today. I am trying to do my part to promote awareness of diabetes, not only through this hearing, but also today the Senate Diabetes Caucus which I chair is holding a free screening for Senate employees and for Senators. It is going to be held in the nurse's station on the first floor between the Hart and Dirksen Senate Buildings, and I encourage anyone to take advantage of the free screening today. I am going to do it myself, although having learned a lot about diabetes, I must say I am a little bit nervous about what the results may be.

In all seriousness, I do want to thank all of our witnesses today. Again, I want to thank you for your dedication to diabetes research, for the excellent work that you are doing in your labs, for the exciting research that you have underway.

I hope that I will be able to hold another hearing 5 years from now, if the voters of the State of Maine have the judgment to send me back for a second term, and that I will be able to hear of the exciting breakthroughs that you have accomplished because we have given you the resources that you need to achieve the goals set out in the Working Group's report. So I want to thank you very much for sharing your experience with us today.

I want to thank all of our witnesses today for coming forward and sharing their unique perspectives. I particularly want to thank the people with diabetes who testified today. I think that it is so

important that we do put the human face on this very serious disease, and without their very eloquent and moving testimony, this hearing would have been far different. So I want to thank particularly our second panel for coming forward today.

I want to thank Dr. Gorden as well, and to assure him that he has the very strong support of Congress, he has that green light that Dr. Kahn referred to. I am very committed to continuing the fight against diabetes. We have learned a great deal today, and I think we have learned there is reason for great hope and optimism, that indeed the research is at a stage where we can see breakthroughs happening.

It is very exciting what is going on, and I think that as long as NIH works with Congress to fully fund the recommendations of the Diabetes Research Working Group, that we will make the kinds of breakthrough that are going to allow us eventually to prevent and cure diabetes, as well as giving improved treatments and improved quality of life for those who are suffering from the disease right now.

I also want to thank my staff, which has worked very hard on this hearing. Priscilla Hanley, of my personal staff, has worked very closely with me on all the initiatives I have undertaken for diabetes, as well as the members of the Subcommittee staff, particularly Lee Blalack, Elizabeth Hays, Mary Robertson, and Justin Tatram.

I also want to thank again the American Diabetes Association and the Juvenile Diabetes Foundation for the expertise that they have provided me. I am going to continue the fight, as well, and I thank you very much for your contributions.

The Subcommittee is now adjourned.

[Whereupon, at 11:57 a.m, the Subcommittee was adjourned.]

A P P E N D I X

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland 20892

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Senate Governmental Affairs Permanent Subcommittee on Investigations

October 14, 1999

Witness

Phillip Gorden, M.D.
Director, National Institute of Diabetes and Digestive and Kidney Diseases

For Release Upon Delivery

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Statement of the Director

National Institute of Diabetes and Digestive and Kidney Diseases

Phillip Gorden, M.D.

Madam Chairman, I am Phillip Gorden, the Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which has lead responsibility for diabetes research at the National Institutes of Health (NIH), within the Department of Health and Human Services. I appreciate the opportunity to testify before the subcommittee about the Department's efforts to combat diabetes.

In both human and economic terms, diabetes is an extremely costly disease. It is widely recognized as one of the leading causes of death and disability in the United States. Diabetes affects an estimated 16 million Americans. About half of them do not know they have diabetes and are not receiving care for the disease. Approximately 800,000 people are diagnosed with diabetes each year including both genders, the young and the old, all races and ethnic groups, the rich and the poor. Although diabetes occurs most often in older individuals, it is one of the most common chronic disorders in children in the United States. About 120,000 children and teenagers age 19 and younger have diabetes. It is the leading cause of kidney failure, new blindness in adults, and non-traumatic amputations. According to the American Diabetes Association, diabetes and its complications of the eye, kidney, nervous system, and heart cost an estimated $98 billion annually. Though there are several interventions currently available to help reduce the burden of this disease, there are no methods

to cure it or prevent its onset. Consistent with today's hearing, I will focus my testimony today mainly on NIH research that is aimed at understanding, treating, preventing, and ultimately curing diabetes.

Diabetes is a disease marked by the body's failure to produce or properly use insulin, a hormone that is needed to convert sugar, starches, and other food into energy essential for daily life. The causes of diabetes are not precisely known, although both genetic and environmental factors play a role. Diabetes occurs in several forms, and has complications that affect virtually every system of the body. The most common forms of this disease are type 1 and type 2 diabetes.

Type 1 diabetes--formerly known as insulin-dependent or juvenile-onset diabetes--most often occurs in children, but can appear at any age. It accounts for 5 to 10 percent of all diabetes in the United States. It occurs equally among males and females, but is more common in Caucasians than in non-Caucasians. Type 1 diabetes is considered an autoimmune disease, which occurs when the body's system for fighting infection--the immune system--turns against itself. In type 1 diabetes, the immune system attacks and destroys the insulin-producing cells in the pancreas. Thus, a person with type 1 diabetes needs daily injections of insulin to live. At present, we do not know exactly what causes the autoimmunity in type 1 diabetes, but we believe that both genetic factors and an environmental trigger are involved.

Type 2 diabetes is the most common form of the disease. Once known as noninsulin-dependent or adult-onset diabetes, it affects about 90 to 95 percent of people with diabetes. In type 2 diabetes, the pancreas usually produces insulin, but for some reason, the body cannot use the insulin effectively. The end result is the same as for type 1 diabetes--an unhealthy buildup of glucose in the blood. Type 2 diabetes is more common in older people, especially older women who are overweight. We know that obesity is a major risk factor for this form of diabetes. It also occurs more frequently among minority

groups, including African Americans, Hispanics, and Native Americans. Recently, we have also witnessed a disturbing increase of type 2 diabetes in children, particularly minority children.

HIGHLIGHTS OF THE DEPARTMENT'S EFFORTS AND STRATEGIES TO COMBAT DIABETES

The Department of Health and Human Services has a multifaceted agenda to combat diabetes. Within the NIH, there are broad research efforts to understand, treat, prevent and cure the disease. Because diabetes and its complications affect so many parts of the body--the heart, the eyes, the kidneys, and the nervous system--it is an important trans-NIH research area, complemented by the programs of other components of the Department, such as the Centers for Disease Control and Prevention and the Indian Health Service. Many organizations outside the Government also support diabetes research and education activities. These organizations include the American Diabetes Association and the Juvenile Diabetes Foundation International, as well as the biotechnology and pharmaceutical industries. The NIH has formed strong and fruitful relationships with these organizations to enhance progress in the fight against diabetes.

I would like to emphasize several scientific points that are central to present and the future biomedical and behavioral research efforts of the NIH to prevent and treat diabetes. We are witnessing rapid advances in the study of the patterns of inheritance of specific traits (genetics) and the development and application of broad, experimental approaches to assess gene function (genomics). These advances help us to pursue our goal to find and eliminate the causes of diabetes, as well as many other diseases. In addition, major new understandings of cell communication are critical to diabetes. Likewise, key advances in clinical research are showing how the control of blood pressure, serum

cholesterol, and other lipids, as well as control of blood glucose, is important in the comprehensive care of patients with diabetes.

The Diabetes Control and Complications Trial sponsored by the NIH clearly demonstrated that the complications of diabetes affecting the eye, kidney and nerves can be ameliorated or prevented through close control of blood glucose levels. These findings have important implications for the treatment of both forms of diabetes and give new emphasis to the value of early treatment in type 2 diabetes. This view was recently confirmed by the United Kingdom Prospective Diabetes Study, which also demonstrated that good blood pressure control produced a major benefit in decreasing complications of the large blood vessels. Collectively, these results complement and extend the clinical progress achieved in treating diabetic eye disease with laser therapy, and the use of drugs--such as ACE inhibitors--for the kidney disease of diabetes. These advances represent major steps forward in our continued quest for a cure. While progress has been made, the seriousness and frequency of complications further emphasize the compelling need to develop better technologies both to manage blood glucose levels and to treat complications more directly and effectively.

IDENTIFYING SCIENTIFIC OPPORTUNITIES AND NEEDS

To identify the most promising avenues of diabetes research, the NIH has a two-step peer review process mandated by law to ensure high scientific standards among funded projects. This process begins with an assessment of scientific and technical merit by an initial review group of non-Federal scientists. Applications are then reviewed by the Institute's National Advisory Council, a group of eminent scientists and lay individuals with expertise in an Institute's areas of research, to consider program needs and the relevance of grant applications to the mission of that Institute.

In addition to the peer review system, the NIH also takes steps to guide and facilitate the development of its programs through a variety of means. In diabetes, for example, we have accelerated and enhanced our efforts by seeking and acting upon scientific advice from a special trans-NIH workshop, "Diabetes Mellitus: Challenges and Opportunities," complemented by the Strategic Plan of the congressionally established Diabetes Research Working Group. We have already initiated many new research projects as a result of these processes and will continue to build upon them in the future. We are also developing a new NIDDK Strategic Plan based on cross-cutting scientific themes that are highly relevant to both type 1 and type 2 diabetes.

SPECIAL INITIATIVES ON DIABETES

The Balanced Budget Act of 1997 provided funds for two major, five-year initiatives within the Department of Health and Human Services. I would like to report briefly on activities being pursued.

Consistent with congressional directives, the first five-year initiative is providing $30 million annually for research on the prevention and cure of type 1 diabetes. This initiative is being administered by the NIH, with participation of the Centers for Disease Control and Prevention. I am pleased to report progress on NIH efforts under this initiative to promote innovative, clinically relevant, multidisciplinary research relevant to all of the scientific opportunities in type 1 diabetes research today, but especially to the development of more effective therapies, which can be easily administered and followed. Through this initiative, we are seeking the best research talent from diverse fields, the most promising research ideas, and the most technologically advanced research tools for combating type 1 diabetes. We are exploiting the fruits of the biotechnology revolution, with special attention to clinical issues. We have solicited new research projects to develop therapies to achieve normal glucose

levels in people with type 1 diabetes and to develop improved glucose sensors for regulating blood glucose. We have also expanded programs to understand the mechanisms by which high glucose levels result in the late complications of diabetes; to apply this information to the development of ways to prevent, limit or reverse complications; and to understand generally the role of factors important in disease development.

This year the special funds for type 1 diabetes research are being used to focus on the mechanisms by which the disease results in painful and disabling neuropathies and other neurological complications; identification of stem cells and factors that regulate development and differentiation of pancreatic beta cells through the establishment of a functional genomics resource in diabetes; and pilot studies for new therapies for type 1 diabetes and its complications.

With funds provided by the Balanced Budget Act, the Centers for Disease Control and Prevention has dedicated $3 million to establish a National Diabetes Laboratory to support emerging scientific efforts on type 1 diabetes. Scientists are working to improve blood test measurements of hemoglobin A1C, an effective blood marker used in the long-term treatment of people with diabetes, and to improve genetic and immunological markers that show if people are susceptible to type 1 diabetes.

In the second, five-year initiative under the Balanced Budget Act, the Indian Health Service is administering $30 million annually for grants aimed at the prevention and treatment of diabetes in American Indians and Alaska Natives. Type 2 diabetes occurs at dramatically higher rates among American Indians and Alaska Natives (2.5 times higher in this population than in the U.S. population). There has been about a 24 percent increase in the American Indian age-adjusted death rate since 1991-1993. The funds provided in the Balanced Budget Act have enabled the Indian Health Service to

expand its clinical diabetes program, which it has supported for 20 years. Although the incidence of various complications of diabetes has continued to rise in Native Americans and Alaska Natives, the Indian Health Service has pioneered a number of innovations including the extensive use of a team approach to prevention and treatment, the use of podiatry services in prevention, culturally distinct dietary interventions, and extensive community-wide diet and exercise interventions. The Indian Health Service is recognized as an international leader in diabetes care.

As a result of the funds provided by the Balanced Budget Act, more than 280 new and innovative programs have been implemented by the Indian Health Service's Tribal/Urban Indian Health Programs. While progress has been made in reducing the rate of increase of blindness and amputations, these complications continue to occur at unacceptably high levels, and end stage renal disease is escalating at a rapid rate. Currently, these programs provide primary and secondary inpatient and outpatient treatment services to Indian beneficiaries with diabetes or who are at high risk for developing diabetes. The Indian Health Service's diabetes care services are consistent with services recommended by the American Diabetes Association and follow what is classified as current "best practices."

Ultimately, the anticipated outcome of the efforts of the Indian Health Service's Tribal/Urban Indian Health Programs is a reduction in the mortality and morbidity of diabetes. In the short term, the commitment is to expand access to both ambulatory and inpatient diabetes services through a multidisciplinary approach. This would include increased access to retinopathy, dialysis, nutrition, weight-loss, and foot-care programs. Promotion of the implementation of diabetes practice guidelines in program settings is a major emphasis.

EXAMPLES OF RESEARCH AVENUES THE NIH IS PURSUING

I would like to describe in detail some of the research avenues the NIH is pursuing to combat diabetes. These include: cell-based therapies; enhanced modalities of treatment; fundamental research; clinical research and clinical trials; prevention and treatment of complications; and type 2 diabetes in children, adolescents, and young adults.

Initiative on Cell-based Therapies for Diabetes:

We are embarking on a new and exciting initiative to restore insulin-producing capacity through transplantation of the whole pancreas, or of insulin-producing islets from the pancreas. This research is being propelled by an impressive series of advances. Recent studies in primates have shown that both insulin-producing cells and kidneys can be transplanted using a highly selective method to control the immune system's rejection of the transplant. This new technology involves what is referred to as "blockade of the co-stimulatory pathway." It allows for a selective form of immune tolerance and, therefore, does not require suppression of the entire immune system, as is required by conventional therapy for organ transplantation.

Paralleling this initiative is a major, new, collaborative effort on immune tolerance within the intramural program of the NIH. The research partnership involves the NIDDK, the Warren Grant Magnuson Clinical Center, the Department of Defense, and the Diabetes Research Institute of the University of Miami. The strategy under study is relevant to both the treatment of type 1 diabetes and kidney transplantation. Furthermore, there is a major, additional joint effort involving the NIDDK, the National Institute of Allergy and Infectious Diseases and the Juvenile Diabetes Foundation International to broaden this program into a network of collaborating institutions.

Initiative to Enhance Modalities of Treatment:

The NIH is working diligently to develop a wide range of new and more effective therapies for avoiding the adverse consequences of low blood glucose levels and for improving the treatment of diabetes. For example, the National Institute of Child Health and Human Development is supporting two comprehensive studies in adolescents to understand how low blood glucose levels affect learning skills and how the undesirable effects of multiple daily insulin injections affect compliance. We are also pioneering the development of glucose sensors and mechanical systems to facilitate insulin administration and thus ease the burden of this therapy for children and adults who are insulin-dependent.

One exciting recent advance may well have important therapeutic implications with respect to the immune system's attack in type 1 diabetes. Researchers have shown that a protein called GAD, which is expressed by insulin-producing cells, controls the development of diabetes in an animal model of human type 1 diabetes. The demonstration that this protein initiates autoimmune diabetes builds upon an earlier NIH-supported advance, which showed that cells specifically reactive against GAD directly produced injury to insulin-producing cells in a mouse model. This avenue of research could have important consequences for the development of new therapies to prevent type 1 diabetes, provided these findings can be extended to human disease.

We also hope that new clinical advances will emerge from other NIH-supported investigations of pancreas and islet transplantation in animals. This work includes studies of ways to regenerate the pancreas; to develop methods to enable the protection and survival of implanted insulin-producing cells; and to discover innovative approaches to prevent graft rejection by induction of immune tolerance, as previously described.

An important research goal is to extend the therapeutic arsenal of safe and effective drugs to treat diabetes. In the United States, five classes of oral medications, each of which works through a different mechanism of action, are currently available to improve blood glucose control in patients with type 2 diabetes, as well as multiple agents for the treatment of lipid and blood pressure disorders. These oral agents complement a variety of new insulin preparations that have been introduced for treatment of type 1 diabetes.

Examples of Fundamental Research Important to Diabetes:

The NIDDK has a major research initiative on obesity, which is a serious risk factor for the development of type 2 diabetes. We funded the initial discovery of the first gene identified as causing obesity in an animal model. The subsequent identification of this gene's protein product, leptin, and the elucidation of leptin's role in appetite and energy regulation spearheaded the discovery of other genes that control critical aspects of both eating and energy regulation. At least five different genetic defects in humans have been linked to obesity. Such important research advances have relevance not only to our understanding of obesity, but also to the inter-relationship of obesity and type 2 diabetes.

To enhance application of improvements in genomic reagents and bioinformatics to diabetes, the NIDDK has expanded its research in the genetics of type 1 and type 2 diabetes, as well as its studies of the genetic factors that underlie progression to diabetic kidney disease. Our investments have already led to the discovery of six genes in which mutations cause rare forms of diabetes. However, the more common forms of diabetes are complex disorders with contributions from multiple genes. To facilitate the discovery of these genes, we have established an International Type 2 Diabetes Linkage Analysis Consortium. Jointly funded by the NIH and the American Diabetes Association, this

is an effort to pool data from multiple studies for collaborative analysis to map diabetes susceptibility genes. A similar collaboration has been initiated with an emphasis on the kidney complications of diabetes. The NIDDK also plans to convene an advisory group to aid in further development and implementation of genetics initiatives.

Another major goal of fundamental research is to gain insights into disease processes in order to create targets for therapeutic intervention. These basic discoveries then provide the platform for drug discovery and testing by the biotechnology and pharmaceutical industries. Thus, NIH basic research helped to generate the knowledge base for development of several of the diabetes drugs I mentioned previously.

Examples of Clinical Research and Clinical Trials:

With the development of screening tests, it is now possible to identify and test therapies that may prove beneficial in preventing or delaying the onset of diabetes. These tools are now being studied in a major multicenter clinical trial, the Diabetes Prevention Trial or DPT-1, cosponsored by the NIDDK, the National Institute of Allergy and Infectious Diseases, the National Institute of Child Health and Human Development, the American Diabetes Association and the Juvenile Diabetes Foundation International.

To foster other clinical studies, the Diabetes Research Working Group recommended establishment of a Diabetes TrialNet. In response, the NIDDK recently provided administrative extensions to the centers involved in the ongoing Diabetes Prevention Trial, while a task force considers approaches for establishing such a network for future studies of prevention and treatment of diabetes.

The findings from the two major clinical trials, described previously, reinforce the importance of our Diabetes Prevention Program, an important primary prevention study now under way, led by the NIDDK, with financial and technical support from the Centers for Disease Control and Prevention. This major, multicenter clinical trial is designed to find out whether onset of type 2 diabetes can be delayed or prevented in at-risk individuals. The trial is comparing the current standard regimen of diet and exercise with a more intense regimen of diet and exercise and metformin, a medication approved for the treatment of type 2 diabetes. Approximately 50 percent of the patients in this trial are from minority populations, who suffer a disproportionate burden from type 2 diabetes.

Diabetes has long been recognized as an independent risk factor for several forms of heart disease in both men and women. Indeed, cardiovascular complications are now the leading cause of illness and death in the diabetic patient. The NIDDK and the National Heart, Lung, and Blood Institute are initiating two clinical trials designed to identify ways to reduce cardiovascular complications of type 2 diabetes. The Prevention of Cardiovascular Disease in Diabetes study will assess the benefits of intensified control of high blood sugar, cholesterol and hypertension. The Study of Health Outcomes of Weight Loss is a large multi-center trial designed to determine if interventions to produce sustained weight loss in obese individuals with type 2 diabetes will improve health. Together, these trials will provide important information about the effectiveness of several new medications and treatment regimens.

Initiative on Prevention and Treatment of Complications:

Multiple NIH institutes are participating in a major initiative to combat the eye, nerve, kidney and vascular system complications associated with type 1 and type 2 diabetes, including the search for

susceptibility genes that predispose patients to these complications. We will also place a new emphasis on understanding and treating diabetic nerve disease, and inaugurate a major clinical trial aimed at reducing the cardiovascular complications of diabetes, as mentioned previously. These research areas have been identified as having high priority by the Diabetes Research Working Group.

Type 2 Diabetes in Children, Adolescents, and Young Adults:

Type 2 diabetes has traditionally been considered a disease of adults because the age of onset is frequently after age 40. In recent years, however, an increasing number of children who appear with elevated blood glucose levels actually have type 2 diabetes. Based on case reports and clinical studies, among children who have diabetes, the percentage who have type 2 diabetes has risen from less than five percent prior to 1994, to 20 to 30 percent after 1994. It appears that these children are not dependent upon insulin injections; however, their cells and tissues are resistant to insulin. Some may require insulin to maintain control of their blood glucose. Not surprisingly, one of the major risk factors for type 2 diabetes in children is obesity. The increase in reports of type 2 diabetes among children parallels a similar rise in the adult population, as obesity has become a major public health concern. In children, the alarming rise in the incidence of type 2 diabetes appears to be occurring largely in minority populations--Hispanic Americans, African Americans, and Native Americans. The NIDDK recently convened a group of epidemiologists and pediatric endocrinologists to address this issue. Based on data presented at that meeting, we plan to solicit research on the pathophysiology, prevention and treatment of type 2 diabetes in children. We also plan to collaborate in a campaign to alert pediatricians to this alarming trend.

OUTREACH AND EDUCATION PROGRAMS

Important parts of the effort to combat diabetes are outreach and education programs. The NIDDK initiated the National Diabetes Education Program with the Centers for Disease Control and Prevention, with support from the NIH Office of Research on Minority Health, and with participation of the diabetes voluntary community. A goal of this program is to improve the treatment and outcome for people with diabetes in order to reduce the illness and death associated with diabetes and its complications. Because survey research showed that the level of awareness of diabetes among the public was low, the program launched a media campaign with the theme, "Control Your Diabetes. For Life." The goal of this campaign was to disseminate the findings from our major clinical trial, which showed that close control of blood glucose levels can prevent or significantly reduce the complications of diabetes. In national and local media outlets across the country, we received excellent coverage of this message. Because of the extremely high incidence of diabetes in all minority groups, the program quickly moved to target those audiences with culturally-sensitive public health messages tailored by minority organizations who collaborate in this program. Complementing these education campaigns is the National Diabetes Information Clearinghouse, established to increase knowledge and understanding about diabetes among patients, health care professionals, and the public. In addition, NIH is collaborating with the American Heart Association and the diabetes voluntary organizations on a major public health statement to alert physicians, patients, and the general public to the increasing significance of diabetes as a major risk factor for cardiovascular disease. In addition to these efforts,

there are a number of ongoing outreach and education programs being implemented throughout the Department. Examples include:

The Department's Health Disparities Initiative:

The Centers for Disease Control and Prevention and the NIH co-chair the Diabetes Work Group of the Department's Health Disparities Initiative. The workgroup assessed the best ways to translate what we know about preventing and controlling diabetes, identified ways to address the gaps in what we know, and developed strategies to eliminate the disparity in the burden of diabetes among selected racial and ethnic minority populations. The Department anticipates that these activities will be used to support the efforts of grantees funded through the Centers for Disease Control and Prevention's "Racial and Ethnic Approaches to Community Health (REACH) 2010 Initiative." This initiative was developed as part of the Department's response to the President's Initiative on Race. Fourteen of the thirty-two grantees funded in FY 1999 are addressing diabetes prevention and control.

TRIAD Study:

In 1999, the Centers for Disease Control and Prevention initiated a multicenter, five-year study to conduct research within managed care organizations that will evaluate and improve the health care and health status of people with diabetes. The Translating Research into Action for Diabetes (TRIAD) study will be recruiting substantial numbers of minorities in an effort to: (1) better understand the current levels of quality of care and health status of minority populations; and (2) better understand the barriers to improved care and health status for minority populations covered by managed care.

In summary, Madam Chairman, I am grateful for the opportunity to share with you some examples of the efforts and progress in combating diabetes that are being made by the National Institutes of Health, the Centers for Disease Control and Prevention, and the Indian Health Service. I have tried to underscore today that we understand the great burden diabetes places on patients, families, and communities. At the same time, I want to share my feelings of encouragement and hope. I believe that our national programs hold the essential key to curing this disease. We have important programs under way, but much more remains to be done. I am pleased to answer any questions you may have.

Juvenile Diabetes Foundation International
The Diabetes Research Foundation

Public Affairs

Testimony of the

Juvenile Diabetes Foundation International

Presented by

Ryan Dinkgrave, Age 16
Livonia, Michigan

before the

Senate Permanent Subcommittee on Investigations

Regarding

Diabetes Research

October 14, 1999

Chairman Collins and members of the Subcommittee, thank you for giving me the opportunity to testify this morning on behalf of the Juvenile Diabetes Foundation International. My name is Ryan Dinkgrave, and I am 16 years old and a student at Stevenson High School.

Before I begin, Chairman Collins, let me thank you on behalf of all of the JDF children and teens with diabetes for all that you are doing with the Senate Diabetes Caucus to help us find a cure.

I was diagnosed with juvenile, or Type 1, diabetes when I was in the fifth grade, just over six years ago. It was one of the scariest things that has ever happened to me. My pediatrician said that my constant thirst and exhaustion were because I had diabetes. I had also lost weight, experienced frequent sluggishness and other common symptoms of diabetes. I had no clue what diabetes was, and I really didn't want to know, but we proceeded directly to the hospital. That day was the first of my six years of trying to live with diabetes.

I was in the hospital for almost a week, and I left with no idea what to expect. It turned out that having diabetes meant my whole life was to be turned upside down and changed in every way. No longer could I just eat what I'd like or when I'd like, no longer could I really do anything without planning. This was because of the constant concern that I would suffer from low-blood sugar that could lead to an insulin reaction or high-blood sugar that could lead to severe health complications.

I began trying to manage my diabetes with two shots a day, which eventually became three shots a day, and then four. Along with the shots came blood glucose tests four times a day. These tests involve pricking my finger to draw a drop of blood. Along with these daily efforts came worries about what could happen if my blood sugar levels were not kept in good control: heart problems, kidney problems, nerve damage, vision problems, blindness and amputations; the list seemed like an impossible thing to avoid. My life would certainly never be the same.

Last November, after doing insulin injections for over five years, I switched to a more advanced type of insulin therapy, called the insulin pump. This is a device that is about the size of a pager which administers insulin through a tube that goes into my body, and has to be moved to a new location every few days. While it has allowed me more freedom, better blood sugar control, and possibly a longer life, it is still not perfect and living with diabetes is still, at best, very difficult. Until there is a cure, nothing will satisfy those who struggle to live daily with this disease.

A common misperception about diabetes is that one with diabetes is healthy. This is because people with diabetes often have no outwardly visible characteristics of the disease. There is no physical evidence of the organ damage and future health concerns of someone with diabetes. Look at any teenager or child with diabetes. They look just like any other person their age. Put a hundred kids in the line, and there is nothing you can see that would allow you to visually distinguish who has diabetes from who does not. It is because of this that many people do not realize the severity of diabetes, and the urgency for a cure, until it is too late, and complications of the disease have set in.

I, personally, have had to struggle a lot with diabetes, both emotionally and physically. I have to worry about future health concerns, and every moment of every day I must be aware of my condition and treat it. I have had three seizures due to low blood sugar. I know that this scared me and my parents like never before with how serious and trying these events have been.

I have done a lot to help spread information on diabetes, and work with others with diabetes like myself. About three and a half years ago I started a website called The Family's Guide To Diabetes at http://diabetes.cbyc.com/ for children and teens with diabetes, and their families. Through the site, and through my speaking to doctors, families, and others about diabetes, I have been able to exchange information and learn about how others live with diabetes. Also, I have participated in the Juvenile Diabetes Foundation's (JDF) Walk to Cure Diabetes for each of the past 5 years. In fact, this year my group, Team Ryan 1999, raised a new high of $4,000, which will go to support curing diabetes through JDF's $75 million research budget.

This past summer I was the Michigan representative for the JDF Children's Congress here in Washington, D.C. The JDF Children's Congress allowed 100 children and teens with diabetes to explain to Congress and the nation how diabetes impacts us and the need for increased research funding for a cure. I learned at the JDF Children's Congress about the Diabetes Research Working Group report that indicated that there are many high-quality diabetes research projects that are not being conducted solely due to a lack of funding. On behalf of all of the children and teens with diabetes, I urge you to ensure that this funding be made available so we can find a cure as quickly as possible. Thank you very much for allowing me the opportunity to testify, and I would be pleased to answer any questions.

TESTIMONY OF PAM FERNANDES

Before The
Permanent Subcommittee on Investigations
Hearing On
CONQUERING DIABETES: ARE WE TAKING FULL ADVANTAGE OF THE SCIENTIFIC OPPORTUNITIES FOR RESEARCH?

October 14, 1999

* * *

My name is Pam Fernandes. I am from Needham, Massachusetts. Thank you for the opportunity to tell you about diabetes, a disease which plagues our country. Many people will give you statistics including the incidence of diabetes and it's complications. These numbers tell you the overwhelming breadth of the problem. Through my story, I hope to also give you a sense of the tragic depth of the problem.

Thirty four years ago I was diagnosed with Type I diabetes. At the age of four, my understanding was quite simplistic. Two painful injections a day, urine tests, and no treats like brownies, cookies or candy. Through my childhood and early adolescence I tried desperately to understand, this disease that made me different from every other child. I still did all the things my friends did. I went to girl scout camp, played varsity sports, and attended football games and dances.

When I was 18, at the very time in my life when options seemed endless and the future was full of exciting promise, diabetes threw me a curve. Two weeks before leaving for college, I went for a routine eye exam. My doctor told me I had a few small hemorrhages in my eyes -- nothing to worry about, but I should see a specialist when I arrived in Boston. Three weeks later I found out I was going blind. The day I walked into that office began eight of the most painful and difficult years of my life.

After laser surgery and five eye operations, I was declared legally blind. I was just 21 years old. Exactly one week before my twenty second birthday I began dialysis treatments. You see diabetes took it's toll on my kidneys as well. I lived on a machine for five years and although everyone said I was doing remarkably well with the treatments, I never felt worse in my life. I couldn't imagine any kind of future, with each day being so emotionally and physically painful. It was then that I lost site of my dreams. . .

After more than thirty operations, too many nights in a hospital bed and two episodes of respiratory arrest, I made a life- changing decision. In 1987 I opted for and received a kidney transplant. The first year was tough, but soon I rediscovered the Pam that was vibrant, alive, and tenacious.

About the time life began looking up for me, my family was hit with an unthinkable tragedy. My oldest brother Mark died from complications of his diabetes. He also had kidney disease, which

lead to his failing health. One of the most painful parts of Mark's death was watching my parents suffer the loss of a child, the hardest loss one can endure. Diabetes claimed the life of a young 32-year-old man who had a wife and a baby girl.

In 1992 I was invited to ride on a tandem bicycle. Little did I realize that this ride would not only change my life, but open doors that I never imagined possible. I rode recreationally for about a year, to have fun and stay fit. I got involved in American Diabetes Association Tour de Cures. These rides are designed to raise money to support education and research in diabetes. The American Diabetes Association is the largest organization representing all people with diabetes. I am very happy to be the National Spokesperson for the American Diabetes Association's Tour de Cures for the next two years.

Bike racing became a part of my life in 1993. I attended a camp for cyclists with disabilities at the U.S. Olympic Training Center. I had one of the most empowering, intimidating and painful (good pain mind you) weeks of my life. Again, a life changing decision for me.

In 1994 I won the U.S. Association Of Blind Athletes it's first international medal in cycling, by capturing the silver medal at the World Championships in Belgium. At the 1996 Atlanta Paralympic Games I earned a bronze medal in the 1 kilometer time trial. I am a five-time National Champion in road and track racing. As if the medals weren't enough, I have been recognized through many awards including The New England Women's Leadership Award in Sports, The Lifescan Prize For Athletic Achievement, and The U.S. Olympic Committee's Athlete Of The Year, Disabled In Sports, Blind Athletes. When I reflect on some of these accomplishments, I marvel at the fact that I can ride at all in spite of what I have been through.

I am in many regards a very lucky girl. This disease hasn't been kind to me, In fact it's been my toughest opponent. but so far, I've come out ahead. I am a living example of how far we've come in research by the mere fact that I am doing what I'm doing. I am also a very sad reminder of how far we have yet to go. My story speaks well to the power of the human spirit, but how many set backs can one's spirit hold up to.

Unfortunately, I am not the rule, but the exception. Many people with diabetes don't have the determination, the desire, the knowledge, the opportunity, or the family support to succeed as I have. That is why it is so important for you as our Congressmen to understand our disease and help us by supporting research to find treatments and ultimately the cure.

You know I learned a very poignant lesson during my first few trips to Washington. I learned the enormous responsibility and power our Congress has as it relates to our nations health. I learned that there is absolutely nothing between me and the cure to my disease but money. There is no lack of researchers and no lack of desire to stop this disease . . . there is only a lack of money. We deserve to have the brilliant researchers who are waiting to cure our disease funded. We deserve to have a cure.

Diabetes must become a national priority. Right now there are more than 16 million people in the United States with diabetes. In the coming years that number will grow because diabetes is not going away. If anything, it is gaining momentum. With the diligent work of the Diabetes Research Working Group, we have identified extraordinary research opportunities. We must find the means to support this research. Diabetes and it's complications are a financial drain on this country. This disease can be slowed and eventually halted, but only through research.

My mom and I made a pact after my brother Mark died. I said I would never give up. She always knew that I was a fighter and a survivor. The sad fact is that I will probably succumb to this disease at some point. Because like it or not, it's got a good track record of shortening people's lives.

For as long as I am able, I promise that I will continue to do whatever I can to stop this disease. Please make that same commitment today. We need your support, your understanding and your wisdom. The battle against diabetes can only be won if all of us work together.

☆ ☆ ☆

Testimony of Gordon Jump

Before the
Permanent Subcommittee on Investigations
of the
Senate Governmental Affairs Committee
Senator Susan Collins, Chair

October 14,1999

Madam Chair, thank you very much for this opportunity to talk about the need for significantly more research dollars for diabetes. I plan to touch on a few of the highlights of my written testimony and would ask that my testimony in its entirety be submitted into the record. With your further permission, I would also like to place into the record a formal statement from the American Diabetes Association explaining why the National Institutes of Health or NIH should increase diabetes research funding in line with the recommendations of the congressionally established, NIH appointed Diabetes Research Working Group.

About twenty years ago, I found out that I am a Type 2 diabetic; it was discovered when I was taking a routine health examination to purchase life insurance.

For the next five years I lived in a state of denial. I have come to understand that this is quite common for most diabetics. Sooner or later, however, you must come to grips with the fact that you have a chronic illness; one that is, at the very least, costly and something of a nuisance and at its worst, life-threatening because of its many complications.

When you finally acquire the gumption to take advantage of the education al programs offered by many hospitals, you will encounter a term one doesn't usually associate with a disease: MANAGE -- you must learn to manage your disease. Managing diabetes, a disease with few overt signs or symptoms, is not an easy task. Management means getting to know your body – every little signal that it gives and every change it undergoes. It means thinking about nutrition – how can something as sweet as sugar possibly be bad for you? So I eat a little too much; what's the harm? Self-discipline (a dirty word to most of us) is the most important part of disease management; for a diabetic, carefully monitoring diet, exercise, body changes and medication requires a diligence that most of us simply don't posses.

This is just the beginning; diabetes affects our lives in ways we hadn't even thought of before our diagnosis. In order simply to survive, we will have to spend money -- and lots of it – to keep the disease under control. Then the complications begin; it is then that we truly understand what a cruel and insidious affliction has taken over our lives.

We discover that diabetes isn't just a single disease to be treated – it has many tentacles that wrap themselves around various and sundry parts of our anatomy. Diabetes affects the cardiovascular

system, the nervous system, neuropathy affects your feet and legs and ultimately other parts of your body. Your eyes can be affected to the point of blindness. Lack of circulation in your limbs can cause you to require amputation.

When you are a diabetic, you are in a constant life-and-death struggle; in the case of type 2 diabetes, onset is usually at a that time of life when you are most productive. This is also the time when you are going under the most stress – climbing the corporate ladder, struggling with teenagers at home, going through a divorce, being down-sized, and maybe even going through a mid-life crisis (whatever that is). It's rather like the chicken and egg thing – which came first, the stress or the disease?

The American Diabetes Association has done a tremendous job in bringing the standard of awareness to a much higher level than it ever has been; yet, and I'm sure they would agree, the standard of awareness isn't nearly high enough. The American Diabetes Association also provides tremendous support to physicians in providing educational services on the disease and its management to their patients.

In the twenty years since I was diagnosed, I have suffered a number of health problems, several of which can be directly attributed to diabetes. For the first eight or ten years of my condition, I simply took pills, "watched" my diet, and saw my endocrinologist when I felt I should - which wasn't too often. Of course, my blood sugar was stable – at about 250! (Good blood sugar is 100 – plus or minus 5.)

By the time I acquired enough sense to seriously consider doing something to maintain my health, my health was already all bad! I had high blood pressure, four-digit triglycerides. And cholesterol numbers that would scare even an actor. Not only did I g o on insulin, but I also needed a lot of other medications – pills for my heart, high blood pressure, triglycerides, cholesterol, digestion, and on and on.

The next difficulty that I uncovered was a condition called "sleep apnea." I went to a well-known sleep clinic on the West Coast to be checked for a sleep disorder at the insistence of my wife; we were newly married at the time and the fact that I stopped breathing many times during the night upset her somewhat. The snoring didn't help either. I don't know if diabetes is a cause of sleep apnea, but many diabetics are overweight and that certainly contributes to the problem.

The problem with sleep apnea is that a closed airway doesn't allow a sufficient amount of oxygen-rich air to get to your lungs. Without enough oxygen, your heart is put under great strain. Did you ever observe that when a heart problem is suspected, the doctor puts a little electrode cap on the finger of the patient? That monitors the amount of oxygen reaching the bloodstream and ultimately the patients' heart. Even if you don't have a heart problem yet, the lack of oxygen in your bloodstream causes extreme fatigue. I used to joke about being able to sleep standing against a doorjamb until I realized my fatigue could have caused me to enter a permanent sleep while driving down the freeway.

I now have a machine that I use during sleep; I call it my "Darth Vader" mask; it covers my nose and mouth and blows air at a rate sufficient to keep my airway open. Sleeping with a contraption on my face isn't a lot of fun, but the fatigue I experience without it isn't fun either. My wife doesn't mind it a bit because I don't snore any more!

Sometimes a severe and sudden change in someone's eyes gives a physician a clue that diabetes may be the ultimate diagnosis for an individual. I've worn glasses for many years and often had to have my prescription changed; the fact that my vision was already somewhat impaired didn't prepare me for what happened about a year ago. When I awoke one morning I realized I was seeing double. After a number of tests had been made to assess the situation, I finally was fitted with glasses that made it possible for me to function. It was a frightening time for me, not knowing whether my sight would ever be restored to single vision. Vision problems, including blindness, is another of the complications of diabetes.

This past June I underwent angioplasty -- triglycerides and cholesterol had finally spoken. My blocked artery was discovered in much the same way my diabetes was – during a physical exam administered near the end of May. I flunked the stress test. I happened to be away when

the cardiologist called my wife and told her to tell me to stop taking a certain medication and to be at the hospital on Tuesday morning at 11:00 am for a heart catheter. I thought that perhaps it was just a routine part of the exam to get a closer look at something that was seen during the exam; after all, I had not had a heart attack or even any chest pains. When the doctor called my wife a second time to make sure I stopped the medication, and a third time-at ten o'clock the evening before the procedure to make sure I showed up-I began to realize the gravity of the situation.

It was not the best time for me to have a procedure that could turn into a situation that might incapacitate me for several weeks. I had a wedding to attend; my daughter was being married on June 5.

The angiogram disclosed an artery that was approximately 95% occluded; at the very least it would require a stint or angioplasty and at the worst, bypass surgery. Fortunately, while the artery's shape and placement didn't allow for emplacement of a stint, an angioplasty was successful. When Friday's wedding rehearsal rolled around, I was still quite t ired, but managed to get through it and the wedding the following day.

Being afflicted with diabetes is not something I would wish even on my worst enemy. I am blessed with excellent insurance, sufficient funds to pay what insurance doesn't cover, and I have access to the finest care. The disease is still costly in many ways: I do pay a lot for things to make my life a little simpler. For example, I buy the insulin pen that doesn't have to be refrigerated and measures the dosage precisely for me. I don't have to search for a way to keep a vial of insulin cool, risk running out of syringes or other supplies because a trip has gone over a day more than I had planned. I have to be vigilant about making sure I have a sufficient supply

of all my medications when I travel; I constantly monitor the state of my prescriptions. Eating out when I am on the road is difficult. Restaurants don't cater to healthful eating habits; portion size is not even a consideration for them and we all know how good fat and sugar taste. I try not to think about the possibility of an adverse insulin reaction, acquiring a wound that won't heal, or losing my eyesight permanently.

I have a number of friends and family who are type II diabetics. They all feel the effects of the complications of diabetes. The disease itself is generally only felt as a number of needle pricks each day. Some are lucky enough to manage with pills; of course the daily testing is not too pleasant. Somehow it just gets to be a habit-you don't think about the needle sticks any more.

My wife's nephew was diagnosed about twelve years ago. He is insulin dependent; his daily amount is 40 units of R and 20 units of N insulin. He checks his blood sugar four times a day. He is fifty-nine years old, a high school teacher who also does custom woodwork in his spare time. His mother was diabetic, but she was not diagnosed until age 70.

John's first complication was to develop extremely high blood pressure; he takes blood pressure medication and a diuretic. He also takes thyroid medication. He suffers from neuropathy in his lower extremities; twice he has suffered infections from wounds that began very small on his right foot. Both times he had to be hospitalized for three days. He required laser surgery to relieve pressure in one of his eyes. Twice he inadvertently overdosed (or mis-dosed) on insulin and paramedics had to be called. This happened because he is the kind of individual who becomes engrossed at the task at hand and forgets to eat; then when he takes his insulin he doesn't adjust for lack of food.

At this point in time, he has pretty decent insurance that covers most of his supplies and doctor visits; it covers all his hospitalizations. His current insurance doesn't cover the cost of the insulin pen; when he goes out for more than a few hours, he has to make provisions to take his supplies along. However, should he become too ill to teach before he reaches Medicare age, he will be without insurance or he will have to pay for insurance himself. In either event, he will be the financial loser.

Then there's Walter, a good friend in his early sixties. Walter's disease almost cost him his foot last year; he was hospitalized for two weeks receiving intravenous antibiotics for an infection that simply didn't want to die. His feet have been a problem for him as long as we've known him. Walter is a deeply religious man who walks the walk of his faith; one of the things he does for our church involves wearing all white clothing, including shoes. His foot problems required that he purchase custom-made shoes that would protect and support his feet; they were $600 per pair. Walter managed to buy the shoes, even the white ones. Walter retired from the Air Force, so much of his care is covered through the military, but not all of it. He worked as a chauffeur and had two young boys and a wife to support. It wasn't just the expense of the shoes and other supplies; every hour of work that he had to miss cost him dearly. He worries that he won't live

to see his boys grow up and that he won't be around to support his immigrant wife. Walter's words were always kind and his spirits always high, but his face always showed his pain.

How much money will be needed for basic research to conquer this insidious disease? How much is the disease itself costing the country in the form of Medicare, Medicaid, disability and other country, state and federal programs?

I calculated what I thought would be the cost of the most basic of diabetes supplies for an insulin-dependant, type 2 diabetic for one month. Assuming checking blood sugar only twice a day using one test strip each time for $1.34 per day, two sterile alcohol swabs at $0.16 daily, and 20 units per day of insulin at $4.20 daily, the cost of one month's basic daily supplies is $184.20. This figure also assumes that no other medications are required and it does not account for doctor visits.

I calculated what the cost of my medications would be (not including doctor, hospital, extra glasses or other devices) if I had no insurance. The cost for one month would be $733.20. Even with insurance, I manage to pay more than $200 per month; the standard co-pay for a prescription is $10. However, because of the price of some medications, the co-pay can be as much as 8 times the usual. For example, one medication (without insurance help) would cost $149.56 and another is $111.82 for one month's supply.

I think about the monetary cost of this disease and wonder how people who are struggling to live on Social Security can possible do an adequate job of caring for themselves even with Medicare. I know there are other programs that help some, but the gap is still way too wide. If it were one disease that remained as one, perhaps it would be sufficient to allow the drug companies to take their time to seek out a cure.

Diabetes takes its toll in the day to day wear-and-tear that it inflicts on the human body – in the form of heart disease, amputations caused by wounds that won't heal, eyes that lose their sight, financial burdens, and sundry other complications. The final blow it administers is the worst one – a parent with type 2 diabetes finds out that his or her child has been diagnosed with the disease and the cycle begins again.

Let's break the cycle; let's put type 2 diabetes out to pasture – with smallpox, polio, whooping cough, and diphtheria. Let's fund the research necessary to find a cure.

Respectfully submitted

Gordon Jump

Testimony
of
WILLIAM H. FULLER, JR.
Virginia Beach, Virginia
Former Professional Football Defensive Lineman
1984-1998
before the
SENATE PERMANENT SUBCOMMITTEE ON INVESTIGATIONS
Regarding
DIABETES RESEARCH
October 14, 1999

Chairman Collins and members of the Subcommittee, thank you for inviting me to testify today regarding diabetes research, an issue I deeply care about.

In 1991, I was in my fourth year of NFL football as a defensive lineman with the Houston Oilers. After playing spot duty for the first years, I was finally getting my long overdue chance at being a starter. Having played two years in the old United States Football League and three with the Oilers, I had already made more money than I could ever imagine.

This success enabled me to buy my mother and father their first house, complete with a satellite dish, after living in apartments. I was the first person in the Fuller family lineage to graduate from college. I had been married for five years and I had a beautiful wife and two young daughters. It should have been one of the better periods in my pro-football career, or life for that matter, but that was not the case, for I was seriously considering retirement.

You see, back in my hometown of Chesapeake, Virginia, a totally different story was unfolding. The people who I owed the most gratitude for my success were suffering—suffering because of diabetes. My father had Type 2 diabetes. His diabetes had already caused him to have a leg amputated, while I was in college. It also caused his kidneys to fail and he had to be hooked to a dialysis machine three days a week for three hours each visit. And now, to make matters worse, he was losing his eyesight.

At six feet three and two hundred and sixty pounds, I knew it was getting harder and harder for my mother to take care of him. She also took care of my sister who could not hear or talk as the result of a bout with spinal meningitis when she was a baby. Until I left for college on a football scholarship, it had always been just the four of us. My wife suggested I get a nurse to help her, but mom kept saying that they were fine and for me not to worry. She promised to let me know if things got too tough, but on a recent trip home a neighbor informed me that my father had fallen down in the bathroom and my mother had to call my neighbor to help get him up.

I told my father of my thoughts about quitting pro football so I could return home and help out. If he could have gotten up and punched me I think he would have. I remember it as being one of the few times I had seen my father cry. He told me how proud he was of the man I had become and that no matter what happened, to promise not to quit because of his situation. He said that my quitting football would do him more harm than diabetes ever could. We decided to get some help for my mother and I promised not to quit. A promise that was made even tougher to keep because of the Oiler's insistence that players live and train in Houston year round.

It was during that same time that I met Milton Slocum at a charity event. He informed me of his business as publicist and marketing agent for several of the Houston Rockets. We agreed to meet the next day. We met and I basically told him what I have just told you. When he asked me specific questions about diabetes, I honestly could not answer them. All I knew was that it was a horrible disease that was wreaking havoc on my father and it has something to do with the fact that his body was not producing enough insulin.

The next week Milton scheduled a meeting with the Juvenile Diabetes Foundation International. It was a meeting that would forever change my life, and I later served on JDF's International Board of Directors and currently serve on its Board of Chancellors. I walked into JDF's office as a helpless and hopeless young man with a lot of questions. I walked out with many answers to my basic questions, but more importantly, I walked out with hope—hope that research would lead to a cure.

I have learned a lot about this disease. I now know that there are over 16 million people with diabetes and that many of them are children. To watch my father suffer was very tough, but I can not imagine the pain if this disease were to attack one of my four daughters. However, over the years, I have met many parents that are dealing with this nightmare on a daily basis. I cannot imagine having to give my two-year old daughter an insulin injection or having to realize the possibilities of blindness, amputation or diabetic comas that she or any of my daughters could face for the rest of their lives.

In almost twenty years of playing college football and pro football, I've learned a lot about teamwork. I sincerely believe that the team of researchers at the National Institutes of Heath, the JDF and other organizations are on the right track to find a cure. I am proud to be a part of that team. Every team needs leaders and the Congress and the NIH—if they provide funding to support all diabetes research opportunities—have the capability of leading the way to a cure. We are ever so close to reaching our Super Bowl—A CURE FOR DIABETES. I thank you for your time and may God bless you all.

TESTIMONY FOR THE SENATE
PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

C. RONALD KAHN, M.D.
October 14, 1999

First, I would like to thank Chairman Collins and Senator Levin for giving me a chance to present the report of the Diabetes Research Working Group to the Senate Subcommittee on Investigations. As you are aware, the DRWG was created in response to House Report (105-205 and 105-635) and Senate Report 105-98 to evaluate the current state of diabetes research in the US and to develop a strategic plan for the nation as to how best to proceed and make progress against this disease. In the next few minutes, I would like to briefly summarize what the Working Group found and indicate what some of our recommendations are.

So, "What is diabetes mellitus and why is it so important?"
As I am sure most of you are aware, diabetes mellitus is not just a single disease, but a group of diseases, which have in common the presence of high blood sugar and many other metabolic abnormalities.

There are two major forms of diabetes

- Type 1 – the insulin-dependent form of diabetes, often with juvenile-onset
- Type 2 – the adult-onset form, often called non-insulin dependent diabetes, even though at least one-third of Type 2 diabetic patients take insulin.

Together, these two forms of diabetes currently affect an estimated 16 million Americans

- Over 700,000 children and young adults have Type 1 diabetes.
- As people age, diabetes becomes even more common. In fact, if we all live to be 80 (and we all hope to live to be 80), 17% of the people in this room will have diabetes.
- As a result of these two forces, about 800,000 new cases of diabetes are diagnosed each year.

In addition, there are many other forms of diabetes, some of which are rare, but others are not. For example, gestational diabetes, that is, diabetes that occurs specifically during pregnancy, affects over 5% of all women in the US who become pregnant.

Diabetes spares no one (from Avi Robbins – the 16 year-old son of my neighbor - to Nicole Johnson, the Miss America for 1999, from our grandchildren to our grandparents, from Italian Americans in Boston to Siberian Yupiks in Alaska, - all are at risk of diabetes.

Indeed, the minority populations of the US, that is the African-Americans, Hispanic-Americans, Native Americans and Asian Americans represent some of the fasting growing segments of the population and are particularly vulnerable to diabetes and its complications. For example, among the Pima Indians of Arizona, over 50% of the adults have diabetes.

Not only does living with diabetes present many day-to-day challenges, diabetes also affects virtually every tissue of the body with long-term and severe damage.

- Diabetic eye disease is the most common cause of blindness in adults.
- Diabetic kidney disease accounts for 42% of cases of end-stage renal disease and is the fastest growing cause of patients requiring kidney dialysis and transplantation.
- Stroke and heart disease are 2-4 times higher in people with diabetes, and especially increased in women.
- Diabetes affects the nervous system leading to impaired sensation, pain, slowed digestion, impotence, and other problems.
- The rate of congenital malformations in offspring of diabetic women is increased 3-4 times.
- More than half of lower limb amputations in the U.S. are secondary to diabetes.

As a result, diabetes is the sixth leading cause of death in the U.S., and the third in some minorities.

Chart 1

One of the surprising findings, even to members of the DRWG, is that since 1980, the age-adjusted death rate due to diabetes has increased by 30 %, while the death rate for other common diseases, such as stroke and cardiovascular disease, has fallen.

And least you think that these are just impersonal statistics, or that diabetes is not really that serious, I would like to point out that there five personal profiles of people with diabetes in this book which I present today. I am saddened to have to tell you that even in the few months that have passed since we began to assemble the final report, one of the individuals with diabetes highlighted in this report, Mr. Jerrold Weinberg of Detroit, has died at the age of 39 from complications of this terrible disease.

Chart 2

The next chart indicates that the economic impact of diabetes is staggering.

- The cost of diabetes to the nation is conservatively estimated at $105 billion annually, and some estimates are as high as $130 billion.
- Between 10% and 14% of all U.S. healthcare dollars are spent for diabetes.
- One of every four Medicare dollar pays for health care of people with diabetes.

Chart 3

Another striking finding of the DRWG was that while healthcare costs for each person in the US affected with diabetes average $6,560 annually, the current investment in diabetes research in only about $30 per person affected per year. That is, less than ½ of one percent of the cost of this disease is invested in R & D in attempt to reduce the burden created by diabetes. This is a small investment for a disease that affects 6 to 7% of the population and accounts for about 10 to 14% of all health care dollars.

Chart 4

With these facts in mind, the Strategic Plan created by the DRWG had multiple goals.
We must -

- Understand the causes of diabetes and its complications
- Develop methods to prevent and treat diabetes and its complications
- Reduce the impact of diabetes in minority populations
- Develop a research infrastructure and train investigators to do the necessary research
- Translate theses findings into clinical practice

In developing an approach to this plan, I took some advice from Lee Iacocca, another strong supporter of diabetes research. When we first met, I told the group, "Imagine we are in the year 2010, and would like to say what we have accomplished for diabetes." "Then given these goals, what would you have to do over the next decade to have at least a chance of accomplishing some of them." Ultimately, what came out of this approach was the 140 page Research Strategic Plan that you have before you today.

Chart 5

There are three major components of the DRWG Strategic Plan:

- Extraordinary Opportunities:
  These represent rapidly expanding and important areas of research in which increased investment or development of new approaches will significantly speed research.

- Special Needs for Special Problems:
  These are equally important, but more focused research areas usually targeted to specific populations, complications, and methodological approaches.

- Resources and Infrastructural Needs:
  A plan for increasing research manpower, technology and other infrastructure elements for diabetes research.

In all, the Plan contains a total of 88 recommendations in 16 different categories.

Let us briefly look at a few of these:

Perhaps one of the most exciting areas in all of research today is the "Genetics of Diabetes and Its Complications." If we identify the genes for diabetes and its complications, we may some day be able to predict and prevent the disease. Understanding the genetics also will give us the opportunity to develop new therapies that are directed at the true central problem of the disease.

The DRWG proposes several initiatives in the area of genetics, including creation of a new National Consortium for the Study of the Genetics of Diabetes. One of the goals of this Consortium would be the development of a diabetes DNA chip. This is a DNA Chip that we are using in my own laboratory to

begin to identify some of the genes which might be altered in diabetes. With the proper investment in research, within a decade a diabetes chip could be developed that, when exposed to DNA from a few drops of blood, will tell us who is likely to develop diabetes, which of our diabetic patients are most likely to develop complications, and who will respond to each specific treatment approach.

A second area is "Autoimmunity and the Beta Cell." This holds the key to Type 1 Diabetes, since type 1 diabetes is an autoimmune disease that destroys insulin-producing β-cells. Important Progress has been made in this area over the past several years, including

- Identifying some of the major genes predisposing to Type 1 diabetes and the components of the beta cell that are attacked
- Developing markers for detection of pre-diabetes
- Demonstrating the critical importance of "tight" control of blood glucose for reducing complications (DCCT)

But there remain many challenges which are critical if we are to conquer this disease. The DRWG report, therefore describes a program to

- Intensify research to understand the immunological basis of Type 1 diabetes
- Develop optimal strategies for blocking immune destruction of beta cells, including both pre-clinical and clinical studies
- Expand research on Transplantation as therapy for Type 1 diabetes. This requires solving critical issues, such as

  ⇒ How are we going to get enough islet cells to treat hundreds of thousands or millions of patients who could benefit from this treatment?
  ⇒ How can we protect the transplanted cells from immunologic rejection?

Other Extraordinary Opportunities include research in "Cell Signaling and Cell Communication" which we believe hold the key for Type 2 diabetes, "Obesity" and the area of "Clinical Research and Clinical Trials" to develop proper evidence based approaches to this disease.

The DRWG has also made special recommendations regarding research into the "Eye, Kidney and Nerve Complications," as well as the "Cardiovascular complications" which are the major killer of people with diabetes. In these areas, we must:

- Define why and how diabetes enhances the atherosclerotic process and other diabetic complications
- Determine why women with diabetes lose their vascular protection
- Identify factors in the heart that lead to increased mortality after a heart attack and develop new therapies to enhance survival
- Develop specific, noninvasive techniques to identify the presence of diabetic complications, predict their progression and assess the response to therapy.

We also describe research programs to better understand the "Impact of Diabetes in the Young and Old, in Women, and in Minority Populations" where there is a need for more basic research, as well as culturally sensitive approaches to applied clinical research.

Chart 6 BUDGET RECOMMENDATIONS

As I have already indicated, the current investment in research is small, and indeed far too small to provide the resources needed to begin to address the research plan.

As requested by Congress, therefore the DRWG has developed budgetary recommendations to accompany this plan. You will see that these recommendations call for five-year step up in the research budget for diabetes from the current level of $443 million to $827 million for the year 2000 rising to $1.6 billion by the year 2004.

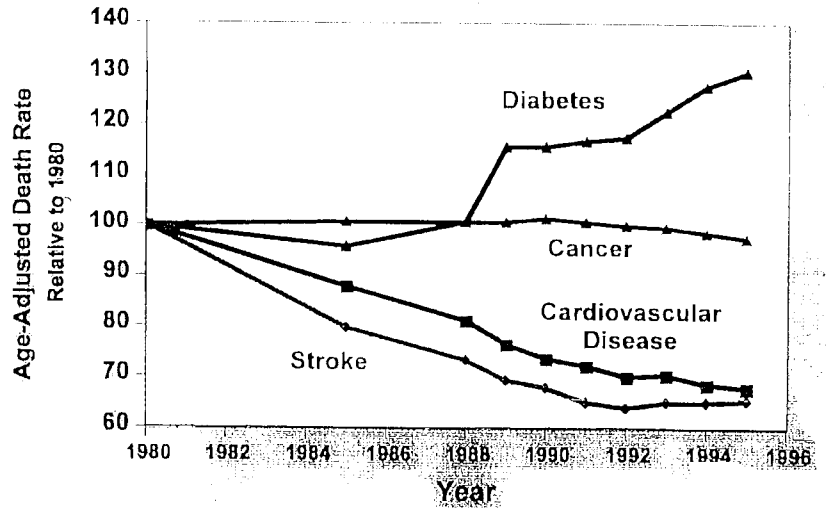
Let me point out to this Committee that these numbers are not arbitrary. They are based on a detailed planning process and what is realistically needed to bring diabetes research to a point where there would, at least be a chance that we could accomplish some of the goals we have set forth over the next ten years.

In the full report, this budget is detailed with project-by-project and Institute by Institute recommendations.

I would also like to point out that the members of the DRWG do not believe that diabetes research should be funded by taking resources from other important biomedical research needs. The DRWG is strongly supportive of the NIH, the Director of NIH, Dr. Harold Varmus, and the Director of NIDDK, Dr. Philip Gorden, and recognize the many challenges which must be faced in utilizing these precious resources. Like the military, however, which must be prepared to fight a battle on at least two fronts, the NIH and the biomedical research community must be prepared to fight the battle of human disease, not just on two fronts, but on many fronts at once - and this will require a significant investment, both immediately and in the long term.

The DRWG is convinced that there is both great urgency and unprecedented opportunities in diabetes research. The DRWG is also convinced that taking action now will save thousands of men, women and children from the severe consequences of diabetes, and save the nation billions of dollars in medical care and lost productivity. We have done the first part of our job by developing the comprehensive plan for diabetes research that you requested. We present this report to you and ask now for your support in going to the next phase – by allowing us to do the research that will be required to conquer this dread disease.

Increasing Deaths Due to Diabetes



Source: U.S. National Center for Health Statistics

DIABETES RESEARCH WORKING GROUP

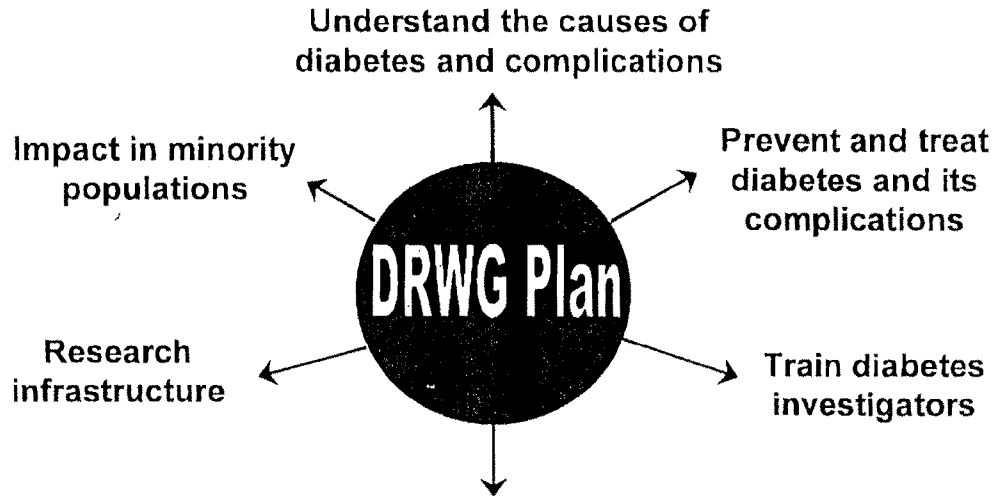
The Economic Impact of Diabetes is Staggering

- The cost of diabetes to the nation is over $105 billion annually.
- Between 10% and 14% of all U.S. healthcare dollars are spent for diabetes.
- One of every four Medicare dollar pays for health care of people with diabetes.

DIABETES RESEARCH WORKING GROUP

10/7/99

Goals of the DRWG Plan



10/7/99

Components of the DRWG Strategic Plan

EXTRAORDINARY OPPORTUNITIES

- Genetics of diabetes and its complications
- Autoimmunity and the beta cell
- Cell signaling and cellular regulation
- Obesity
- Clinical Research and Clinical Trials of Critical Importance

SPECIAL NEEDS FOR SPECIAL PROBLEMS

- Micro- And Macrovascular Complications
  - Diabetic Nephropathy
  - Diabetic Retinopathy
  - Diabetic Neuropathy
  - Diabetes and Macrovascular Disease
  - Oral Complications Of Diabetes
- Methods To Optimize Glucose Control
- Genetic Engineering
- Diabetes in Minority Populations
- Diabetes In Women, Children And The Elderly
- Diabetes And The Environment
- Behavioral And Health Services Research

RESOURCES AND INFRASTRUCTURE

- Human resource needs
- Infrastructural Needs
- Taskforces for review, planning, and technology

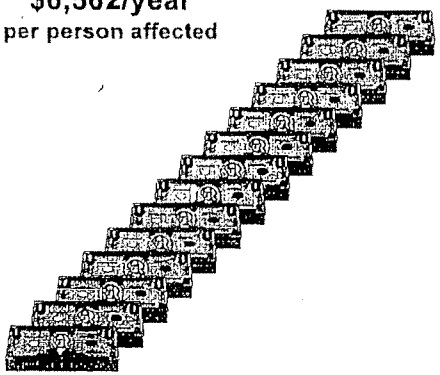
DIABETES RESEARCH WORKING GROUP

THE ECONOMICS OF DIABETES

[redacted]

[redacted]

$6,562/year
per person affected



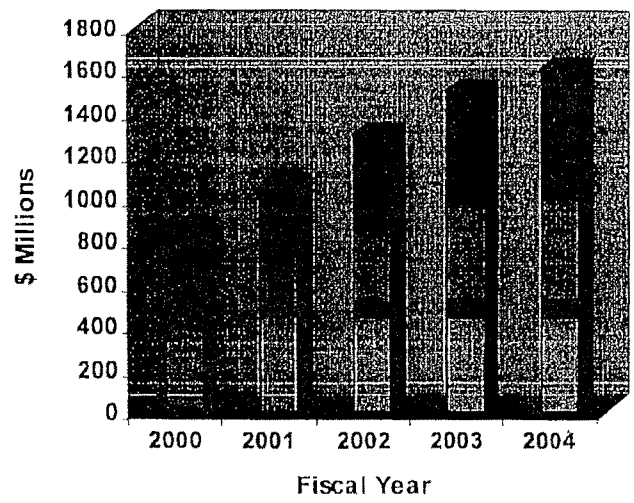
$30/year
per person affected

[redacted]

DIABETES RESEARCH WORKING GROUP

10/7/99

BUDGET RECOMMENDATIONS



DIABETES RESEARCH WORKING GROUP

MEMORANDUM

TO: Senator Susan M. Collins

FROM: Edward H. Leiter, Ph.D., Senior Staff Scientist
The Jackson Laboratory
Bar Harbor, ME 04609

Date: October 6, 1999

Re: Statement to the Committee Regarding Scientific Opportunities in Diabetes Research

I have been a member of the Research Staff of The Jackson Laboratory in Bar Harbor, Maine, for the past 25 years. The Jackson Laboratory, located on the rocky coast of Maine, is a world leader in mammalian genetics. My work has concentrated on the development and characterization of mouse models for the study of type 1 (insulin dependent) and type 2 (non-insulin dependent) diabetes in humans. The fact that diabetes occurs in different forms means that it is a complex disease. Despite the genetic complexity underlying the development of diabetes in an individual, either type 1 or type 2, the terrible secondary complications that arise from diabetes are common--kidney failure, heart disease and stroke, blindness, and loss of limbs. My interest in conducting research on both forms of this devastating disease is based upon my personal family history. My grandfather had type 2 diabetes, and his son, my uncle, Frank Black, of Los Angeles, California, has been struggling valiantly with his type 1 diabetes since he was first diagnosed in 1942. He was one of the first recipients of the insulin pump, a device that provides only therapy and not a cure. It is my concern for my uncle, and for the millions of other Americans who now suffer from diabetes, or will develop diabetes, that leads me to appear before you today.

We now know that most cases of type 1 diabetes in humans presents an autoimmune disease wherein a "rogue" immune system escapes from its normal control and attacks the body in which it resides. We have an excellent mouse model for autoimmune type 1 diabetes. It is the NOD mouse. Research support from the National Institutes of Health, the Juvenile Diabetes Foundation, International, and the American Diabetes Association has enabled myself and other investigators throughout the United States to understand the genetic and environmental requirements for this little animal's immune system to become autoaggressive against the insulin-producing beta cells in the

207-288-6000
600 Main Street
Bar Harbor, ME 04609-1500

pancreas. Cells of the immune system called T lymphocytes invade the pancreas and destroy the insulin-producing beta cells. However, the genetic program that sets the insulin-producing beta cells up for the destructive "hit" by the T lymphocytes is expressed at another level of the immune system. Immune cells called antigen presenting cells should be educating the T lymphocytes to leave the mouse's insulin-producing beta cells alone. However, in NOD mice, this education is impaired. But one of the most important lessons we have learned from the NOD mouse model is that this genetic program is not immutable such that autoimmune diabetes is a preventable disease. The "rogue" immune system can be contained by many different environmental stimuli during the prediabetic phase so that diabetes is prevented or diabetes onset is greatly retarded. It was this finding, along with similar scientific discovery in another rodent model, called the BB rat, that clinical researchers, working through the aegis of the National Institutes of Health, are now engaged in clinical trials to prevent type 1 diabetes from developing in individuals at high risk. One of the most exciting developments in my laboratory comes from genetic analysis of a close relative of the NOD mouse. Based upon a genetic scan, this mouse has the "right" program to develop type 1 diabetes. But why doesn't it do so? The answer seems to be that the insulin-producing beta cells of this mouse are incredibly resistant to immune-mediated insult. With support from the American Diabetes Association and The Juvenile Diabetes Foundation, International, we are working hard to identify the factor that is protecting these insulin-producing beta cells. We hope that our findings can be extrapolated to make human islets more resistant to damage by a "rogue" immune system.

Of equal importance in my research are the mouse models for obesity and type 2 diabetes. In this type of diabetes, the immune system is not at fault. Rather, a collection of different genes regulating glucose and fat metabolism are not working well together. The consequence often is that the body fails to respond normally to insulin; obesity develops, and the insulin-producing beta cells of the pancreas become overworked. I am constructing new mouse models of type 2 diabetes that exhibit these pathologies. We are identifying genes in different strains of mice that predispose them to what is termed "impaired glucose tolerance", a clinical phase in the development of type 2 diabetes. We then take these separate genetic liabilities, and by selective breeding, combine them into new strains of mice. These new strains not only develop impaired glucose tolerance, but transit into overt diabetes. Such new models are of tremendous importance in the testing of pharmaceuticals to be used in the treatment of human type 2 diabetes. For example, these mice are helping us to identify genetic targets that respond favorably to a given pharmaceutical agent, as well as identifying the genetic make-up of individuals that would suffer adverse side effects if treated with an anti-diabetes drug.

I would like to end my remarks with some thoughts about the recommendations made to the Congress by the Diabetes Research Working Group. Obviously, as a recipient of NIH funding to do my own diabetes research, and having participated in the development of the Diabetes Research Working Group recommendations, I am biased in my hope that the recommendations could be implemented by NIH. Although considerably more NIH funds have been designated for diabetes-related research in the past year than ever before, the research dollars allocated are inadequate to fund all the meritorious investigator-proposed grant applications in the areas identified by the Diabetes Research Working Group. I have personally served on peer-review panels evaluating diabetes research, and have observed that the competition for grant funding today is so stringent that many scientific avenues that could be explored are not being explored. I am absolutely convinced that if Drs. Frederick Banting and Charles Best, the discoverers of insulin, were to apply for an NIH grant today, offering only their interesting hypothesis that the pancreas made a substance that controlled blood glucose, and offering their surgical expertise and an animal model system to test this hypothesis, their proposal would not be funded. Why would it not be funded? The answer is that with the National Institutes of Health's rather limited resources devoted to diabetes research, only those investigators receive funding who can demonstrate with preliminary studies that the hypothesis they are proposing to test is correct. This review process assures the Congress and the American taxpayers that NIH monies are being wisely spent. However, it also means that the process of scientific discovery, which entails considerable trial and error, and often, even serendipity, on the path to "eureka" is not being promoted to its fullest extent. Thus, progress on the path to better therapies and an eventual prevention of diabetes is not as rapid as it might be if all the Diabetes Research Working Group recommendations could be implemented.

So, in closing, let me thank the committee and especially the Senator from my own State of Maine, Senator Collins, for inviting me to testify. We are now in an unparalleled age of discovery in molecular genetics in mice and in humans. The human genome project, which the Congress has so wisely supported, will provide a genetic "blueprint" on which a massive structure of new knowledge can be built. This new knowledge will certainly contain the key to new therapies not only to control diabetes, but more importantly, to identify individuals at risk to develop diabetes, and thereby permit interventions to prevent diabetes from happening. This is a reality now in my mouse models. Let us work to make it a reality in the human family as well.

Testimony

Presented by

Jeffrey A. Bluestone, Ph.D.
Director, Ben May Institute for Cancer Research, University of Chicago
Director, Collaborative Network for Clinical Research on Immune Tolerance and the
JDFI Center for Islet Transplantation at the University of Chicago and University of Minnesota

Before the

Senate Permanent Subcommittee on Investigations

Regarding

Diabetes/Immune Tolerance Research

14 October 1999

Good morning Chairman Collins and other members of the Subcommittee. My name is Jeffrey Bluestone and I am Chair of the Committee on Immunology and Director of the Juvenile Diabetes Foundation Islet Transplant Center at the University of Chicago and the University of Minnesota. I am addressing you today on behalf of my scientist and clinician colleagues whose continued pursuit of a cure for diabetes and many other debilitating autoimmune diseases depends heavily on the federal government's efforts to support basic and clinical research. In my short presentation here, I hope to impart to you, my personal sense of optimism that, with your continued and enhanced support, we have indeed turned a corner in the fight to conquer autoimmune diseases, such as Type 1, or juvenile, diabetes. I would also like to share with you just a few of the reasons behind my optimism.

The research in my laboratory focuses on the study of the basic processes of the immune system. Our particular emphasis is on the study of organ transplantation and autoimmune diseases. Our research goals are to empower clinical researchers to apply the basic research discoveries to the development of novel approaches to treating immune disorders.

For instance, my laboratory has worked to develop new approaches that would allow the transplantation of pancreatic islet cells—the cells that are destroyed in Type 1 diabetes patients—to restore normal insulin production in the body without the debilitating effects of current drug therapies. Unlike the daily regimens of insulin injections that individuals with diabetes are currently dependent upon, islet transplantation offers the hope of a true cure for diabetes. We are now refining methods of isolating islet cells from healthy donors, of assessing their suitability for transplant, and of transplanting pancreatic islets into Type 1 diabetes patients. I believe we are rapidly approaching the point where islet transplantation will become a routine clinical procedure.

Despite this progress, however, islet transplantation still offers only the *hope* of a cure. The destruction of islet cells by an overzealous immune system, the cause of Type 1 diabetes in the first place, continues following transplantation, and results in the subsequent destruction of the transplanted cells and a return to insulin dependence. The procedure is further complicated by the body's immune response, which naturally rejects foreign tissues. The result is that, right now, most transplants last less than a year. If we are to solve the remaining problems in islet transplantation, we must continue to investigate the basic elements of the immune response that is responsible for diabetes and for transplant rejection.

T cells are the body's front line of defense in disease prevention. They normally seek out and destroy foreign invaders like bacteria, viruses, and unfortunately, transplanted tissues. When they malfunction, they may also seek out and destroy the body's own tissues, causing autoimmune diseases like lupus, rheumatoid arthritis, and Type 1 diabetes.

Normally, T cells are trained to recognize foreign invaders by what resembles a lock-and-key mechanism. Receptors found on the surface of T cells act as a lock; the invader's key takes the form of molecules on its surface known as "antigens". When the right key is fitted into the lock, the T cell can become "activated", beginning a sequence of events that causes the immune system to seek out and destroy all other cells with similar keys, or antigens. In diabetes, the defective T cells recognize keys known as autoantigens – molecules found on the body's own tissues.

Over the last two decades, scientists have made important strides in treating transplant rejection. A series of immunosuppressive therapies designed to stem the tide of T cells directed against the transplants have revolutionized the fields of kidney and liver transplantation. These immunosuppressive drugs work exactly as advertised—they completely suppress the immune system. Unfortunately, treatment with these drugs is akin to using a shotgun just to get rid of a fly. This shotgun approach suppresses the entire immune system, not just the cells causing the autoimmune disease or graft rejection. In the process of suppressing the T cells that cause the islet cell rejection, good parts of the immune system that protect us from infection and cancer are adversely affected. Moreover, many of the current immunosuppressive drugs are "toxic", or poisonous, particularly to pancreatic islet cells. Therefore, the present challenge for researchers in islet transplantation is to induce a state of "immune tolerance," where only the immune cells responsible for the islet cells' demise are suppressed, and where the good, disease and infection-preventing cells are spared.

Very recently, efforts to selectively interfere with this lock-and-key mechanism have shown early signs of success. Although it has been difficult to determine the precise shape of the lock on the harmful T cells because the number of shapes is endless, more specific drugs have now been developed that target only the autoimmune T cells. We have discovered that T cells have more than one lock. We now know that antigen is not enough to activate T cells—that a second key, a "costimulatory signal" is needed in order for T cells to become activated. Just like a double-locked front door, both keys are needed to get in. What is so intriguing about this second lock, or receptor, is that they are the same from person to person—that is, the same keys, or signals, are at work in different people. A therapy that interferes with this signal could work in everyone.

This clearer understanding of the regulation of our immune system has resulted in the development of several promising new drugs aimed at inducing a state of immune tolerance. The treatments have been designed to interfere with the receptors (locks)—much like putting a wad of bubble gum into a lock—to prevent the key from being inserted. The T cells, which have already detected an autoantigen, never receive the second signal and therefore cannot continue on their destructive way. In effect, they die waiting. The new drugs, successfully used in pre-clinical studies in mouse and monkeys, have fundamentally changed our approach to the induction of immune tolerance.

It was these exciting new approaches to the treatment of immune disorders that led the NIH and JDF to fund a bold, new initiative—The Immune Tolerance Network (ITN). Over the next seven years, the ITN (which I am fortunate to lead) will conduct

clinical trials of new tolerance therapies in autoimmune diseases, allergy & asthma, and islet and kidney transplantation at clinical sites across the country—and the world. It is medical science on a remarkable scale - a combined and concerted effort led by over 70 of the world's top clinicians and immunologists interested in tolerance. The National Institutes of Allergy and Infectious Diseases, in collaboration with the Juvenile Diabetes Foundation and the National Institute of Diabetes and Digestive and Kidney Diseases, has committed over $140,000,000 to the effort. It is a testament to the confidence of the clinical research community that we are indeed close to altering the course of immune-mediated diseases.

It bears emphasizing that the exciting clinical opportunities we see today are a reflection of the much deeper understanding of our immune system that has been generated by fundamental research discoveries. Often overlooked are the basic discoveries that reveal central processes at work in diabetes and other autoimmune diseases. It is this basic scientific research that continues to be the engine that drives our progress towards eliminating diabetes.

Moreover, basic research has a much broader impact than is apparent at first glance. The fundamental immune processes at work in diabetes, and in islet transplantation rejection, are the same fundamental processes that lie at the heart of numerous other common afflictions. Lupus, Rheumatoid Arthritis, asthma, allergy, kidney transplantation, psoriasis. Even cancer. Research that leads to successful islet transplantation promises therefore, not only to eliminate diabetes, but to alter the course of literally dozens of diseases affecting millions of Americans.

There is no doubt that the recent scientific developments represent remarkable progress in our understanding of human disease and have yielded new tools with which we may now take a fresh approach to the treatment of diabetes and related diseases. But, it is not simply scientific achievement that has fueled my hopefulness. Indeed, much of my optimism lies in the new opportunities that have been created to capitalize on these discoveries. Initiatives like the Immune Tolerance Network are symbolic of the Congress' new understanding that the innovative efforts by our research scientists must be partnered with forward thinking clinical research. Such efforts reflect very real and very positive changes in the nature of health research. Yet, as our understanding of the biological bases of disease continues to expand, increased levels of funding are necessary to ensure that we continue to create new knowledge and exploit it to its fullest extent. Only in this way will our past investments in basic research fully mature into improvements in public health.

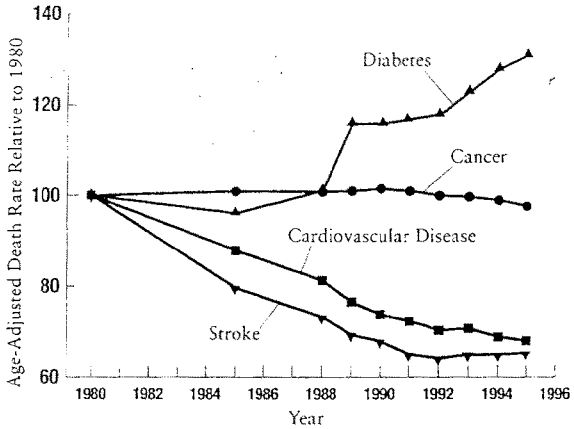
In particular, I urge Congress and the NIH to implement the recommendations of the Diabetes Research Working Group. If we can ensure that all diabetes research opportunities are sufficiently funded, we will be able to help millions of Americans avoid further suffering from diabetes and other devastating illnesses. I sit before your committee full of enthusiasm and optimism. I am confident that fifty years from now, when we look back to the turn of the century, it will not be remembered as a time when we argued over the management of our public health system. It will be regarded as an era of discovery and innovation—a golden age of biology that marked the beginning of the end for so many diseases. And, like the industrial revolution, the biological revolution will be remembered as a time of innovation and discovery when diseases like diabetes are only a memory.

Thank you.

Senate Permanent Subcommittee
on Investigations

EXHIBIT # 1

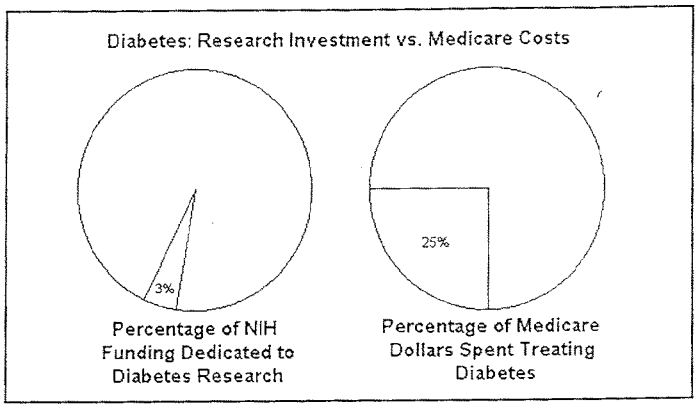
Increasing Deaths Due to Diabetes



Source: U.S. National Center for Health Statistics

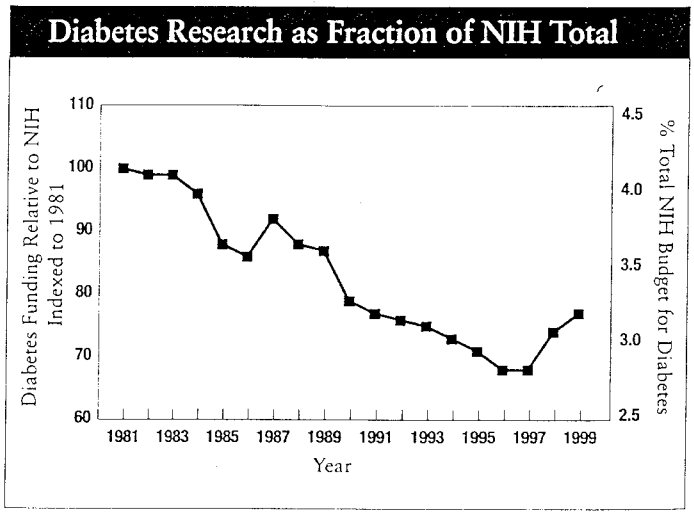
Senate Permanent Subcommittee
on Investigations

EXHIBIT # 2



Senate Permanent Subcommittee
on Investigations

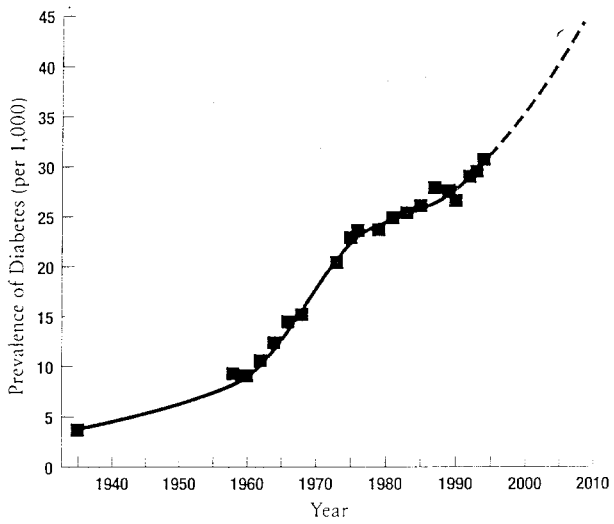
EXHIBIT # 3



Senate Permanent Subcommittee
on Investigations

EXHIBIT # 4

Rising Prevalence of Diabetes in the U.S.



Source: Modified from *Diabetes in America*, 2nd Ed.

Senate Permanent Subcommittee
on Investigations
EXHIBIT # 5

free copies of DIABETES DIGEST now
Please click here!

The Family's Guide To Diabetes

http://diabetes.cbyc.com/

Visit The Diabetes Bookstore!
*more than just diabetes books!
*an affiliate of barnesandnoble.com!
*5% funds this site!

DiabetiChat chatroom Discussion bulletin board

TOPICS

Ketones Hypoglycemia Foods Orthodontics Hyperglycemia School And Diabetes My Poem:"Hypoglycemia" Halloween! When I'm Cured... Could You Be Diabetic?

FEATURES

The JDF Children's Congress Feature!
The Pump Feature! Diabetes Bookstore! DiabetiChat! Diabetes Discussion! Guest Article:Young Children

SITE INFO

Disclaimer Feedback! NEW: Media / Awards Diabetes Resources On The Internet

The Family's Guide To Diabetes Poll!

Q: If you are a Type I diabetic, at what age were you diagnosed?

- 0-5 Years
- 6-10 Years
- 11-15 Years
- 16-20 Years
- 21+ Years

View Results

Past Poll Results

What's New?

- **Recent Happenings:** Wow! I recently returned from The Juvenile Diabetes Foundation's Children's Congress in Washington, D.C. which was a great experience! I am working on a HUGE feature on it, and so any delegates or their families with pictures I can use, please email me at diabetes@cbyc.com! You can see the first few sections of this feature now, by clicking here. Also, I am in the preliminary stages of redesigning this site, have any ideas? Let me know by emailing diabetes@cbyc.com. Thanks!
- **About the Webmaster:** Hi! My name is Ryan Dinkgrave. I am 16 years old and I am the editor and webmaster of *The Family's Guide To Diabetes*. Thanks again for visiting the site!
- **Diabetes Bookstore:** Be sure to visit our new Diabetes Bookstore, an affiliate of Barnesandnoble.com, where 5% of your purchase will fund The Family's Guide To Diabetes, and make it better! **NEW DESIGN AND FEATURES FOR BOOKSTORE COMING SOON!**
- **LINKS:** I have recently introduced a new links section, and I am adding other diabetes sites only when a link is requested by the site administrators. If you are the administrator of a diabetes site that you wish to have added to my links page, please email me at diabetes@cbyc.com. Thanks!
- **Interact!!!** Talk with other diabetics in our **chat room** through TalkCity (Sign up here for free!). Or, post questions, and maybe answers, on our **bulletin board!**
- **Diabetes Awareness Stamp:** The Juvenile Diabetes Foundation International (JDF) is spearheading a national campaign to procure a Diabetes Awareness U.S. Postage Stamp. You can make diabetes a national priority, and help "stamp" out diabetes, by clicking here!
- **In Search Of A Gray Ribbon:** If you know where a good gray ribbon image is available, one which I can use on this site, please email me at diabetes@cbyc.com. Thanks!

Search This Site!

GO!

This Site The Web

Get your own free Search Engine

Send E-Mail

Netscape Now!

advertise on this site!

email the webmaster:
diabetes@cbyc.com

Medinex

Home E-Mail Feedback Disclaimer

© 1996-1999 diabetes@cbyc.com

TRATEGIC PLAN FOR THE 21ST CENT

Summary

of the Report and

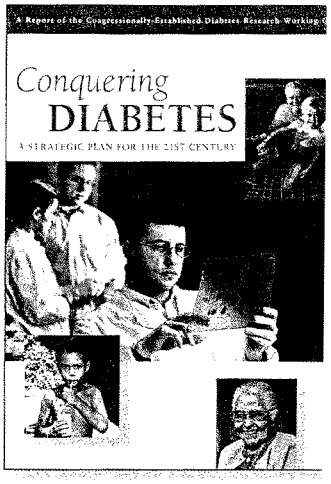
Recommendations of

the Congressionally-

Established

Diabetes Research

Working Group



TRANSMITTAL TO THE CONGRESS

In accordance with directives from the House and Senate Appropriations Committees, I am pleased to transmit to the Congress the summary of the Strategic Plan for NIH-funded diabetes research developed by the congressionally-established Diabetes Research Working Group.* As specified by the Congress, this Research Plan includes recommendations for future diabetes research directions and corresponding overall budget estimates for implementing the proposed new research initiatives.

The Diabetes Research Working Group is an independent panel composed of twelve scientific experts in diabetes and four representatives from the lay diabetes community. In developing its Strategic Research Plan, the Working Group held plenary meetings and subcommittee discussions, analyzed the existing NIH diabetes research portfolio, sought the expertise of *ad hoc* scientists, and enlisted public commentary. The Diabetes Research Working Group believes that the culmination of this year-long, in-depth planning process is a set of recommendations that will be of value to the Congress and to the NIH.

Clearly, the congressional action calling for the establishment of the Diabetes Research Working Group and the development of its Research Plan reflects the strong and continuing commitment of the Congress to conquering diabetes. The implementation of the research initiatives recommended in this Strategic Research Plan is the next vital step toward attaining that objective.

C. Ronald Kahn, M.D.
Chairman
Diabetes Research Working Group

*Note: The congressional directives calling for the establishment of the Diabetes Research Working Group and the development of its Strategic Research Plan can be found in Senate Report 105-58 (1998, p. 76, p. 110), House Report 105-205 (1998 , p. 69, p. 98) and House Report 105-635 (1999, p. 69). The charge to the Diabetes Research Working Group called for the development of a comprehensive plan for all NIH-funded diabetes research efforts, including the recommendation of future diabetes research initiatives and directives. Congressional language specifically asked the Working Group to include overall cost estimates to accomplish its recommendations in the final research plan.

This Strategic Research Plan for diabetes research funded by the National Institutes of Health has been developed by an independent, congressionally-established Diabetes Research Working Group, with input from diabetes investigators, diabetes patients, and other members of the broad diabetes research community. The Working Group is composed of scientific and lay experts external to the National Institutes of Health, as well as leaders of major diabetes voluntary organizations. The views, conclusions, and recommendations expressed in this document are solely those of the members of the Diabetes Research Working Group and do not necessarily reflect the positions or judgments of the National Institutes of Health, the Department of Health and Human Services, or the Administration, which must weigh the competing requirements of multiple programs and activities. (NIH Publication No. 99-4398)

DIABETES RESEARCH WORKING GROUP

Art/Photo Credits
The photographs in this document are not available for republication and may not be reproduced in either print or electronic format without the express written consent and permission of the photographer.
Cover: Robert Reichert *(Center)*, Mark Tuschman *(Top right)*, American Diabetes Association, Honolulu *(Lower left)*, Bristol-Myers Squibb *(Lower right)*
Page 4: Peter F. Kador, National Eye Institute

The Challenge

Sixteen million people in the United States have diabetes mellitus. In both human and economic terms, it is one of our nation's most costly diseases. Diabetes is the leading cause of kidney failure, blindness in adults, and amputations. It is a major risk factor for heart disease, stroke, and birth defects, shortens average life expectancy by up to 15 years, and costs the nation in excess of $100 billion annually in health-related expenditures. At present, more than one of every ten health-care dollars and about one of every four Medicare dollars are spent on people with diabetes. Over the next decade these numbers will grow as the number of people afflicted by diabetes continues to increase at an accelerating rate. At present, there is no method to prevent or cure diabetes, and available treatments have only limited success in controlling its devastating consequences.

This problem is made more complex by the fact that diabetes mellitus is not a single disease, but occurs in several forms, and has complications that affect virtually every system of the body. The most common forms are Type 1 (insulin-dependent) diabetes, which usually starts in childhood or adolescence, and Type 2 (non-insulin dependent) diabetes, which typically affects adults and increases dramatically with age and obesity.

Congress has clearly recognized the gravity of diabetes through the establishment of a bipartisan Diabetes Caucus and has concluded that the only way to reduce the tremendous burden of this disease is through intensified biomedical research. Over the past three years, Congress has emphasized diabetes research in funding increases provided to the NIH and through other special initiatives. Realizing the critical need to build upon these important steps, the Congress directed the establishment of the Diabetes Research Working Group (DRWG) and charged it with developing a comprehensive plan for diabetes research. This plan is intended to help increase the effectiveness of NIH-funded diabetes research and find solutions to the extremely serious problems posed by this disease. During 1998, the DRWG and its subcommittees held a series of meetings, consulted with a wide range of experts in the field, and heard public commentary. It evaluated all aspects of the diabetes problem in an effort to develop a comprehensive plan for submission to the Congress. This document summarizes the Strategic Research Plan of the Diabetes Research Working Group.

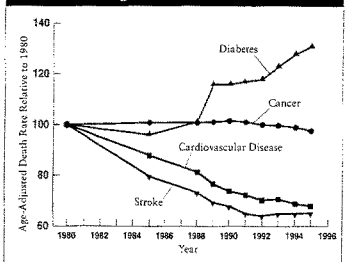
Based on its extensive review and deliberations, the DRWG recognizes both great urgency and unprecedented opportunities in diabetes research. The seriousness of the disease and the widespread problems associated with it demand accelerated and expanded research programs, not only to discover the means to prevent and cure diabetes, but also to develop better and more effective treatment strategies. Meeting these challenges requires a well-thought-out and continuously updated research plan; a cadre of talented researchers and physician-scientists; a supportive infrastructure; and appropriate budgetary resources. The DRWG is convinced that taking action now to increase significantly NIH support of diabetes research will save many thousands of men, women and children from the severe consequences of a dangerous, often disabling and potentially even fatal illness, and will also save the nation many billions of dollars in medical care and lost productivity. From both human and scientific perspectives, now is the time for the United States to move swiftly and decisively to begin to ensure a future for America without diabetes.

Magnitude of the Problem

The magnitude of the problem created by diabetes is clearly defined by a few simple facts:

- **Diabetes currently affects an estimated 16 million Americans, and about 800,000 new cases are diagnosed each year.**
- **Diabetes spares no group—attacking men, women, children, the elderly and people from every racial background.**
  - African, Hispanic, Native and Asian Americans, some of the fastest growing segments of the U.S. population, are particularly vulnerable to diabetes and its most severe complications.
  - Diabetes strikes both ends of the age continuum. Children and young adults with Type 1 diabetes face a lifetime of daily insulin injections and the possibility of early complications whose severity will likely increase with duration. Elderly diabetics are frequently debilitated by multiple complications.
- **Diabetes affects virtually every tissue of the body with long term and severe damage.**
  - Diabetic eye disease (retinopathy) is the most common cause of blindness in working age adults.
  - Diabetic kidney disease (nephropathy) accounts for 42 percent of new cases of end-stage renal disease, and is the fastest growing cause of kidney dialysis and transplantation (over 100,000 cases per year).
  - Nervous system damage (neuropathy) affects over 60 percent of diabetics, causing impaired sensation or pain in the feet or hands, slowed digestion of food in the stomach, impotence, and other problems.
  - More than half of lower limb amputations in the United States occur among people with diabetes. From 1993 to 1995, about 80,000 amputations were performed each year on people with diabetes.
  - Heart disease death rates in adults with diabetes are about 2 to 4 times those of people without diabetes. Premenopausal women lose their protection from heart disease and have even more markedly increased risk.
  - High blood pressure affects over 60 percent of people with diabetes. As a result of the combination of hypertension and diabetes the risk of stroke is increased 2 to 4 times.
  - Pregnancy related problems confront diabetic women. The rate of major congenital malformations and death of the fetus and newborn are increased 3 to 4 times.
  - Higher rates of infection, periodontal disease, and many other problems occur in people with diabetes.

Increasing Deaths Due to Diabetes



Source: U.S. National Center for Health Statistics

- **Diabetes is the sixth leading cause of death due to disease in the U.S., and the third leading cause in some minority groups.**
  - Since 1980, the age-adjusted death rate due to diabetes has increased by 30 percent while the death rate has fallen for other common multifactorial diseases, such as cardiovascular disease and stroke.
  - Life expectancy of people with diabetes averages 10 to 15 years less than that in the general population.
- **The economic impact of diabetes is staggering.**
  - The cost of diabetes to the nation is over $105 billion annually.
  - More than one of every ten U.S. healthcare dollars is spent for diabetes.
  - One of about four Medicare dollars pays for health care of people with diabetes.

The Federal Investment in Diabetes Research

Reducing the tremendous health and human burden of diabetes and its enormous economic toll depends upon identifying the factors responsible for the disease and developing new methods for treatment and prevention. These advances can only occur through increased biomedical research. Although Federal support for diabetes research has produced a number of major advances in the past two decades, many scientific opportunities are not being pursued due to insufficient funding, lack of appropriate mechanisms, and a shortage of trained researchers. Improvements in technology and the general growth in scientific knowledge offer unprecedented opportunities for advances that might lead to better treatments, prevention and possibly cure. Unfortunately, the current funding, level of effort, and scope of diabetes research fall far short of what is needed to capitalize on these opportunities.

The U.S. Government, through the National Institutes of Health (NIH), will spend an estimated $443 million in FY 1999 on diabetes-related research. While this amount has steadily increased since 1981, there is unanimous agreement in the DRWG that this funding level is far short of what is required to make progress on this complex and difficult problem. In fact, the current federal budget for diabetes research represents less than one-half of one percent (0.5 percent) of the annual cost of diabetes to the U.S. economy. When compared with the 5 to 15 percent budgets for research and development in other high-technology sectors, the investment in diabetes research is trivial.

Meeting the challenges posed by diabetes requires investment of additional resources to conduct the needed research and a well-conceived, comprehensive research plan for its effective use. This Plan by the DRWG is the first step in this direction.

The Federal Investment in Diabetes Research

- Represents about 3 cents out of each dollar, that is about 3 percent of the NIH research budget. Although there is no accepted method for determining appropriate levels of research funding, this is clearly a small investment for a disease that affects 6 to 7 percent of the population and accounts for more than 10 percent of all health care dollars.
- The proportion devoted to diabetes research, relative to the whole NIH budget, has decreased by more than 30 percent since 1981, at a time when the death rate due to diabetes has increased by 30 percent.
- Represents only about $30 per person affected with diabetes per year--less than two people might spend for a movie and a pizza.

The Research Plan

The Diabetes Research Working Group is convinced that a significant investment in research today will greatly speed progress in understanding and conquering this disease and its complications. The Strategic Research Plan set forth has two overarching goals:

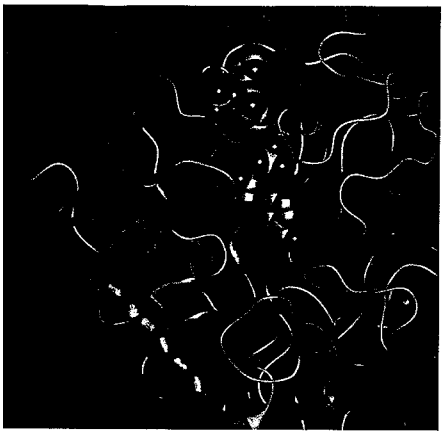
- Understand the causes and define approaches to prevent the development of Type 1 and Type 2 diabetes and their complications.
- Develop methods for optimal management, treatment and ultimate cure of diabetes and its complications.

The DRWG has divided this Research Plan into the following three major components, and provided specific recommendations concerning the types of efforts, budgetary requirements and program mechanisms that should be pursued to realize compelling research goals:

- Extraordinary Opportunities: Rapidly expanding, crosscutting areas in which increased investment or development of new mechanisms will significantly speed research.
- Special Needs for Special Problems: Equally important, but more focused research areas targeted to specific populations, complications, and methodological approaches.
- Resource and Infrastructural Needs: A bold plan for increasing research manpower, technology and other infrastructure elements for diabetes-related research.

Extraordinary Opportunities

Exciting and rapid research advances in recent years have opened the door to a new understanding of diabetes. The next decade offers important research opportunities that, if seized now, can vastly improve the lives of people with or at risk for diabetes. The Diabetes Research Working Group has identified five areas that offer extraordinary opportunities for making genuine and significant progress toward understanding, more



Computer-generated image of molecule associated with complications of diabetes. This imaging technology enables researchers to gain new insights into the disease process at the molecular level.

effectively treating, and ultimately preventing and curing diabetes. They are: the genetics of diabetes and its complications; autoimmunity and the beta cell; cell signaling and cell regulation; obesity; and clinical research and clinical trials of critical importance.

Genetics of Diabetes

Because Type 1 and Type 2 diabetes and their complications have strong genetic determinants, defining the specific genes involved is essential to prevention and could lead to new and better therapies. Defining the genes for diabetes and its complications will also help isolate the environmental factors involved in the disease and may identify genetic factors that contribute to variations in response to medications. Thus, a major goal for the coming decade must be to identify these predisposing genes.

Although most of the basic tools for genetic studies are in place and much progress has been made, current approaches are inadequate to tackle the vital genetics questions in a reasonable time frame. Three major impediments are inadequate resources; the lack of an appropriate mechanism to bring together the groups of researchers and patient samples to conduct the necessary studies; and fragmented genetic repositories.

Recommendations:

- **Establish a National Consortium for the Study of the Genetics of Diabetes to create a strong, coordinated effort for analysis of the role of genetics in diabetes and its complications.**
- **Enhance research in laboratory animals and humans to discover the biochemical mechanisms by which diabetes genes function to create susceptibility to diabetes and its complications.**

Autoimmunity and the Beta Cell

Type 1 diabetes is an "autoimmune" disease in which the body's own defense system mistakenly attacks and destroys insulin-producing beta cells of the pancreas. Important discoveries and concepts have emerged during the past decade from research in basic immunology, cell biology, and autoimmune diseases, including Type 1 diabetes. Based on this solid research foundation, the DRWG believes that aggressive pursuit of three scientific areas over the next decade could lead to dramatic improvements in diabetes therapy and prevention.

Recommendations:

- **Define the immunological basis of Type 1 diabetes and develop methods for prevention of the disease.**
  - Intensify research to understand the immunological basis of Type 1 diabetes.
  - Complete mapping of T cell specificity of autoimmune responses to major pancreatic islet cell proteins and identify optimal strategies for immunotherapy.
  - Expand the scope of efforts to identify immune response markers that reliably detect individuals predisposed to Type 1 diabetes in the population at large.
  - Conduct additional clinical trials of immunoprevention of Type 1 diabetes using antigen-specific, cytokine- or antibody-based immunotherapy.
- **Advance research on islet cell transplantation for treatment of diabetes.**
  - Establish Centers for Islet Transplantation with appropriate funding to undertake immediate clinical trials of islet transplantation in patients with Type 1 diabetes and to evaluate various methods of immune intervention.

- Support an expanded system for national collection of human pancreas for isolation and distribution of islets for clinical studies and clinical trials, and establish a Task Force to make recommendations on approaches to enhance this process.

➤ **Develop methods to stimulate beta cell growth and regeneration.**

- Increase basic research on the control and regulation of islet cell differentiation, growth and development, and devise methods for stimulating growth or regeneration of islet cells.
- Create Interdisciplinary Centers for Beta Cell Biology to expand current efforts and bring new investigators into the field. These Centers should be applicable to research efforts on both Type 1 and Type 2 diabetes.

Cell Signaling and Cell Regulation

Intracellular and intercellular communication is the basic mechanism for the regulation of all cells. Disturbances in cell signaling are central to disturbances in insulin secretion and action, which lead to diabetes and to both micro- and macrovascular complications. Basic research in this area is not only essential to understanding diabetes, but is also critical to understanding many diabetes-related complications. Most importantly, this type of "discovery" research can identify important targets for new treatments. It would also complement the important new information about the genetic underpinnings of disease.

Recent progress in research on signaling systems and in the ability to use genetic methods to study these pathways has created an extraordinary opportunity to determine the exact mechanisms of signal communication and its alterations in diabetes. A parallel opportunity exists to identify the molecular events responsible for the insulin resistance characteristic of Type 2 diabetes.

The DRWG has identified five areas of opportunity in cell signaling and regulation that warrant increased research. These are: dissection of insulin and hormone signaling pathways; understanding and countering insulin resistance; defining mechanisms regulating beta cell function; metabolic staging of diabetes; and defining alterations in signaling pathways that lead to development of diabetes complications.

Recommendations:

➤ **Complete the dissection of hormone signaling pathways, particularly the pathways of insulin action, and define their alterations in diabetes, including insulin resistance.**

- Significantly increase research in the fundamental science of cellular signaling as it relates to diabetes and its complications.
- Remove the limits currently present on research project (RO1) and program project (PO1) grants, such as budget caps, limitations on growth of programs, and considerations of average grant size, to maximize the opportunity for effective research teams to be formed.
- Establish research centers to focus on development of methods to study cellular signaling at the molecular and genetic level in humans with diabetes to allow correlation between the physiological defects and the molecular alterations.
- Expand research to identify the underlying genetic and biochemical basis of insulin resistance, and to develop interventions to prevent, reverse and ameliorate it in Type 2 diabetes and obesity.

➤ **Define mechanisms regulating beta cell function and their alterations in Type 2 diabetes.**

- Increase research on signaling pathways involved in the regulation of normal beta cell function and their derangements in diabetes.
- Use the proposed Interdisciplinary Centers for Beta-Cell Biology to study the alterations in signaling in Type 2 diabetes.

➤ **Allow metabolic staging of diabetes and identify the mechanisms of complications.**

- Develop a program of research to allow metabolic staging of Type 2 diabetes, and to detect individuals at high risk for this form of the disease and its complications.
- Expand support of interdisciplinary research to identify the mechanisms of the complications of diabetes, including interactive mechanisms and program project grants, which bring together investigators with different areas of expertise.

Obesity–Critical in Diabetes and a Major Problem of Its Own

Obesity is a major risk factor for the development of Type 2 diabetes and insulin resistance, as well as a major cause of morbidity and mortality in the U.S. One of every two Americans is overweight, and the prevalence has increased 30 percent in the past decade alone. Obesity disproportionately affects minorities. Over 60 percent of African American, Mexican American, and Native American women meet the criteria of being overweight and between 33 and 37 percent are obese. Moreover, obesity in children and adolescents is increasing at alarming rates, leading to occurrence of Type 2 diabetes in these groups.

Obesity results from an imbalance between energy intake and energy expenditure. The recent discovery of the fat cell hormone, leptin, and other appetite-regulating hormones has demonstrated that certain types of obesity are not simply due to overeating, but are the result of misregulated pathways that control the balance between appetite and energy expenditure. These new discoveries have provided a revolutionary understanding of obesity at the molecular level, thus leading to extraordinary opportunities in biomedical and behavioral research.

Recommendations:

- **Increase the size, scope, number and funding level of NIH sponsored Obesity Research Centers to meet appropriately the severity of this problem in the U.S.**
- **Significantly increase research in the basic sciences underlying obesity to capitalize on recent advances in hormonal control of appetite, energy regulation, metabolism, and adipocyte development.**
- **Develop stronger industry-NIH relationships to support obesity-related research.**
- **Enhance behavioral research in obesity.**

Clinical Research and Clinical Trials of Critical Importance

Translation of basic research into human therapies depends on an active and vigorous clinical research program. Studies in test tubes, cells and animals can answer questions of fundamental importance, and often provide the basis for development and initial testing of potential interventions. However, it is clinical studies in patients with diabetes that are essential for validating these observations and their relevance to human disease. In addition, clinical studies give key insights into the genetic, immune, hormonal, metabolic and environmental factors involved in the disease, and allow true testing of therapeutic strategies. Several prevailing forces, however, have significantly hampered clinical research and clinical trials in diabetes. Investigator-initiated clinical research is decreasing as a result of decreasing numbers of clinical investigators, limitations on funding of clinical research, the high cost of clinical research, and the complexity of clinical challenges. A major factor hampering clinical trials is the lack of infrastructure to organize and support them.

For diabetes, the long-term nature of the complications adds to the complexity of clinical trials. In most clinical studies, it is difficult to have adequate representation of high-risk minority groups due to the *ad hoc* nature of the organization of clinical trials. For robust and effective clinical research, additional well-trained clinical investigators and increased funding of meritorious clinical studies are required. Also needed are efficient systems for clinical research to provide the necessary numbers of patients and the stability of operations for long-term studies, and opportunities to include sufficient numbers of appropriate minority groups.

A comprehensive program for tackling a major public health problem such as diabetes requires a major investment, not only in basic research, but also in clinical research and clinical trials. The latter are particularly needed to document the safety and efficacy of various therapeutic strategies and generate the knowledge base for "evidence based medicine" that will lead to better treatment of diseases. There are two major needs to achieve these goals. The first is creation of an infrastructure to facilitate clinical trials—both improving efficiency and lowering cost. This need is especially apparent in diabetes where clinical trials to "hard endpoints" may take many years and even decades. The second need is a commitment to using clinical trials as a mechanism to develop the proper base of knowledge and to assure steady improvement in the care of people with diabetes.

Recommendations:

- **Establish a national diabetes trial network (Diabetes TrialNet) of cooperative clinical research groups to create the stable, high-quality infrastructure necessary for the conduct of effective and efficient clinical trials in diabetes.**

  In addition, the Diabetes Research Working Group recommends that NIH:
  - Increase funding of meritorious clinical trials of emerging new therapies for diabetes and its complications.
  - Support critical trials on how to most effectively apply the current methods of therapy and identify new, more generally applicable methods for achieving tight blood glucose control without hypoglycemia.
  - Support clinical trials on the prevention of microvascular and macrovascular disease, the major causes of morbidity and death in people with diabetes.
  - Develop effective partnerships among the NIH, academia and industry for collaboration and co-funding of clinical trials in diabetes and to provide training in the science of clinical trials.

- **Increase funding of meritorious clinical research for physiological studies and development of new technologies for metabolic assessment. These should include efforts to:**
  - Initiate clinical studies of promising new therapies for diabetes, such as gene therapy, or tissue-specific approaches to microvascular complications.
  - Initiate studies to determine the reasons that women and some minority populations with diabetes have higher risks for diabetic complications.
  - Increase opportunities for and support of clinical research training in diabetes.
  - Perform clinical studies to establish and validate surrogate endpoints for the complications of diabetes to be used in clinical research and clinical trials.

Special Needs for Special Problems

Micro- and Macrovascular Complications

The different types of diabetes and the array of complications they present offer a wide range of specific research needs unique to each. The micro- and macrovascular complications of diabetes are responsible for most of the morbidity and mortality in both Type 1 and Type 2 diabetes. Their prevention and reversal will greatly reduce the burden of this disease on individuals and on the nation. Understanding and combating the complications of diabetes will require significantly expanded research in mechanisms involved in the development and progression of the complications of diabetes. Several promising research avenues must be pursued through intensified basic and clinical research. This will require an increased effort from the existing community of scientists working in diabetes, as well as important new input from scientists in immunology, genetics, neurology, atherosclerosis, obesity and maternal and child health.

Recommendations on Diabetic Kidney Disease:

- **Increase the study of the basic mechanisms involved in diabetic nephropathy, including studies of extracellular matrix, growth factors, cytokines and genetic factors, and develop strategies to prevent and reverse this process.**
- **Initiate clinical studies to establish and validate additional markers for staging of disease and use in clinical trials on diabetic nephropathy, including functional imaging and other minimally invasive approaches.**
- **Establish multidisciplinary centers for the study of diabetic nephropathy in order to expand basic and clinical research studies and identify leads for prevention and treatment.**

Recommendations on Diabetic Eye Disease:

- **Increase basic and clinical research on the role of hormones, growth factors and other molecules in the development and progression of diabetic retinopathy.**
- **Increase research into the potential for tissue-specific gene therapy and drug delivery, including approaches for regeneration and rescue of retinal function.**
- **Increase basic and clinical research to develop and improve prosthetics and transplantation technology for diabetic retinopathy.**

Recommendations on Diabetic Nerve Disease:

- **Significantly increase the investment in fundamental research to determine the mechanisms of the nerve damage in diabetes, to expand research on nerve regeneration and rescue, and to evaluate methods to enhance peripheral and autonomic function.**
- **Initiate clinical studies to establish and validate surrogate markers for use in clinical trials on diabetic neuropathy, including new technologies that will aid in the measurement and evaluation of nerve function in people with diabetes.**
- **Establish new multidisciplinary centers for the study of metabolic nerve diseases, with an emphasis on diabetic neuropathy, to develop leads for prevention and treatment.**

Recommendations on Macrovascular Complications:

- **Increase research on the mechanisms by which diabetes and insulin resistance enhance the atherosclerotic process and on the mechanisms of angiogenesis and its use in the treatment and prevention of macrovascular disease.**
- **Increase research to determine the mechanisms responsible for the loss of the vascular-protective effect in premenopausal women.**
- **Increase basic and clinical research to study myocardial function and the cardiac and micrometabolic environment in diabetic heart disease in order to identify the mechanisms that lead to the high mortality in the peri-infarction period and in patients undergoing surgery, and to develop effective preventive interventions.**
- **Support research to develop appropriate animal models of diabetes and atherosclerosis.**
- **Support further analysis of existing studies and new clinical research to identify the presence, predict the progression, and assess the response to therapy of macrovascular complications in patients with diabetes.**
- **Create multidisciplinary Centers for Diabetes and Vascular Disease.**

Methods to Optimize Glucose Control

Despite the findings of clinical trials and other studies that have demonstrated the importance of tight glucose control to minimize the risk of long-term complications, many patients continue to have far less than optimal control. This is due in part to the risk of hypoglycemia, which increases with intensified therapy, and in part to the difficulty of obtaining optimal control in a general clinical setting. The Diabetes Research Working Group believes that identification of methods that promote implementation of these standards of treatment should be a high priority of current clinical research.

Recommendations:

- **Increase basic and clinical research to discover novel approaches for controlling hyperglycemia in diabetes. These approaches should include designing small, orally bioavailable molecules mimicking insulin action; overcoming insulin resistance or stimulating insulin secretion in a physiologic manner; and developing technologies that enable administration of insulin by routes other than injection. This research could involve enhanced collaboration with the pharmaceutical and biotechnology industry.**
- **Develop a focused, multi-disciplinary research program on hypoglycemia and hypoglycemic unawareness. This research should include the neuroendocrine and neuroscience mechanisms that underlie these problems, and increased clinical research to find simple, reliable techniques to identify patients at greatest risk for severe hypoglycemia.**
- **Initiate immediate review of the research program to develop mechanical approaches to insulin replacement by the Diabetes Technology Taskforce (see "Resource and Infrastructural Needs").**

Diabetes and the Environment

The environment appears to play important roles in Type 1 diabetes as a trigger for the autoimmune response and in Type 2 diabetes as a modifier of pre-existing genetic risk. While the latter influence is partly understood, but difficult to control, the former influence has been difficult to define in any specific way. Identification of these environmental factors would provide important information for any preventive strategies for either form of diabetes.

Recommendations:

- **Hold a series of conferences and workshops to explore new methods to search for the environmental triggers of Type 1 diabetes and other autoimmune diseases.**
- **Perform epidemiologic analysis of suspected triggering factors, such as latent or endogenous viruses (including retroviruses) or other substances, whose activation may initiate the autoimmune process.**
- **Explore with the Centers for Disease Control and Prevention the possibility of a national registry for Type 1 diabetes as a mechanism to enhance epidemiologic research.**
- **Support research to develop and apply new technologies to provide accurate, affordable, quantitative measures in normal, living humans of individual-specific energy expenditure, energy intake and macronutrient composition, which contribute to obesity and Type 2 diabetes.**
- **Initiate new epidemiological studies taking into account genetic susceptibility to help identify additional environmental risk factors for Type 2 diabetes, such as stress levels and bacterial/viral infectious agents.**
- **Study environmental factors responsible for the increase in Type 2 diabetes in children and ways to modify them.**

Diabetes in Women, Children and the Elderly

Diabetes mellitus presents additional problems to women with its impact on reproductive health and vascular complications. Children and the elderly present special problems in management and may have additional physiological variables that must be addressed through specific research.

Recommendations:

- **Increase basic and clinical research to identify the mechanisms by which the intrauterine environment, including the diabetic environment, affects the immediate and long-term health outcomes for children and their risks of diabetes and obesity.**
- **Support research to determine the impact of Type 1 and Type 2 diabetes on women, including their reproductive health; risk of cardiovascular disease; the relationship of insulin resistance syndrome and polycystic ovarian disease; and the risk of diabetes following gestational diabetes mellitus.**
- **Increase studies about specific psychosocial issues that face women, children and the elderly with diabetes, including eating disorders, impact of school settings on diabetes, and the management of diabetes in assisted-living situations.**
- **Increase studies of how to implement effectively the principles of the Diabetes Control and Complications Trial (DCCT) in children with Type 1 diabetes in an effort to improve glucose control and reduce the complications of disease.**
- **Increase studies on age-related changes in the development of Type 2 diabetes, and the effects of these changes on responses to treatment and prevention strategies in older persons.**

Diabetes in Minority Populations

Minority populations, including African Americans, Hispanics, Native Americans, and Asians, have the highest incidence of diabetes and the highest rates of complications of the disease. Current research has only begun to address the reasons for this in a very limited way. These groups are rapidly growing segments of the population and specific research must address the reasons for the disproportionate impact of diabetes they bear.

Recommendations:

- **Increase efforts in genetic studies in minority populations as part of the proposed National Consortium for the Study of Genetics of Diabetes.**
- **Support research to identify physiologic and environmental determinants for development of Type 2 diabetes and its complications in minority populations, including in children and adolescents.**
- **Support research to identify risk factors, co-morbidities, and primary and secondary prevention strategies for micro- and macrovascular complications of diabetes in minority populations.**
- **Initiate research to develop culturally sensitive, preventive and therapeutic approaches utilizing appropriate, innovative communication and education techniques applicable in relevant, "real world" settings, for example, rural clinics, county clinics, and urban health centers.**

- **Design and conduct studies in partnership with minority communities to understand more fully the cultural, familial, and other factors that influence adoption of health-promotion, and to change high risk behaviors in those with or at risk for Type 2 diabetes.**

Genetic Engineering

The ability to modify the function of cells through genetic engineering opens up tremendous opportunities for new therapeutic approaches to diabetes and its complications. The Diabetes Research Working Group recommends that several applications of this technology be explored.

Recommendations:

- **Increase research to explore the possible use of genetic engineering as a strategy for beta-cell replacement and immunomodulation of transplanted cell lines.**
- **Expand research to explore the potential for gene therapy for Type 2 diabetes.**
- **Bolster research to explore unique applications of gene therapy for tissue-specific approaches to micro- and macrovascular complications.**

Behavioral and Health Services Research

Lifestyle variables, such as dietary intake and physical activity, represent important risk factors for Type 2 diabetes. Type 1 diabetes management can also be influenced by behavioral patterns and can greatly influence personal, family and social dynamics.

Recommendations:

- **Intensify clinical behavioral research to develop interventions to improve patients' adherence to diabetes treatment and their quality of life, and promote sustained improvements in lifestyle behaviors, particularly diet and exercise, which will effectively prevent and reduce the risk for diabetes.**
- **Extend research and development of valid methodologies to measure psychosocial and behavioral factors in diabetes.**
- **Integrate behavioral and pharmacological approaches to reduction of risk factors for diabetes and its complications.**
- **Develop interdisciplinary research teams and training programs to bring together individuals who have training in behavioral sciences with those who have training in diabetes, nutrition, and exercise physiology.**
- **Study the effectiveness of different clinical practices, interventions and technologies; and identify deficiencies in access to care for diabetic patients.**
- **Support research to address lifestyle risk factors and behavioral modification/counseling programs, including obesity, unhealthful dietary preferences, and smoking cessation.**

Oral Complications of Diabetes

Oral complications of diabetes include periodontal diseases, mucosal infections, salivary gland dysfunction, and neurological disorders. These complications are extremely common, as well as problematic. In addition, they are difficult to treat and greatly interfere with essential daily tasks such as eating and speaking.

Recommendations:

- **Establish multidisciplinary Centers for Oral Complications of Diabetes and identify means for prevention and treatment.**
- **Increase studies of the oral complications of diabetes, particularly with respect to the chronic destruction of gingival tissues, the immune response to oral bacteria, salivary dysfunction, healing of oral wounds, and oral neuropathies.**

Resource and Infrastructural Needs

An effective program of diabetes research can exist only if there is a supportive infrastructure. New and expanded initiatives are required to address issues of human resources, clinical research, special needs for animal research, high-cost technology, and other components of infrastructure. Also essential are mechanisms for ongoing review, evaluation, and advice regarding implementation of all of the recommendations in the Strategic Research Plan set forth by the Diabetes Research Working Group.

Recommendations:

For Strengthening Human Resources for Research

- **Create new mechanisms and significantly modify existing programs to maximize recruitment, research training, and research career development of diabetes investigators, including special initiatives to promote clinical research and to attract investigators from other disciplines.**

For Enhancement of the Diabetes Research Centers

- **Create new Comprehensive Diabetes Research Centers (CDRCs) to provide enhanced infrastructure support, and enhance the effectiveness of existing Diabetes Centers (DERCs and DRTCs) by significantly increasing their funding levels and expanding their mission.**

For Developing and Harnessing New Technologies

- **Create a National Diabetes Technology Task Force.**
- **Create new regional centers with advanced technologies required for metabolic and functional imaging studies, such as nuclear magnetic resonance (NMR), positron emission tomography (PET), and related technologies, which are required for contemporary diabetes research, and provide ongoing support for their operation.**

For Animal Models for Study of Diabetes

- **Establish regional Centers for Animal Models of Diabetes and Related Disorders.**
- **Support mechanisms to develop and characterize larger animal models of Types 1 and 2 diabetes and their complications, and distribute these models for enhanced approaches to genetic and metabolic studies and the full range of diabetes complications.**

For Human Materials for Diabetes Research

- **Expand support of programs for procurement of human tissues and organs in order to serve cutting-edge diabetes research; to provide adequate numbers of pancreases for islet cell clinical trials and research; to obtain appropriate tissues for study of diabetes complications and genetic research; and to ensure availability of a range of human tissues required to establish DNA and RNA libraries.**

For NIH–Pharmaceutical and Biotechnology Interactions

- **Establish a NIH–Industry–Academia Task Force to foster interactive research initiatives.**

For the Intramural Programs of the NIH

- **Create an advisory panel, established by the Director of the National Institutes of Health, to review and make recommendations concerning intramural NIH diabetes research efforts in all Institutes and Centers.**

For Extramural Research and Ongoing Strategic Planning

- **Create a Task Force on Strategic Planning in Diabetes Research that would report biennially to the Congress and the Directors of NIH and NIDDK.**

SUMMARY OF BUDGET RECOMMENDATIONS

The Diabetes Research Working Group has conducted a careful review of NIH-funded diabetes research and believes that this enterprise is a strong and valuable component of U.S. biomedical research efforts. However, the nation is far from achieving its maximal potential with this difficult problem. Limitations are created in part by under-funding of diabetes research, and by the design of existing research mechanisms and infrastructure. The Diabetes Research Working Group believes that progress over the past decade, coupled with the explosion of information in science, makes this an appropriate time to increase significantly the nation's investment to conquer this disease. To implement its recommendations, the Diabetes Research Working Group calls upon the Congress and the American people to increase research funding through new appropriations to NIDDK and other Institutes and Centers of NIH.

The table on the following page summarizes these budgetary recommendations. They call for stepwise expansion of funding for diabetes research providing an increment of $384.5 million for FY2000 rising to an increment of $1.166 billion by FY2004. Built on a base of diabetes research funding for FY1999 of $442.8 million, this proposed budget increment would result in an approximate four-fold increase in overall NIH funding for diabetes research over the coming five-year period. The Diabetes Research Working Group believes that such a budget increase is necessary for implementation of the programs presented in this Research Plan, consistent with the rising impact of diabetes on the U.S. in both human and economic terms, and that the proposed budget is more in line with the levels of research funding for other major disease areas. Most importantly, the Diabetes Research Working Group believes that such an investment has the potential to reduce dramatically the personal, societal and economic burden of diabetes for the American people in the 21st century.

Summary of Budget Recommendations

	Year 1 2000	Year 2 2001	Year 3 2002	Year 4 2003	Year 5 2004
	(in millions of dollars)				
Extraordinary Opportunities					
Genetics of Diabetes	40.5	72.0	85.0	99.0	101.0
Autoimmunity and the Beta Cell	30.0	45.0	58.0	66.0	79.0
Cell Signaling and Cell Regulation	38.0	57.0	73.0	86.0	94.0
Obesity	15.0	25.0	37.0	46.0	52.0
Clinical Research and Clinical Trials	87.0	139.0	191.0	252.0	280.0
Sub-Total	**210.5**	**338.0**	**444.0**	**549.0**	**606.0**
Special Needs for Special Problems					
Microvascular Complications	51.0	80.0	106.5	124.0	129.5
Macrovascular Complications	34.0	58.0	79.0	95.0	102.0
Optimization of Glucose Control	9.5	16.0	24.0	29.0	36.0
Diabetes and the Environment	3.0	4.0	6.0	8.0	10.0
Special Needs in Women, Children and the Elderly	20.0	40.0	60.0	80.0	80.0
Special Needs in Minority Populations	9.0	15.0	22.5	30.0	32.0
Genetic Engineering	8.0	15.0	22.0	28.0	35.0
Behavioral and Health Services Research	8.0	13.5	20.0	27.0	40.0
Oral Complications of Diabetes	1.0	1.5	2.0	2.5	3.0
Sub-Total	**143.5**	**243.0**	**342.0**	**423.5**	**467.5**
Resource and Infrastructural Needs					
Research Training and Manpower Development	3.0	5.0	8.0	10.0	10.0
Diabetes Research Centers Program	6.0	15.0	25.0	40.0	40.0
Technology Taskforce	13.0	17.0	21.0	13.0	13.0
Regional Centers for Animal Models	5.0	10.0	16.0	26.0	26.0
Human Material for Diabetes Research	2.0	2.0	2.0	2.0	2.0
NIH-Pharmaceutical and Biotechnology Interactions	0.5	0.5	0.5	0.5	0.5
Review of Intramural Programs of NIH	0.5	0.5	0.5	0.5	0.5
Taskforce for Strategic Planning	0.5	0.5	0.5	0.5	0.5
Sub-Total	**30.5**	**50.5**	**73.5**	**92.5**	**92.5**
Increment over FY99 Base to Implement Recommendations in DRWG Strategic Research Plan	384.5	631.5	859.5	1065.0	1166.0
FY99 Base for Diabetes Research	442.8	442.8	442.8	442.8	442.8
Grand Total for Diabetes Research	**827.3**	**1074.3**	**1302.3**	**1507.8**	**1608.8**

More detailed budgetary information presented in terms of the specific scientific recommendations and the corresponding additional funds proposed for individual Institutes and Centers of the National Institutes of Health will be found in the full Strategic Plan of the Diabetes Research Working Group.

DIABETES RESEARCH WORKING GROUP

C. Ronald Kahn, M.D., Chairman
Director, Joslin Diabetes Center
Mary K. Iacocca Professor of Medicine
Harvard Medical School

Jose Caro, M.D.
Lilly Research Laboratories

Nancy Cox, Ph.D.
University of Chicago

Lee Ducat
National Disease Research Interchange/
Human Biological Data Interchange

Joyce C. Dugan
Eastern Band of Cherokee Indians

Robert N. Frank, M.D.
Wayne State University School of Medicine

James R. Gavin III, M.D., Ph.D.
Howard Hughes Medical Institute

Willa Ann Hsueh, M.D.
University of California, Los Angeles

Hugh O. McDevitt, M.D.
Stanford University

Douglas Melton, Ph.D.
Harvard University

Christopher B. Newgard, Ph.D.
University of Texas SW Medical Center

Daniel Porte, Jr., M.D.
University of Washington and
Seattle Veterans Affairs Medical Center

Stephen Smith
American Diabetes Association

Emily Spitzer
Juvenile Diabetes Foundation International

Michael P. Stern, M.D.
University of Texas Health Science Center at San Antonio

Rena Wing, Ph.D.
University of Pittsburgh School of Medicine and
Brown University

Lester B. Salans, M.D., LBS Associates, New York, served as Senior Medical Advisor.

AD HOC CONSULTANTS TO THE CONGRESSIONALLY-ESTABLISHED DIABETES RESEARCH WORKING GROUP

Kelly J. Acton, M.D., M.P.H., F.A.C.P.
Indian Health Service

Michael A. Brownlee, M.D.
Albert Einstein College of Medicine

Thomas A. Buchanan, M.D.
University of Southern California
School of Medicine

Patrick Concannon, Ph.D.
University of Washington

Donald Coustan, M.D.
Brown University School of Medicine

George S. Eisenbarth, M.D., Ph.D.
University of Colorado Health Sciences
Center

Edwin Fisher, Ph.D.
Washington University

Michael S. German, M.D.
University of California - San Francisco

Marvin C. Gershengorn, M.D.
Cornell University Medical College

Daryl K. Granner, M.D.
Vanderbilt University School of
Medicine

Thomas C. Hohman, Ph.D.
Wyeth-Ayerst Research

George L. King, M.D.
Harvard University

John Kitzmiller, M.D.
Good Samaritan Hospital

S. Robert Levine, M.D.
Juvenile Diabetes Foundation
International

Michael Mauer, M.D.
University of Minnesota Medical
School

Boyd E. Metzger, M.D.
Northwestern University

Richard Nesto, M.D.
New England Deaconess Medical
Center

Jerrold M. Olefsky, M.D.
University of California, San Diego

Jeffrey E. Pessin, Ph.D.
University of Iowa

Kenneth S. Polonsky, M.D.
The University of Chicago

E. Albert Reece, M.D.
Temple University School of Medicine

Douglas L. Rothman, M.D., Ph.D.
Yale University School of Medicine

Christopher D. Saudek, M.D.
Johns Hopkins University

Gerald I. Shulman, M.D., Ph.D.
Yale University School of Medicine

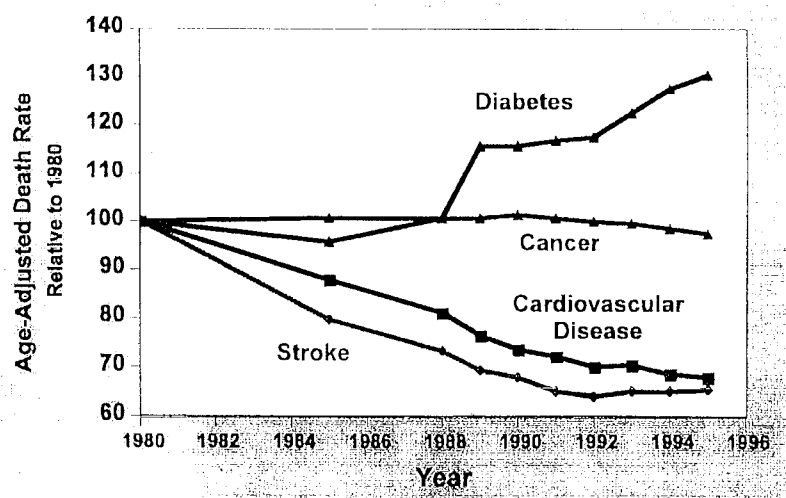
Anders A.F. Sima, M.D., Ph.D.
Wayne State University School of
Medicine

Lorraine Valdez
Indian Health Service Diabetes
Program

Senate Permanent Subcommittee on Investigations

EXHIBIT # 7a

Increasing Deaths Due to Diabetes



Source: U.S. National Center for Health Statistics

DIABETES RESEARCH WORKING GROUP

10/7/99

Senate Permanent Subcommittee on Investigations
EXHIBIT #
75

The Economic Impact of Diabetes is Staggering

- The cost of diabetes to the nation is over $105 billion annually.
- Between 10% and 14% of all U.S. healthcare dollars are spent for diabetes.
- One of every four Medicare dollar pays for health care of people with diabetes.

DIABETES RESEARCH WORKING GROUP

10/7/99

Senate Permanent Subcommittee on Investigations

EXHIBIT # 7c.

THE ECONOMICS OF DIABETES

[redacted]

[redacted]

$6,562/year
per person affected

$30/year
per person affected

[redacted]

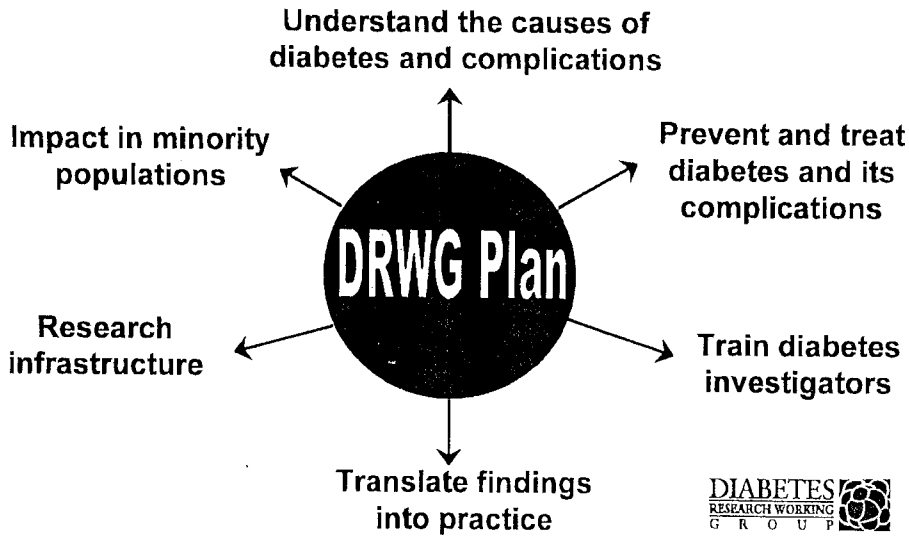
DIABETES RESEARCH WORKING GROUP

10/7/99

Senate Permanent Subcommittee on Investigations

EXHIBIT #_____ 7d.

Goals of the DRWG Plan



10/7/99

Senate Permanent Subcommittee on Investigations
EXHIBIT #_____

Components of the DRWG Strategic Plan

EXTRAORDINARY OPPORTUNITIES

- Genetics of diabetes and its complications
- Autoimmunity and the beta cell
- Cell signaling and cellular regulation
- Obesity
- Clinical Research and Clinical Trials of Critical Importance

SPECIAL NEEDS FOR SPECIAL PROBLEMS

- Micro- And Macrovascular Complications
  - Diabetic Nephropathy
  - Diabetic Retinopathy
  - Diabetic Neuropathy
  - Diabetes and Macrovascular Disease
  - Oral Complications Of Diabetes
- Methods To Optimize Glucose Control
- Genetic Engineering
- Diabetes In Minority Populations
- Diabetes In Women, Children And The Elderly
- Diabetes And The Environment
- Behavioral And Health Services Research

RESOURCES AND INFRASTRUCTURE

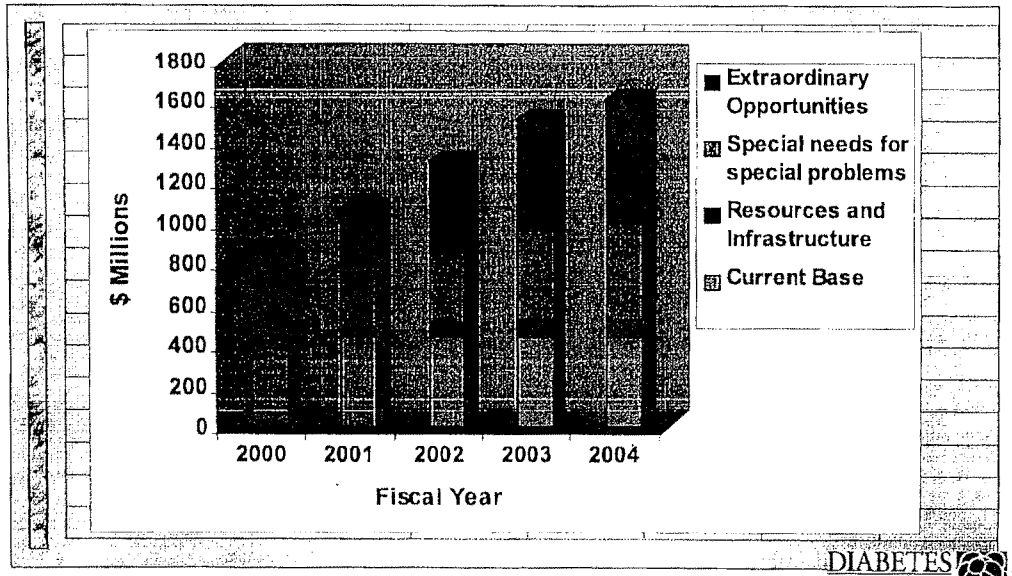
- Human resource needs
- Infrastructural Needs
- Taskforces for review, planning, and technology

DIABETES RESEARCH WORKING GROUP

10/7/99

Senate Permanent Subcommittee
on Investigations
EXHIBIT #_____
7F

BUDGET RECOMMENDATIONS



DIABETES RESEARCH WORKING GROUP

10/7/99

Senate Permanent Subcommittee on Investigations
EXHIBIT # 8

Mission
to prevent and cure diabetes
and to improve the lives of all
people affected by diabetes.

Statement presented by

the

American Diabetes Association

on the

NIH Allocation Process
and the need for more diabetes funding at NIH

before the

Senate Governmental Affairs Committee
Permanent Subcommittee on Investigations

Senator Susan Collins, Chair

Thursday October 14, 1999

National Office
1701 N. Beauregard Street • Alexandria, Virginia 22311
Tel: (703) 549-1500
For Diabetes Information Call 1-800-DIABETES • http://www.diabetes.org
The Association gratefully accepts gifts through your will.

Madam Chair and members of the subcommittee, thank you for the opportunity to present this written testimony on the important issue of the National Institutes of Health (NIH) allocation process and the need for significantly more diabetes research funding at NIH.

In 1997, Congress directed NIH to put together a team of "the best and the brightest" diabetes experts and develop a comprehensive plan that would lead to the elimination of diabetes. This spring, *Conquering Diabetes*, the final report of the Diabetes Research Working Group (DRWG), was presented to Congress.

Conquering Diabetes identifies the challenges associated with diabetes and provides compelling evidence attesting to the magnitude of the problem. It also analyzes the federal government's current commitment to diabetes research. Most importantly, *Conquering Diabetes* identifies hundreds of scientific opportunities that could lead to better treatments and hopefully, a cure.

Since 1997, the issue of how NIH allocates its multi-billion annual budget has been explored internally by NIH, by the National Academy of Science's Institute of Medicine and by a subcommittee of the Senate Labor and Human Resources Committee.

During this time, NIH has stated that it uses five criteria in setting research priorities:

- Public health needs.
- Scientific quality of the research.
- Potential for scientific progress.
- Portfolio diversification.
- Adequate support of infrastructure.[i]

According to NIH, "two of the most important of these…are public health needs and scientific opportunities."[ii] Each year, according to NIH, "deciding how and where to distribute [its] money…requires a fresh assessment of the nation's health needs and renewed evaluation of scientific opportunity."[iii]

Based upon the findings of the DRWG, diabetes exceedingly meets these two criteria. Yet despite meeting them, the DRWG found that diabetes research has been, and continues to remain, significantly underfunded by NIH.

PRESSING PUBLIC HEALTH NEEDS

In terms of incidence, severity and cost, there can be no doubt that diabetes imposes a significant burden on our nation and the world.

INCIDENCE -- Sixteen million Americans have diabetes.[iv] Approximately 500,000 have type 1, formerly known as juvenile, diabetes and the rest, predominantly older Americans, have type 2 diabetes.[v] Each year, another 800,000 will develop the disease.[vi]

Since 1959, the number of Americans diagnosed with diabetes has increased nearly 700%.[vii] This trend will continue as our nation ages and becomes more sedentary. According to the World

Health Organization (WHO), nearly 22 million Americans will have diabetes by 2025 – a 37.5% increase.[viii] This has led the Centers for Disease Control and Prevention (CDC) to call diabetes "the epidemic of our time."[ix]

This epidemic is also evident worldwide. According to WHO, the worldwide incidence of diabetes is expected to rise from its current level of 135.5 million to 300 million by 2025. This growth will be especially pronounced in developing countries, which are expected to see a 170% increase in the number of people affected with diabetes over the next 25 years.[x]

According to WHO's Director-General, Dr. Gro Harlem Brundtland, these statistics "are yet another scientific testimony of a transition the world is experiencing at the moment, the transition from communicable to noncommunicable diseases. In the 21st century," she stated, "the impact of this transition on the public health and economic sectors will be especially noticeable in developing countries."[xi]

SEVERITY -- Diabetes is the sixth deadliest disease in America, killing over 193,000 Americans annually. Diabetes is deadly because it affects virtually every tissue of the body with long-term and severe damage. For example, in the United States:

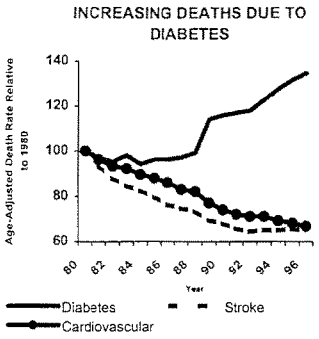
- Diabetes-related eye disease is the most common cause of blindness in working age adults.
- Diabetes-related kidney disease accounts for 42% of new cases and is responsible for 100,000 cases of dialysis and transplantation each year.
- More than 50% of lower limb amputations, approximately 80,000 cases a year, are caused by diabetes.
- Heart disease death rates in adults with diabetes are 2-4 times greater.
- The risk of stroke in adults with diabetes is 2-4 times greater.
- The rate of major congenital malformations and death of the fetus and newborn are 3-4 times greater in a woman with diabetes.[xii]

Given the systemic damage diabetes imposes, it is no surprise that the life expectancy of a person with the disease averages 10-15 years less than that of the general population.[xiii]

Unlike cancer and other acute medical conditions, the damage caused by diabetes typically occurs over a period of years as opposed to months. Because a person with diabetes can live with the disease for years, it creates the mistaken impression that diabetes is not serious.

Medical research has shown that careful control of diabetes can diminish the individual's risk for developing complications. But diminished risk is not equivalent to immunity from risk. As the DRWG correctly stated, "available treatments have only limited success in controlling its devastating complications."[xiv]

Unlike other diseases and medical conditions, the DRWG found that diabetes has not experienced a diminution in the rate at which it kills. According to the U.S. National Center for Health Statistics, the age-adjusted death rates for cardiovascular disease and stroke have each declined more than 35% since 1980.[xv]



Yet diabetes has not declined. According to the U.S. National Center for Health Statistics, the age-adjusted diabetes death rate has increased more than 30% since 1980.[xvi] Furthermore, people with diabetes have not benefited equally from the national decline in heart disease death rates.

A recent study published in the Journal of the American Medical Association found that while heart disease deaths declined 36% in nondiabetic men from 1971-93, they fell just 13% in men with diabetes. The study also found that heart disease deaths rose 23% in women with diabetes despite a 27% drop in heart disease deaths in non-diabetic women.[xvii]

COST -- In addition to the extraordinary personal burden, diabetes exacts an equally staggering economic burden on our nation. According to *Conquering Diabetes*, the cost of diabetes to the nation is over $105 billion a year. The DRWG also found that more than 1 of every 10 health care dollars is spent for diabetes.[xviii]

The federal government is held hostage to these exorbitant medical costs. According to the DRWG, about one in every four Medicare dollars pays for the health care of people with diabetes.[xix] A recent study found that the federal government spends more than $40 billion a year treating people with diabetes through Medicare, Medicaid, FEHBP and veterans programs.[xx]

If this $40 billion was returned to the taxpayers through tax relief, it would provide a $400 rebate to every working American or nearly $600 to every American family. It could also be used to provide computers to every public school, save Social Security or help pay down the debt.[xxi]

How do the economic consequences of diabetes compare to other diseases? In 1998, NIH sought to answer this question in a report titled "HHS and National Costs for Thirteen Diseases and Conditions." The data in the following table (right) is taken directly from the report.[xxii]

Disease	**Direct cost (in billions)**
Heart diseases	97.9
Diabetes	**44.1**
Stroke	28.3
Cancer	27.5
Kidney diseases	26.2
Chronic pulmonary diseases	21.6
Depression	19.9
Pneumonia/ Influenza	17.5
Arthritis	15.2
HIV/AIDS	10.3
Septicemia	4.9
Acute respiratory distress syndrome	2.6
Chronic liver diseases	1.2

Clearly, diabetes imposes a significant burden upon our nation's health unlike any other and meets NIH's first criteria on determining how to allocate research funding. Diabetes also satisfies NIH's second criteria, the availability of scientific research opportunities.

SCIENTIFIC OPPORTUNITIES

In *Conquering Diabetes*, the members of the DRWG stated their conviction that "a significant investment in research today will greatly speed progress in understanding and conquering this disease and its complications." Their Strategic Research Plan set forth two goals:

1. To understand the causes and define approaches to prevent the development of type 1 and type 2 diabetes and their complications.

2. To develop methods for optimal management, treatment and ultimate cure of diabetes and its complications.[xxiii]

The DRWG's Strategic Research Plan is more than a "professional judgement" budget, the documents provided to Congress each year by NIH institutes that outline the maximum amount of money that could be spent in the upcoming year. Instead, it is a peer-reviewed document that sets forth a comprehensive plan of attack against diabetes.

According to the DRWG, exciting and rapid research advances in recent years have opened the door to a new understanding of diabetes. In their judgement, the next decade offers important research opportunities that, if seized now, can vastly improve the lives of people with diabetes.

Towards this goal, the DRWG identified five areas that offer extraordinary opportunities for making genuine and significant progress toward understanding, more effectively treating, and ultimately preventing and curing diabetes:

1. **Genetics of Diabetes** -- Because type 1 and type 2 diabetes have strong genetic determinants, defining the specific genes involved is essential to prevention and could lead to new and better therapies.

2. **Autoimmunity and the Beta Cell** -- Type 1 diabetes is an "autoimmune" disease in which the body's own defense system mistakenly attacks the insulin-producing cells of the pancreas. Aggressive pursuit of the following areas could lead to dramatic improvements in diabetes therapy and prevention: (1) Define immunological basis of type 1 diabetes and develop methods for prevention. (2) Advance research on islet cell transplantation. (3) Develop methods to stimulate beta cell growth and regeneration.

3. **Cell Signaling and Regulation** -- Disturbances in cell communication are central to disturbances in insulin secretion and action. The DRWG has identified five areas of opportunity that warrant increased research: (1) Dissection of insulin and hormone signaling pathways. (2) Understanding and countering insulin resistance. (3) Defining mechanisms regulating Beta cell function. (4) Understanding metabolic staging. (5) Defining alterations in signaling pathways that lead to complications.

4. **Obesity** -- Obesity is a major risk factor for type 2 diabetes and results from an imbalance between energy intake and expenditure. New discoveries have provided a revolutionary understanding of obesity at the molecular level, thus leading to extraordinary opportunities in research.

5. **Clinical Research and Trials** -- Translation of basic research into human therapies depends on an active and vigorous clinical research program. A comprehensive program for tackling diabetes requires a major investment in order to document the safety and efficacy of different therapies and to increase the knowledge base of diabetes. There are two major needs to meet these goals: (1) The creation of an infrastructure to facilitate clinical trials in diabetes. (2) A commitment to these trials as a way to increase understanding of diabetes.

In addition to these extraordinary opportunities, the DRWG Strategic Research Plan includes two additional components necessary to make significant inroads against diabetes:

1. **Special Needs for Special Problems** -- Equally important, but more focused research areas, targeted to specific populations, complications and methodological approaches.

2. **Resources and Infrastructure Needs** -- A bold plan for increasing research manpower, technology and other infrastructure elements for diabetes-related research.

Conquering Diabetes provides NIH with the "scientific opportunities that offer the best prospects for new knowledge and better health." Furthermore, being drafted by the world's leading diabetes researchers, it virtually assures that, if funded, NIH will be able to keep its commitment to supporting "work of the highest scientific caliber."[xxiv]

NIH FUNDING

In addition to outlining the magnitude of the problem and the scientific opportunities available in diabetes research, the DRWG thoroughly analyzed the current federal investment in diabetes research. They found that despite the pressing public health needs and the myriad scientific opportunities available to researchers, diabetes research is significantly underfunded at NIH:

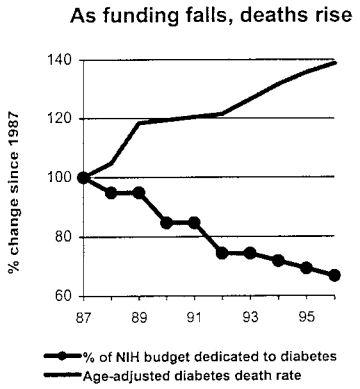
- NIH funding for diabetes research has risen from $134 million in FY 1980 to an estimated $442.8 million for FY 1999. When adjusted for inflation, however, the actual amount of growth has been only 34.4 percent over 20 years, or less than 2 percent per year.[xxv]

- From FY 1980-99, the diabetes research budget, expressed as a percentage of the total NIH budget, has never exceeded 4.1%, although diabetes-related illness amounts during the same period represented 10% of the health care expenses in the United States.[xxvi]

- Diabetes research represents less than 3% of the NIH research budget. Although there is generally no accepted methodology for determining appropriate levels of research funding, this is a small investment for a disease that affects 6-7% of the population and accounts for about 10% of all health care dollars.[xxvii]

- Relative to the whole NIH budget, the amount devoted to diabetes research has decreased by more than 30% since 1981, at a time when the death rate due to diabetes has increased by 30% (see chart, right)[xxviii]

- Diabetes research represents only about $30 per person affected with diabetes per year -- less than two people might spend for a movie and a pizza.[xxix]



Based upon their analysis of the federal government's current commitment to diabetes research, the DRWG concluded that:

> Although federal support for diabetes research has produced a number of major advances in the past two decades, many scientific opportunities are not being pursued due to insufficient funding, lack of appropriate mechanisms and a shortage of trained researchers. Improvements in technology and the general growth in scientific knowledge offer unprecedented opportunities for advances that might lead to better treatments, prevention and possibly a cure.
>
> While [funding for diabetes research] has increased steadily since 1981, there is a strong consensus in the DRWG that this funding level is far short of what is required to make optimal progress on this complex and difficult problem. In fact, the current federal budget for diabetes research represents less than one-half of one percent (0.5 percent) of the annual cost of diabetes to the US economy. When compared with the 5 to 15 percent budgets for research and development in other high-technology sectors, this investment in diabetes research is trivial.[xxx]

CONCLUSION

The science and data of the DRWG demonstrates that diabetes research is severely underfunded by NIH despite meeting its published criteria for allocation of resources.

As the DRWG concluded, "conquering diabetes and its complications represents a formidable task." The budgetary recommendations of the DRWG are "not only more consistent with the impact of diabetes on the U.S. population from both human and economic perspectives, but is what would be required to have a robust and effective diabetes research effort – one which will reduce the rising burden created by this debilitating disease."[xxxi]

The American Diabetes Association continues to strongly support fully funding diabetes research at $827 million, the amount recommended by the DRWG. Equally, or perhaps even more important, is that Congress take the steps necessary to ensure that the DRWG Strategic Research Plan is fully implemented by NIH by FY 2004.

The American Diabetes Association appreciates this opportunity to testify on behalf of the 16 million Americans with diabetes.

REFERENCES

[i] Institute of Medicine, "Scientific Opportunities and Public Needs: Improving Priority Setting and Public Input at the National Institutes of Health." National Academy Press: Washington, D.C.: 1998.

[ii] "Biomedical Research Priorities: Who Should Decide?" Hearing before the Subcommittee on Public Health and Safety of the Committee on Labor and Human Resources, United States Senate. May 1, 1997, p. 8.

[iii] "Setting Research Priorities at the National Institutes of Health," National Institutes of Health, September 1997: p. 7.

[iv] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 2.

[v] National Institutes of Health. Diabetes in America: 2nd Edition, 1995, p. 1.

[vi] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 2.

[vii] Ibid., p. 16.

[viii] World Health Organization. GLOBAL BURDEN OF DIABETES: WHO Projects a 170% Growth in the Number of People with Diabetes in Developing Countries by 2025. September 14, 1998 Press Release.

[ix] 1999 Congressional Appropriations Justification, p. 45.

[x] World Health Organization. GLOBAL BURDEN OF DIABETES: WHO Projects a 170% Growth in the Number of People with Diabetes in Developing Countries by 2025. September 14, 1998 Press Release.

[xi] Ibid.

[xii] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 2.

[xiii] Ibid.

[xiv] Ibid., p. 1.

[xv] Ibid., p. 2

[xvi] Ibid., p. 2.
[xvii] Gu, Ken, Ph.D. and Cowie, Catherine C., Ph.D., MPH and Harris, Maureen I., Ph.D., MPH. "Diabetes and Decline in Heart Disease Mortality in US Adults." *Journal of the American Medical Association*. April 14, 1999.
[xviii] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 2.
[xix] Ibid.
[xx] Economic Consequences of Diabetes Mellitus in the U.S. in 1997. *Diabetes Care*, February 1998: 296-309.
[xxi] The World Almanac and Book of Facts: 1999. World Almanac Books.
[xxii] Department of Health and Human Services. February 23, 1998.
[xxiii] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 3.
[xxiv] "Biomedical Research Priorities: Who Should Decide?" Hearing before the Subcommittee on Public Health and Safety of the Committee on Labor and Human Resources, United States Senate. May 1, 1997, p. 8.
[xxv] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 3.
[xxvi] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 49.
[xxvii] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 3
[xxviii] Ibid.
[xxix] Ibid.
[xxx] Ibid.
[xxxi] Diabetes Research Working Group. 1999. Conquering Diabetes: A Strategic Plan for the 21st Century, p. 118.

Senate Permanent Subcommittee on Investigations
EXHIBIT # 9

AMERICAN ASSOCIATION OF DIABETES EDUCATORS
100 W. Monroe Street, 4th Floor, Chicago, Illinois 60603-1901 312/424-2426 Fax: 312/424-242

Testimony Submitted to the
United States Senate Permanent Subcommittee on Investigations
Public Hearing on Diabetes Research
October 14, 1999

Statement of the American Association of Diabetes

Senator Susan M. Collins; Chair
Senator Carl Levin; Ranking Member

The American Association of Diabetes Educators thanks you for the opportunity to furnish testimony for the record of this hearing of the Subcommittee on Investigations.

Who we are:

The *American Association of Diabetes Educators* is a multi-disciplinary organization of over 11,000 members, including nurses, dietitians, pharmacist, physicians, mental health professionals, and others. The mission of AADE is to *Advance the Role of the Diabetes Educator and Improve the Quality of Diabetes Education and Care.*

Why we are here:

We are here because we believe that the role and impact of diabetes education in diabetes care has long been held to be an integral intervention for successful outcomes, however it has been inadequately studied. In contrast, those who are developing models of healthcare delivery are challenging the need for educational services while they streamline care and reduce cost. It is important now that we examine educational interventions on their own and establish a sound scientific base for the practice of diabetes education if it to be embraced as a standard of care for diabetes.

Pivotal clinical research in diabetes care and its complications has provided little practical information on self-care interventions. The Diabetes Control and Complications Trial answered critical questions about diabetes management but left many unanswered questions about how patients were supported in their self care practices, and what providers and roles were critical for patients to be able to sustain excellent glucose control over an extended period of time. The recently completed trials in the United Kingdom barely addressed the issues of educational methods and provider skills.

The complexity and challenges of behavior change and diabetes self- management are not adequately appreciated. Simplistic educational services cannot achieve the same results as well designed programs and services provided by skilled educators. It has been a struggle to assure that education and behavioral care are included in national and organizational policies and guidelines.

Behavioral and educational research is slowly increasing. But evolution has been too slow.

What is needed:

We must define education and what educators do. Those who practice as Diabetes Educators are an increasingly diverse group with representation from a variety of professional and educational backgrounds, practice settings, ethnic groups, methods, and philosophies. The increasing variability may pose some difficulties in consistency of care and unity of practitioners. We must clarify expected skills and outcomes of practice. It is imperative that future research defines the core elements of quality education and practitioner skills.

The *American Association of Diabetes Educators* and partner diabetes organizations convened a *Educational and Behavioral Research Summit* in May 1999 to review the status of current research, identify gaps, and begin strategies to promote more studies that address key issues in diabetes education. The gaps in research that were identified include:

- Special populations such as children, adults, elderly
- Community based interventions
- Models of combined educational and behavioral methods
- Economic impact
- Adoption of self-care behavior in ethnic oriented learners, and learners with chronic disease.
- Enabling and blocking factors associated with adoption of self-care behavior.
- Studies of representative populations
- Literacy, gender, age, attitude, autonomy and cultures effect on health care behaviors related to chronic disease
- General aspects of behavior related to all chronic disease such as; context, quality of life, satisfaction, intent to change, coping, and social support.
- Outcomes research specifically measuring the effect of education and counseling

In general, we need larger longitudinal studies so that we can understand the most effective interventions for subgroups of learners. In particular we need to learn:

- how to sustain improvements following interventions.
- more about educational provider skills, therapeutic relationship, and the role of peer or community providers
- about the care team, provider communications, the effect of the setting, and the impact of the overlap of provider and health system.

Behavioral study designs must be improved so that the dollars spent result in useful quality information. Cost/benefit studies for educational interventions are also needed.

Research into Diabetes Education Fits into Existing Government Priorities:

We believe that education and adoption of self-care behaviors is a clearly cross cutting issue for the National Institutes of Health. Behavioral care is currently provided as a secondary and tertiary interventions for people with diabetes. However with our increased understanding of the insulin resistance syndrome, educational skills are and will increasingly be needed in primary prevention interventions at the point of obesity, insulin resistance and glucose intolerance where nutritional and activity behaviors are needed.

Barriers:
Significant barriers exist to research in diabetes education and behavior change. These barriers are both structural and institutional.

Infrastructure:
The problems of infrastructure for basic or clinical studies are doubled for those interested in careers in behavioral research. Training for investigators is needed. Centers of behavioral excellence could assist multiple institute initiatives. Educators are eager to assist with pilot and feasibility trials as exemplified by the response of over 250 sites to a recent request of our organization to participate in beta-testing an outcomes measurement tool for diabetes education. These are projects of the scope that busy clinicians can accommodate.

Science base:
Much more needs to be understood about the "complex interactions" between self care behaviors, and treatment recommendations for diabetes.

Volunteers:
Partnerships of our educational centers of excellence with behavioral scientists could enhance resource utilization, facilitate volunteer recruitment and provide "real world" test sites of the "unique and complex nature" of diabetes self care which can only be studied in humans affected by the disease and where models do not apply.

Use of science in other disease populations:
Diabetes care and education has provided positive examples for the management of other chronic diseases. Diabetes affects multiple organ systems, is lifelong and its care intrudes into all aspects of daily living. Successful intervention strategies may be useful in management of less demanding or less invasive disease states.

Applying state of the art methods:
As with clinical treatment, adoption of state of the art diabetes behavioral intervention is slow. We need to learn how to change educator/ provider behavior so that disparities between populations served are reduced.

What we will do as a volunteer association:

Not having large research dollars, AADE will continue to fund small, pilot and feasibility studies as resources permit. With clearer research priorities, our Foundation plans to direct research efforts towards the areas of need in the future. We will continue to educate our members on the utilization of research findings. But our practitioners need the science that only major studies can provide. We will continue to partner with others in the diabetes community to promote funding, training and dissemination of educational and behavioral research .Our goal is to provide evidence of the best methods for educating consumers and providers and the anticipated and predictable results of quality diabetes education.

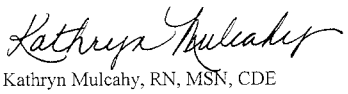
What government can do:

We would like to challenge the National Institutes of Health to apply the same standards and questions to issues of behavioral and educational science that are applied to disease research. Congress and the Administration can provide the large scale study grants directed at behavioral care. The Administration through its various healthcare and research agencies can create training opportunities. The Federal government can facilitate the research that allows our growing and changing population with diabetes, the self-care behaviors that prevent the worst effects of the disease.

We are on the cusp of the most exciting period of discovery into the role of behavioral and educational science in the treatment of diabetes. Research into behavior change and diabetes self-management and its benefits to people with diabetes is too important to shortchange. A fairer, more balanced approach to research for diabetes is needed to realize the potential of the opportunities that confront us.

We welcome the opportunity to work with the Chair and the Senators on the Subcommittee in meeting the challenges that face us.

Respectfully submitted,



Kathryn Mulcahy, RN, MSN, CDE
Immediate Past President

Senate Permanent Subcommittee
on Investigations

EXHIBIT # 10

Statement of
Arnauld E. Nicogossian, M.D.
Associate Administrator
Office of Life and Microgravity Sciences and Applications
National Aeronautics and Space Administration

Permanent Investigations Subcommittee
of the Senate Committee on Governmental Affairs

October 14, 1999

As a partner in NASA's Human Exploration and Development of Space (HEDS) Enterprise, Office of Life and Microgravity Sciences and Applications (OLMSA) seeks to increase commercial and scientific knowledge, to develop space for human enterprise, to effectively transfer knowledge and technologies to the private sector, and to improve the quality of life on Earth. As we move towards the utilization of the International Space Station (ISS), new opportunities for conducting research in space will become available to improve and expand knowledge, advance technology and research products in a wide range of disciplines. The experience gained in the past few years has helped us forge new domestic and international alliances both in academia and the commercial sector, as well as further develop our ground-based activities.

NASA's research and technology is not just about distant galaxies, astronauts and super-sonic aircraft. The science and engineering that make NASA's programs possible touch lives every day. This influence is most apparent in the field of medicine where innovative thinking has made it possible to adapt deep space technology to understanding diabetes. NASA's research is designed to learn how to fly higher and faster, and about how to live and work in space. Its application, however, often hits much closer to home.

NASA is providing this testimony to make the committee aware of NASA's ongoing contributions to biomedical research, and in particular, diabetes research. OLMSA contributes to Diabetes research through collaborations with the Juvenile Diabetes Foundation International (JDFI) and the National Institutes of Health.

JDFI/NASA/NIH Collaboration

The Juvenile Diabetes Foundation International (JDFI) and the National Aeronautics and Space Administration (NASA) are working to support research on diabetes and its devastating complications. The JDFI/NASA partnership was instituted in July 1997 under a Space Act Agreement to initiate joint research activities in the following areas: non-invasive glucose measurement/insulin delivery; islet cell growth/transplantation; and early detection of diabetes-related eye problems. By combining efforts, JDFI and NASA, may be able to stimulate research to overcome the many scientific obstacles faced in these areas.

JDF and NASA have instituted several joint workshops to focus the research communities on the central issues in diabetes research and to identify the cutting-edge technologies that could make a

difference in surmounting the obstacles to further progress. JDF and NASA collaborated with NIH Institutes 1 to sponsor a Workshop on Beta-Cell Replacement in Washington, DC on December 2-3,1997 (Beta-cells are the insulin-producing cells that are destroyed in individuals with Type 1 diabetes). In April, 1998, NASA, JDFI and the NIH sponsored a workshop entitled "Non-Invasive and Minimally Invasive Measurement Of Physiological Analytes. The sponsoring agencies sought technologies to improve or enable an ability to measure physiological analytes such as glucose levels without drawing blood. These technologies support both the goals of JDFI for glucose monitoring and of NASA for crew health care and biomedical research.

Finally, JDF and NASA collaborated with NIH Institutes (NIDDKD, NEI, NINDS) to sponsor a workshop on Diabetic Retinopathy in Washington, DC on March 30-31,1999. The meeting covered a variety of research areas and technologies including retinal imaging, screening, and early detection; compositional analysis of eye tissues, functional analysis of the retina; and novel therapies.

NASA/NIH Collaboration and NASA-developed Technology

The detrimental effects of diabetes include the formation of cataracts and diabetic retinopathy. NASA is currently working with the National Eye Institute (NEI) under an Interagency Agreement to apply a NASA-developed laser-light scattering instrument to the early detection of cataracts and other diabetes-related eye problems. The NASA probe was originally developed for space experiments on-board the Space Shuttle and is now being applied to study eye diseases in collaboration with NEI/NIH and the Food and Drug Administration (FDA). These studies are focused on non-invasive early diagnosis of cataracts and diabetic retinopathy. A new generation of probes based on NASA technology have been shown to detect a growing cataract at the molecular level; i.e., several orders of magnitude earlier than the current clinical capabilities. NASA has delivered and set up a compact laser-light scattering system in the laboratories of the NEI. This system will be used by NEI researchers in the characterization of lens proteins that lead to cataracts. Researchers are also using these probes to study the diabetic corneas. The probes should allow researchers to detect diabetic retinopathy non-invasively and quantitatively.

NASA Research

Although NASA does not have a federal diabetes research program, the agency does pursue a variety of research that may help to support the fight against diabetes. For example, NASA is sponsoring research in the areas of protein crystal growth and analysis, three-dimensional tissue culturing, and non-invasive detection of glucose that could support future therapeutic treatments. These efforts take advantage of NASA developed technologies and the unique environment of space to expand our knowledge and capabilities in fields relevant to diabetes treatment.

Space-grown protein crystals are improving our understanding of drugs that improve insulin delivery. Researchers use the crystals to produce detailed maps of the structures of insulin and certain drugs as they interact. This information is helping researchers develop improved formulations of insulin with better time-release characteristics.

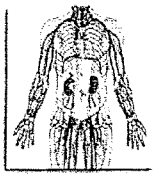
NASA is developing Raman Spectroscopy as a means for analyzing chemical compounds at low concentrations. This technology is being optimized and miniaturized at NASA microelectronics laboratories to support the search for life on other planets and for use in non-invasive health monitoring technology. NASA's Jet Propulsion Laboratory is conducting a four year program to develop a non-invasive glucose monitor based on Raman Spectroscopy. The monitor would shine a very low power laser light into a patient's eyes. Scattered light would then be collected and analyzed to provide an accurate estimate of the glucose level and the patient would see the a numeric readout of his or her glucose reading. If successfully developed, this system could improve care for more than 15 million diabetic patients in the U.S. In addition, such an instrument may also be used to monitor the levels of other physiologically important compounds in the body, providing an advanced new device for use in general health monitoring.

NASA recently signed a Cooperative Agreement with the Foundation for Transplantation Research to use NASA bioreactor technology to grow insulin producing cells outside the body for transplantation to treat diabetes. Research teams are using the NASA-developed bioreactor technology to culture human insulin-secreting pancreas cells which would then be encapsulated in special materials. The encapsulated cells would then be transplanted as a treatment for diabetes. This approach could replace insulin therapy by introducing functional insulin-secreting pancreatic tissue into patients with insulin-dependent diabetes.

For more information, contact Dr. Eugene Trinh, Director of OLMSA's Microgravity Research Division at 358-0649.

[1]National Eye Institute (NEI), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Child Health and Human Development (NICHD), National Institute of Neurological Disorders and Stroke (NINDS), National Center for Research Resources (NCRR)

Senate Permanent Subcommittee
on Investigations
EXHIBIT # 11



Diabetes Overview

NIDDK National Diabetes Information Clearinghouse

Publications

NIDDK

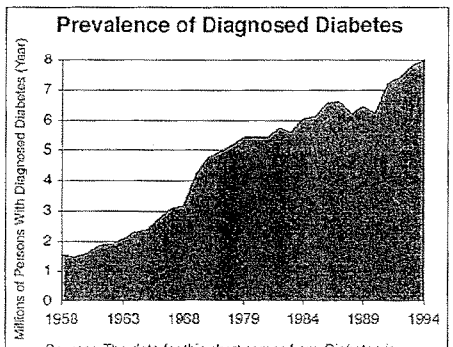
Also see:

Easy-to-Read
Do Your Level Best: Start Controlling Your Blood Sugar Today

- What Is Diabetes?
- What Are the Different Types of Diabetes?
- What Is the Scope and Impact of Diabetes?
- Who Gets Diabetes?
- How Is Diabetes Managed?
- What Is the Status of Diabetes Research?
- What Will the Future Bring?
- Where Is More Information Available?
- Points to Remember

Almost every one of us knows someone who has diabetes. An estimated 16 million people in the United States have diabetes mellitus--a serious, lifelong condition. About half of these people do not know they have diabetes and are not under care for the disorder. Each year, about 798,000 people are diagnosed with diabetes.

Although diabetes occurs most often in older adults, it is one of the most common chronic disorders in children in the United States. About 123,000 children and teenagers age 19 and younger have diabetes.



Source: The data for this chart comes from *Diabetes in America. 2nd Edition* (p. 63) by National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1995.

What Is Diabetes?

Diabetes is a disorder of metabolism--the way our bodies use digested food for growth and energy. Most of the food we eat is broken down by the digestive juices into a simple sugar called glucose. Glucose is the main source of fuel for the body.

After digestion, the glucose passes into our bloodstream where it is available for body cells to use for growth and energy. For the glucose to get into the cells, insulin must be present. Insulin is a hormone produced by the pancreas, a large gland behind the stomach.

When we eat, the pancreas is supposed to automatically produce the right amount of insulin to move the glucose from our blood into our cells. In people with diabetes, however, the pancreas either produces little or no insulin, or the body cells do not respond to the insulin that is produced. As a result, glucose builds up in the blood, overflows into the urine, and passes out of the body. Thus, the body loses its main source of fuel even though the blood contains large amounts of glucose.

What Are the Different Types of Diabetes?

The three main types of diabetes are

- Type 1 diabetes
- Type 2 diabetes
- Gestational diabetes.

Type 1 diabetes

Type 1 diabetes (once known as insulin-dependent diabetes mellitus or juvenile diabetes) is considered an autoimmune disease. An autoimmune disease results when the body's system for fighting infection (the immune system) turns against a part of the body. In diabetes, the immune system attacks the insulin-producing beta cells in the pancreas and destroys them. The pancreas then produces little or no insulin.

Someone with type 1 diabetes needs daily injections of insulin to live. At present, scientists do not know exactly what causes the body's immune system to attack the beta cells, but they believe that both genetic factors and viruses are involved. Type 1 diabetes accounts for about 5 to 10 percent of diagnosed diabetes in the United States.

Type 1 diabetes develops most often in children and young adults, but the disorder can appear at any age. Symptoms of type 1 diabetes usually develop over a short period, although beta cell destruction can begin years earlier.

Symptoms include increased thirst and urination, constant hunger, weight loss, blurred vision, and extreme tiredness. If not diagnosed and treated with insulin, a person can lapse into a life-threatening coma.

Type 2 diabetes

The most common form of diabetes is type 2 diabetes (once known as noninsulin-dependent diabetes mellitus or NIDDM). About 90 to 95 percent of people with diabetes have type 2 diabetes. This form of diabetes usually develops in adults over the age of 40 and is most common among adults over age 55. About 80 percent of people with type 2 diabetes are overweight.

In type 2 diabetes, the pancreas usually produces insulin, but for some reason, the body cannot use the insulin effectively. The end result is the same as for type 1 diabetes--an unhealthy buildup of glucose in the blood and an inability of the body to make efficient use of its main source of fuel.

The symptoms of type 2 diabetes develop gradually and are not as noticeable as in type 1 diabetes. Symptoms include feeling tired or ill, frequent urination (especially at night), unusual thirst, weight loss, blurred vision, frequent infections, and slow healing of sores.

Gestational Diabetes

Gestational diabetes develops or is discovered during pregnancy. This type usually disappears when the pregnancy is over, but women who have had gestational diabetes have a greater risk of developing type 2 diabetes later in their lives.

What Is the Scope and Impact of Diabetes?

Diabetes is widely recognized as one of the leading causes of death and disability in the United States. According to death certificate data, diabetes contributed to the deaths of more than 193,140 persons in 1996.

Diabetes is associated with long-term complications that affect almost every major part of the body. It contributes to blindness, heart disease, strokes, kidney failure, amputations, and nerve damage. Uncontrolled diabetes can complicate pregnancy, and birth defects are more common in babies born to women with diabetes.

Diabetes cost the United States $98 billion in 1997. Indirect costs, including disability payments, time lost from work, and premature death, totaled $54 billion; medical costs for diabetes care, including hospitalizations, medical care, and treatment supplies, totaled $44 billion.

Who Gets Diabetes?

Diabetes is not contagious. People cannot "catch" it from each other. However, certain factors can increase one's risk of developing diabetes. People who have family members with diabetes (especially type 2 diabetes), who are overweight, or who are African American, Hispanic, or Native American are all at greater risk of developing diabetes.

Type 1 diabetes occurs equally among males and females, but is more common in whites than in nonwhites. Data from the World Health Organization's Multinational Project for Childhood

Diabetes indicate that type 1 diabetes is rare in most Asian, African, and American Indian populations. On the other hand, some northern European countries, including Finland and Sweden, have high rates of type 1 diabetes. The reasons for these differences are not known.

Type 2 diabetes is more common in older people, especially older women who are overweight, and occurs more often among African Americans, Hispanics, and American Indians. Compared with non-Hispanic whites, diabetes rates are about 60 percent higher in African Americans and 110 to 120 percent higher in Mexican Americans and Puerto Ricans. American Indians have the highest rates of diabetes in the world. Among Pima Indians living in the United States, for example, half of all adults have type 2 diabetes. The prevalence of diabetes is likely to increase because older people, Hispanics, and other minority groups make up the fastest growing segments of the U.S. population.

How Is Diabetes Managed?

Before the discovery of insulin in 1921, all people with type 1 diabetes died within a few years after the appearance of the disease. Although insulin is not considered a cure for diabetes, its discovery was the first major breakthrough in diabetes treatment.

Today, daily injections of insulin are the basic therapy for type 1 diabetes. Insulin injections must be balanced with meals and daily activities, and glucose levels must be closely monitored through frequent blood sugar testing.

Diet, exercise, and blood testing for glucose are also the basis for management of type 2 diabetes. In addition, some people with type 2 diabetes take oral drugs or insulin to lower their blood glucose levels.

People with diabetes must take responsibility for their day-to-day care. Much of the daily care involves trying to keep blood sugar levels from going too low or too high. When blood sugar levels drop too low--a condition known as hypoglycemia--a person can become nervous, shaky, and confused. Judgment can be impaired. Eventually, the person could pass out. The treatment for low blood sugar is to eat or drink something with sugar in it.

On the other hand, a person can become very ill if blood sugar levels rise too high, a condition known as hyperglycemia. Hypoglycemia and hyperglycemia, which can occur in people with type 1 diabetes or type 2 diabetes, are both potentially life-threatening emergencies.

People with diabetes should be treated by a doctor who monitors their diabetes control and checks for complications. Doctors who specialize in diabetes are called endocrinologists or diabetologists. In addition, people with diabetes often see ophthalmologists for eye examinations, podiatrists for routine foot care, dietitians for help in planning meals, and diabetes educators for instruction in day-to-day care.

The goal of diabetes management is to keep blood glucose levels

as close to the normal (nondiabetic) range as safely possible. A recent Government study, sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), proved that keeping blood sugar levels as close to normal as safely possible reduces the risk of developing major complications of diabetes.

The 10-year study, called the Diabetes Control and Complications Trial (DCCT), was completed in 1993 and included 1,441 people with type 1 diabetes. The study compared the effect of two treatment approaches--intensive management and standard management--on the development and progression of eye, kidney, and nerve complications of diabetes. Researchers found that study participants who maintained lower levels of blood glucose through intensive management had significantly lower rates of these complications.

Researchers believe that DCCT findings have important implications for the treatment of type 2 diabetes, as well as type 1 diabetes.

What Is the Status of Diabetes Research?

NIDDK supports basic and clinical research in its own laboratories and in research centers and hospitals throughout the United States. It also gathers and analyzes statistics about diabetes. Other institutes at the National Institutes of Health also carry out research on diabetes-related eye diseases, heart and vascular complications, pregnancy, and dental problems.

Other Government agencies that sponsor diabetes programs are the Centers for Disease Control and Prevention, the Indian Health Service, the Health Resources and Services Administration, the Bureau of Veterans Affairs, and the Department of Defense.

Many organizations outside of the Government support diabetes research and education activities. These organizations include the American Diabetes Association, the Juvenile Diabetes Foundation International, and the American Association of Diabetes Educators.

In recent years, advances in diabetes research have led to better ways to manage diabetes and treat its complications. Major advances include:

- New forms of purified insulin, such as human insulin produced through genetic engineering.
- Better ways for doctors to monitor blood glucose levels and for people with diabetes to test their own blood glucose levels at home.
- Development of external and implantable insulin pumps that deliver appropriate amounts of insulin, replacing daily injections.
- Laser treatment for diabetic eye disease, reducing the risk of blindness.
- Successful transplantation of kidneys in people whose own kidneys fail because of diabetes.
- Better ways of managing diabetic pregnancies, improving

chances of successful outcomes.

- New drugs to treat type 2 diabetes and better ways to manage this form of diabetes through weight control.
- Evidence that intensive management of blood glucose reduces and may prevent development of microvascular complications of diabetes.
- Demonstration that antihypertensive drugs called ACE-inhibitors prevent or delay kidney failure in people with diabetes.

What Will the Future Bring?

In the future, it may be possible to administer insulin through nasal sprays or in the form of a pill or patch. Devices that can "read" blood glucose levels without having to prick a finger to get a blood sample are also being developed.

Researchers continue to search for the cause or causes of diabetes and ways to prevent and cure the disorder. Scientists are looking for genes that may be involved in type 2 diabetes and type 1 diabetes. Some genetic markers for type 1 diabetes have been identified, and it is now possible to screen relatives of people with type 1 diabetes to see if they are at risk for diabetes.

The new Diabetes Prevention Trial-- type 1 diabetes, sponsored by NIDDK, identifies relatives at risk for developing type 1 diabetes and treats them with low doses of insulin or with oral insulin-like agents in the hope of preventing type 1 diabetes. Similar research is carried out at other medical centers throughout the world.

Transplantation of the pancreas or insulin-producing beta cells offers the best hope of cure for people with type 1 diabetes. Some pancreas transplants have been successful. However, people who have transplants must take powerful drugs to prevent rejection of the transplanted organ. These drugs are costly and may eventually cause serious health problems.

Scientists are working to develop less harmful drugs and better methods of transplanting pancreatic tissue to prevent rejection by the body. Using techniques of bioengineering, researchers are also trying to create artificial islet cells that secrete insulin in response to increased sugar levels in the blood.

For type 2 diabetes, the focus is on ways to prevent diabetes. Preventive approaches include identifying people at high risk for the disorder and encouraging them to lose weight, exercise more, and follow a healthy diet. The Diabetes Prevention Program, another new NIDDK project, will focus on preventing the disorder in high-risk populations.

Where Is More Information Available?

For more information about type 1 diabetes, type 2 diabetes, and gestational diabetes, as well as diabetes research, statistics, and education, contact:

National Diabetes Information Clearinghouse

1 Information Way
Bethesda, MD 20892-3560
(301) 654-3327.

The following organizations also distribute materials and support programs for people with diabetes and their families and friends:

American Association of Diabetes Educators
100 West Monroe Street, 4th Floor
Chicago, IL 60603
(800) 338-3633 or (312) 424-2426
www.aadenet.org

American Diabetes Association
ADA National Service Center
1660 Duke Street
Alexandria, VA 22314
(800) 232-3472
(703) 549-1500

Juvenile Diabetes Foundation International
120 Wall Street, 19th Floor
New York, NY 10005
(800) 223-1138
(212) 785-9500.

Points to Remember

What Is Diabetes?

- A disorder of metabolism--the way the body digests food for energy and growth.

What Are the Different Types of Diabetes?

- Type 1 diabetes
- Type 2 diabetes
- Gestational diabetes.

What Is the Scope and Impact of Diabetes?

- Affects 16 million people
- A leading cause of death and disability
- Costs $98 billion per year.

Who Gets Diabetes?

- People of any age
- More common in older people, African Americans, Hispanics, and American Indians.

National Diabetes Information Clearinghouse

1 Information Way

Bethesda, MD 20892-3560
E-mail: ndic@info.niddk.nih.gov

The National Diabetes Information Clearinghouse (NDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health under the U.S. Department of Health and Human Services. Established in 1978, the clearinghouse provides information about diabetes to people with diabetes and their families, health care professionals, and the public. NDIC answers inquiries; develops, reviews, and distributes publications; and works closely with professional and patient organizations and government agencies to coordinate resources about diabetes.

Publications produced by the clearinghouse are reviewed carefully for scientific accuracy, content, and readability.

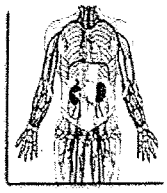
This e-text is not copyrighted. The clearinghouse encourages users of this e-pub to duplicate and distribute as many copies as desired.

Publications

NIDDK

NIH Publication No. 96-3873
November 1998

e-text last updated: 14 June 1999



Diabetes Statistics

NIDDK National Diabetes Information Clearinghouse

Publications

NIDDK

- What is diabetes?
- Prevalence of diabetes
- Incidence of diabetes
- Deaths among people with diabetes
- Prevalence of diabetes by age
- Prevalence of diabetes by sex in people 20 years or older
- Prevalence of diabetes by race/ethnicity in people 20 years or older
- The four types of diabetes
- Complications of diabetes
- Cost
- New diagnostic criteria for diabetes
- Treatment of diabetes
- Impaired fasting glucose
- Appendix
- References
- Acknowledgments

What is diabetes?

Diabetes mellitus is a group of diseases characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Diabetes can be associated with serious complications and premature death, but people with diabetes can take measures to reduce the likelihood of such occurrences.

Prevalence of diabetes*

Total: 15.7 million people--5.9 percent of the population--have diabetes.

Diagnosed: 10.3 million people
Undiagnosed: 5.4 million people

* For further information on prevalence, see the Appendix.

Incidence of diabetes

New cases diagnosed per year: 798,000.

Deaths among people with diabetes

- Studies have found death rates to be twice as high among middle-aged people with diabetes as among middle-aged people without diabetes.
- Based on death certificate data, diabetes contributed to

193,140 deaths in 1996.

- Diabetes was the seventh leading cause of death listed on U.S. death certificates in 1996.
- Diabetes is believed to be underreported on death certificates, both as a condition and as a cause of death.

Prevalence of diabetes by age

Age 65 years or older: 6.3 million. 18.4 percent of all people in this age group have diabetes.

Age 20 years or older: 15.6 million. 8.2 percent of all people in this age group have diabetes.

Under age 20: 123,000. 0.16 percent of all people in this age group have diabetes.

Prevalence of diabetes by sex in people 20 years or older*

Men: 7.5 million. 8.2 percent of all men have diabetes.

Women: 8.1 million. 8.2 percent of all women have diabetes.

*These figures do not include the approximately 123,000 cases of diabetes in children and teenagers in the United States.

Prevalence of diabetes by race/ethnicity in people 20 years or older

Non-Hispanic whites: 11.3 million. 7.8 percent of all non-Hispanic whites have diabetes.

Non-Hispanic blacks: 2.3 million. 10.8 percent of all non-Hispanic blacks have diabetes. On average, non-Hispanic blacks are 1.7 times as likely to have diabetes as non-Hispanic whites of similar age.

Mexican Americans: 1.2 million. 10.6 percent of all Mexican Americans have diabetes. On average, Mexican Americans are 1.9 times as likely to have diabetes as non-Hispanic whites of similar age.

Other Hispanic/Latino Americans: On average, Hispanic/Latino Americans are almost twice as likely to have diabetes as non-Hispanic whites of similar age. (Sufficient data are not currently available to derive more specific estimates.)

American Indians and Alaska Natives: 9 percent of American Indians and Alaska Natives have diagnosed diabetes. On average, American Indians and Alaska Natives are 2.8 times as likely to have diagnosed diabetes as non-Hispanic whites of similar age.

Asian Americans and Pacific Islanders: Prevalence data for diabetes among Asian Americans and Pacific Islanders are limited. Some groups within this population are at increased risk for diabetes. For example, data collected from 1988 to 1995 suggest that Native Hawaiians are twice as likely to have diagnosed diabetes as white residents of Hawaii.

The four types of diabetes

Type 1 diabetes was previously called insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes. Type 1 diabetes may account for 5 to 10 percent of all diagnosed cases of diabetes. Risk factors are less well defined for type 1 diabetes than for type 2 diabetes, but autoimmune, genetic, and environmental factors are involved in the development of this type of diabetes.

Type 2 diabetes was previously called non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes. Type 2 diabetes may account for about 90 to 95 percent of all diagnosed cases of diabetes. Risk factors for type 2 diabetes include older age, obesity, family history of diabetes, prior history of gestational diabetes, impaired glucose tolerance, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans and Pacific Islanders are at particularly high risk for type 2 diabetes.

Gestational diabetes develops in 2 to 5 percent of all pregnancies but disappears when a pregnancy is over. Gestational diabetes occurs more frequently in African Americans, Hispanic/Latino Americans, American Indians, and persons with a family history of diabetes. Obesity is also associated with higher risk. Women who have had gestational diabetes are at increased risk for later developing type 2 diabetes. In some studies, nearly 40 percent of women with a history of gestational diabetes developed diabetes in the future.

"Other specific types" of diabetes result from specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses. Such types of diabetes may account for 1 to 2 percent of all diagnosed cases of diabetes.

Complications of diabetes

Heart disease

- Heart disease is the leading cause of diabetes-related deaths. Adults with diabetes have heart disease death rates about 2 to 4 times higher than those of adults without diabetes.

Stroke

- The risk of stroke is 2 to 4 times higher in people with diabetes.

High blood pressure

- An estimated 60 to 65 percent of people with diabetes have high blood pressure.

Blindness

- Diabetes is the leading cause of new cases of blindness in adults 20 to 74 years old.
- Diabetic retinopathy causes from 12,000 to 24,000 new

cases of blindness each year.

Kidney disease

- Diabetes is the leading cause of end-stage renal disease, accounting for about 40 percent of new cases.
- 27,851 people with diabetes developed end-stage renal disease in 1995.
- In 1995, a total of 98,872 people with diabetes underwent dialysis or kidney transplantation.

Nervous system disease

- About 60 to 70 percent of people with diabetes have mild to severe forms of nervous system damage (which often includes impaired sensation or pain in the feet or hands, slowed digestion of food in the stomach, carpal tunnel syndrome, and other nerve problems).
- Severe forms of diabetic nerve disease are a major contributing cause of lower extremity amputations.

Amputations

- More than half of lower limb amputations in the United States occur among people with diabetes.
- From 1993 to 1995, about 67,000 amputations were performed each year among people with diabetes.

Dental disease

- Periodontal disease (a type of gum disease that can lead to tooth loss) occurs with greater frequency and severity among people with diabetes. Periodontal disease has been reported to occur among 30 percent of people age 19 years or older with type 1 diabetes.

Complications of pregnancy

- The rate of major congenital malformations in babies born to women with preexisting diabetes varies from 0 to 5 percent among women who receive preconception care to 10 percent among women who do not receive preconception care.
- Between 3 and 5 percent of pregnancies among women with diabetes result in death of the newborn; the rate for women who do not have diabetes is 1.5 percent.

Other complications

- Diabetes can directly cause acute life-threatening events, such as diabetic ketoacidosis* and hyperosmolar nonketotic coma.*
- People with diabetes are more susceptible to many other illnesses. For example, they are more likely to die of pneumonia or influenza than people who do not have diabetes.

*Diabetic ketoacidosis and hyperosmolar nonketotic coma are medical

conditions that can result from biochemical imbalance in uncontrolled diabetes.

Cost

Total (direct and indirect): $98 billion (United States, 1997).

Direct medical costs: $44 billion.

Indirect costs: $54 billion (disability, work loss, premature mortality).

This estimate, provided by the American Diabetes Association, is in contrast to higher estimates cited elsewhere that are based on all health care costs incurred by people with diabetes, including costs not resulting from diabetes.

New diagnostic criteria for diabetes*

The new diagnostic criteria for diabetes include the following changes:

- The routine diagnostic test for diabetes is now a fasting plasma glucose test rather than the previously recommended oral glucose tolerance test. (However, in certain clinical circumstances, physicians may still choose to perform the oral glucose tolerance test.)
- A confirmed** fasting plasma glucose value of greater than or equal to 126 milligrams/deciliter (mg/dL) indicates a diagnosis of diabetes. Previously, a value of greater than or equal to 140 mg/dL had been required for diagnosis.
- In the presence of symptoms of diabetes, a confirmed** nonfasting plasma glucose value of greater than or equal to 200 mg/dL indicates a diagnosis of diabetes.
- When a doctor chooses to perform an oral glucose tolerance test (by administering 75 grams of anhydrous glucose dissolved in water, in accordance with World Health Organization standards, and then measuring the plasma glucose concentration 2 hours later), a confirmed** glucose value of greater than or equal to 200 mg/dL indicates a diagnosis of diabetes.

In pregnant women, different requirements are used to identify the presence of gestational diabetes.

*For further information about the new diagnostic criteria for diabetes, please see the "Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus," in the References.

** Except in certain specified circumstances, abnormal tests must be confirmed by repeat testing on another day.

Treatment of diabetes

Diabetes knowledge, treatment, and prevention strategies advance daily. Treatment is aimed at keeping blood glucose near normal levels at all times. Training in self-management is integral to the treatment of diabetes. Treatment must be individualized and must

address medical, psychosocial, and lifestyle issues.

- **Treatment of type 1 diabetes:** Lack of insulin production by the pancreas makes type 1 diabetes particularly difficult to control. Treatment requires a strict regimen that typically includes a carefully calculated diet, planned physical activity, home blood glucose testing several times a day, and multiple daily insulin injections.

- **Treatment of type 2 diabetes:** Treatment typically includes diet control, exercise, home blood glucose testing, and often requiring oral medication and/or insulin. Approximately 40 percent of people with type 2 diabetes require insulin injections.

Impaired fasting glucose

Impaired fasting glucose is a new diagnostic category in which persons have fasting plasma glucose values of 110–125 mg/dL. These glucose values are greater than the level considered normal but less than the level that is diagnostic of diabetes. It is estimated that 13.4 million adults, 7.0 percent of this population, have impaired fasting glucose. Scientists are trying to learn how to predict which of these persons will go on to develop diabetes and how to prevent such progression.

Appendix

How were the estimates in this fact sheet derived?
Periodically, the Federal Government conducts surveys to determine the health of Americans. Such surveys involve questionnaires and medical tests. Most of the diabetes prevalence and incidence estimates presented in this fact sheet were developed by analyzing the newest available national survey data and then adjusting for changes in the population based on 1997 census estimates. The prevalence of diagnosed diabetes represents the number who said they had diabetes. The prevalence of undiagnosed diabetes represents the number of people who said they did not have diabetes, but when given a fasting plasma glucose test, they did in fact have abnormally elevated blood glucose levels (defined as fasting plasma glucose levels greater than or equal to 126 mg/dL). Other estimates presented in this fact sheet were based on individual surveys, research projects, and registry data. A listing of references and additional data sources is below. Most of the national diabetes prevalence estimates are based on Harris MI, et al.

Has the number of persons with diabetes changed since the Diabetes Statistics Fact Sheet issued in 1995?
Between the 1995 and 1997 fact sheets, the number of persons with diagnosed diabetes increased from 8 million to 10.3 million, but the number of persons with undiagnosed diabetes decreased. For the 1995 Diabetes Statistics Fact Sheet, the number of persons with undiagnosed diabetes was estimated from research using the oral glucose tolerance test to identify undiagnosed diabetes. In contrast, for the present Diabetes Statistics Fact Sheet, the number of persons with undiagnosed diabetes was estimated from research using the fasting plasma glucose test, according to recently enacted

recommendations. These tests are not equivalent, however, and fewer cases of undiagnosed diabetes are identified using the fasting plasma glucose test.

An enhanced national effort to identify previously undiagnosed persons may also have contributed to a decrease in the number of persons with undiagnosed diabetes. Continued efforts to identify persons with undiagnosed diabetes, the implementation of new guidelines for screening, and the use of an easier and less expensive diagnostic test are all likely to lead to even further decreases in the number of persons with undiagnosed diabetes and increases in the number of persons with diagnosed diabetes.

References

American Diabetes Association. Economic consequences of diabetes mellitus in the U.S. in 1997. *Diabetes Care* 1998; 21(2): 296–309.

Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. *Diabetes Care* 1998; 21(4): 518–524.

National Diabetes Data Group, National Institutes of Health. *Diabetes in America*, 2nd Edition. Bethesda, MD: National Institutes of Health, 1995. NIH Publication No. 95-1468.

Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997; 20(7):1183–97.

U.S. Department of Health and Human Services. *Physical Activity and Health: A Report of the Surgeon General.* Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.

U.S. Renal Data System. USRDS 1997 *Annual Data Report.* Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1997.

Acknowledgments

The following organizations collaborated in compiling the information for this fact sheet:

American Association of Diabetes Educators
http://www.aadenet.org

American Diabetes Association
http://www.diabetes.org

Centers for Disease Control and Prevention
http://www.cdc.gov/diabetes
http://www.cdc.gov/nchswww

Department of Veterans Affairs

http://www.va.gov/health/diabetes

Health Resources and Services Administration
http://www.hrsa.dhhs.gov

Indian Health Service
http://www.ihs.gov

Juvenile Diabetes Foundation International
http://www.jdfcure.org

National Diabetes Education Program: A joint program of NIH & CDC
http://ndep.nih.gov
http://www.cdc.gov/diabetes

National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health
http://www.niddk.nih.gov

U.S. Department of Health and Human Services Office of Minority Health
http://www.omhrc.gov

National Council of La Raza
http://www.nclr.org

National Diabetes Information Clearinghouse

1 Information Way
Bethesda, MD 20892–3560
E-mail: ndic@info.niddk.nih.gov

The National Diabetes Information Clearinghouse (NDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). NIDDK is part of the National Institutes of Health under the U.S. Department of Health and Human Services. Established in 1978, the clearinghouse provides information about diabetes to people with diabetes and their families, health care professionals, and the public. NDIC answers inquiries; develops, reviews, and distributes publications; and works closely with professional and patient organizations and Government agencies to coordinate resources about diabetes.

Publications produced by the clearinghouse are reviewed carefully for scientific accuracy, content, and readability.

This e-text is not copyrighted. The clearinghouse encourages users of this e-pub to duplicate and distribute as many copies as desired.

Senate Permanent Subcommittee on Investigations
EXHIBIT # 12

The Vision Of Pam Fernandes

Pam Fernandes' message: Don't let your disease or its complications dictate your attitudes about life.

By Marcia Levine Mazur

"Don't make this a pity party," pleads Pam Fernandes of Needham, Mass., an energetic 37-year-old who radiates a joy of life.

Still, it's difficult not to picture Pam on that September day in 1979 when—like thousands of others—she visited her doctor for a routine pre-college physical.

Unlike the others, however, Pam's examination was far from routine. The news was, in fact, astounding. She was going blind. She had one year of sight left, maybe two. Frightening new words were suddenly added to her vocabulary: retinopathy, hemorrhaging, laser treatments.

continued on page 48

continued from page 46

Fourteen years of diabetes—years when diabetes management was more mystery than science—had taken its toll.

She had been diagnosed with type 1 diabetes when she was four.

That was back in the '60s, when blood sugars were gauged by imprecise urine tests and a diabetic diet had little resemblance to the all-encompassing healthy food plan of the '90s. Peanut butter-and-jelly sandwiches, for example, were forbidden. ("Too much sugar.") Pam has still never had one.

Worse: Few people had even heard of a diabetes specialist, let alone visited one. And self-monitoring blood glucose at home seemed a distant fantasy.

Kids probably suffered most. "Don't forget, this was 37 years ago, and although my mom was a nurse and understood that children should be involved in their own diabetes care, there were few resources intended specifically for the child with diabetes," Pam explains.

"A tandem bike is **perfect** for a blind person."

Nothing Hurt

For unknown reasons, the lack of modern diabetes treatment took a particularly heavy toll on Pam. Still, she grew up loving sports, and her world fairly glowed when she made her high school basketball and softball varsity teams.

Then she packed her bags for college, saw her doctor, and discovered the price she'd paid for not being able to track her daily blood sugars or understand the interplay of insulin, diet, and exercise.

"The real shock was that nothing hurt," Pam recalls. "I even had 20/20 vision. Most of my body was functioning perfectly. Only I was going blind."

Were there treatments doctors

A "Q & A" With Pam Fernandes

Q How difficult is it for a blind person to become a world-class tandem cyclist, especially one with have diabetes?

A You might think blindness is my major problem as a bike rider. But it's not. The diabetes is. My blindness is always the same, but my blood sugars vary with travel, tough races, and arduous workouts. That's what demands my attention.

Q Do you carry anything for your diabetes control when you ride?

A I have water as well as glucose in the form of power gels with me when I *race*. But when I *train*, I also carry my glucose meter and insulin.

On a training ride if I don't feel good, I always stop. In a race, I keep going. If you stop in a race, you lose, and I don't plan to be a loser.

Q Do you give yourself an insulin injection before a race?

A When I hang around, stretching, warming up, waiting maybe four hours for my race to begin, I take insulin if I need it. But I try to work it so I am not eating or taking insulin close to race time.

Q How often do you test your blood sugar on race days?

A Generally, I test four to six times a day, but on race days I have been known to test up to 12 times. I think not knowing your blood sugar is like playing Russian roulette with your diabetes.

Q Do you eat before a race?

A I don't like to eat too close to a race. I don't want to feel full. You can get a very unsettled stomach if you are very physical when you're full.

Q How long does a race last?

A On a velodrome—that's an embanked bike-racing track—the race might be as quick as 11 seconds or as long as my longest velodrome race, about 4 minutes.

On the road, my shortest race would be about 30 to 40 minutes, and my longest would be about 2½ hours. They run the gamut, though, which makes it hard to train and monitor your blood sugars for each race.

Q How fast do you go?

A On the velodrome, I race between 35 and 40 miles an hour.

On the road, it's very different, of course, depending on whether it's downhill, uphill, or flat. The maximum speed I've ever done outside was in the desert going downhill with a tailwind. It was 65 mph. That's very, very fast for anyone on a tandem bike.

Q When do you train?

A I am a full-time athlete and I train year-round. In winter, I ride outdoors two days a week and weight train. In nice weather, I ride outdoors five or six days a week.

Of course, I have many understanding people who help me, including my pilot, Kenny Williams, who is a world-class rider and an awesome person.

—MLM

could try? Yes, painful three-hour eye exams and massive laser surgeries—1,195 laser "zaps" in one eye alone. But none of them helped.

Still, neither the diagnosis nor the treatments stopped the determined 19-year-old and she enrolled in the freshman class of Boston's Wheelock College as planned.

But even as she was working towards her degree, the predictions proved accurate. The right eye went first, then the left, and in her sophomore year—at age 21—Pam Fernandes was legally blind.

Quit school? No way.

She learned braille, continued to control her diabetes, and earned a BA in education. After graduating (she received a standing ovation), Pam went to work for the Massachusetts Association for the Blind.

More bad news. Her kidneys, which had given her some trouble in college, now failed completely. As a result, Pam was forced to undergo dialysis three times a week.

Even then, she helped found the "Team With A Vision," composed of blind and sighted runners who still compete in the Boston Marathon to raise money for the Massachusetts Association for the Blind. She considers this one of her greatest accomplishments.

Transplant

At age 27, five years after she'd gone on dialysis, Pam had enough. She decided on a kidney transplant.

That was an especially difficult decision for her and for the Fernandes family, because her older brother Mark—the only one of her six siblings to be diagnosed with type 1 diabetes—had also had a kidney transplant. And he was not doing too well. (Mark passed away several years later.)

Pam's surgery, however, was a resounding success.

Less than two months after she left the hospital, she was overflowing with energy and the joy of being forever free of the dialysis treatments. Charging back into the athletic life, she participated in walk-a-thons, road races, and any other athletic activities she could manage.

Then, four years later, Pam's world changed as Lady Luck provided her a whole new roll of the dice. Or perhaps "turn of the wheel" is more accurate.

Bicycle Built For Two

A civil engineer who had built a tandem bike wanted to test it with a blind person on the back. Pam agreed to be the guinea pig, and climbed aboard.

For world-class athlete Pam Fernandes, nothing equals the joy of riding a bike.

In her heart, she has never gotten off; Pam had found her joy.

"A tandem bike is perfect for a blind person," she explains. "You are the stoker, that is, the person in back, which means you pedal but you don't steer. The pilot in front does that.

"Of course, the two of you have to pedal in unison, and there must be a strong bond of trust between you," she adds.

Pam quickly moved into tandem bike competition and has practically set the pace for the sport. She's been in more than 90 races, and won more prizes, awards, and honors than she cares to mention. She was named

Pam was named 1994 U.S. Olympic Committee Athlete of the Year in the category of Disabled in Sports: Blind Athletes.

TOUR DE CURE

Pam Fernandes, international tandem bike-racing champion, is the national honorary spokesperson for the American Diabetes Association's year 2000 Tour de Cure, among the Association's premier fundraising events.

The Tour de Cure events will be held in selected areas across the country between April and June next year. For more information on how you can pedal your way in your local Tour de Cure, call 1-888-DIABETES.

1994 U.S. Olympic Committee Athlete of the Year in the category of Disabled in Sports; Blind Athletes.

She is a four-time national champion of the United States Association of Blind Athletes in tandem cycling.

The sport even introduced her to her husband, Paul Miller, also an avid cyclist. Pam recalls, "We were on a casual group bike ride, riding on tandems side by side. He had his son, Andrew, on the back. We hit it off right away. Paul didn't even know I was blind at first, and he has certainly never considered me disabled."

Pam and Paul are now married and live in Needham, Mass., with Andrew.

Australia, Here I Come

Pam has not slowed down.

A bronze medallist in the 1996 International Paralympic Games, she is now training for gold in the year 2000 Paralympic Games in Sydney.

The Paralympic Games are held in conjunction with the Olympics, but are for people with physical disabilities. Like the Olympics, the Paralympics rank among the world's major athletic events.

Teaching, Talking

Pam feels that her real calling lies in another area. She has a need to teach, talk, and tell people about diabetes. "They really understand what this disease is about when I tell them my own experiences," she says.

"I have spoken in front of many organizations, including Congress. I tell everyone that it will take all of us to win the war against diabetes: Congress, researchers, fundraisers, doctors, educators, and the families of people with diabetes."

She adds, "Being able to bring this message to groups all over the country is a mission, a passion for me. I consider it a gift to be able to do it."

Loving Life

"So, don't waste any pity on me," Pam concludes. "This is a triumphant, not a sad, story. I am doing what I love to do, racing tandem and educating people."

To those with diabetes, she adds, "We *will* have a cure one day, but don't wait for it. Make the most of your life today. Don't let your disease or complications define you. And never forget the incredible control you can have over your own diabetes.

"As for me," she says, "I am in the best health I have ever known and living the happiest years of my life." ▲

Marcia Levine Mazur is senior editor of Diabetes Forecast.

Talking Book Program Offers *Diabetes Forecast* On Disc

Free subscriptions to *Diabetes Forecast*, including articles, but not advertisements, are available on a talking book disc at the National Library Service for the Blind and Physically Handicapped of the Library of Congress. However, you must be enrolled in the talking book program to obtain the discs.

The Library provides the *Forecast* disc within a few weeks of publication, as well as a record player free of charge to anyone who cannot read standard print because of a permanent or temporary visual or physical disability.

For more information about eligibility, and the location of your closest public library with this service, call (202) 707-5100 or (800) 424-8567. You can also e-mail the program at nls@loc.gov or visit their Web site at http://www.loc.gov/nls.