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JUVENILE DIABETES: EXAMINING THE PERSONAL TOLL ON FAMILIES, FINANCIAL COSTS TO THE FEDERAL HEALTH CARE SYSTEM, AND RESEARCH PROGRESS TOWARD A CURE

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COMMITTEE ON GOVERNMENTAL AFFAIRS UNITED STATES SENATE

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TUESDAY, JUNE 24, 2003

U.S. SENATE,
COMMITTEE ON GOVERNMENTAL AFFAIRS,
Washington, DC.

The Committee met, pursuant to notice, at 10:05 a.m., in room SH–216, Hart Senate Office Building, Hon. Susan M. Collins, Chairman of the Committee, presiding.

Present: Senators Collins, Coleman, Specter, Bennett, Fitzgerald, Durbin, Lautenberg, and Pryor.

Also Present: Senator Nelson.

OPENING STATEMENT OF CHAIRMAN COLLINS

Chairman COLLINS. The Committee will come to order.

Good morning. Good morning particularly to all the children who have joined us from around the country today. We are so glad to have you here.

As one of the co-Chairs of the Juvenile Diabetes Research Foundation's 2003 Children's Congress, I am very pleased this morning to hold this hearing to examine the devastating impact that juvenile diabetes has had on American children and their families. In addition to hearing about the personal toll that this disease imposes, we will also take a look at the tremendous economic costs to our Federal health programs of caring for people with diabetes. And, finally, we will discuss the promising breakthroughs in juvenile diabetes research that holds such hope for a cure. Particularly, we will examine pancreatic islet cell transplantation.

The work that I have done in the Senate on behalf of the 17 million Americans with diabetes has been truly rewarding. It has been a privilege to work with the families, with the Juvenile Diabetes Research Foundation, whose commitment to finding a cure for this serious disease is truly inspiring. I want to welcome our distinguished witnesses today, but especially the 188 delegates to the Children's Congress. They have traveled to Washington from every State in the Union to tell us what it is like to have diabetes, just how serious the disease is, and how important it is that we fund the research necessary to find a cure.

I particularly want to welcome the delegate from my home State of Maine, 16-year-old Katie Halasz of Wells. Katie will be testifying

on our second panel this morning, and I am looking forward to her testimony.

As the founder and the co-Chair of the Senate Diabetes Caucus, I have learned a great deal about this disease and the difficulties and heartbreak that it causes for so many American families as they await a cure. Diabetes is a devastating, lifelong condition that affects people of every race, every age, and every nationality. It is the leading cause of kidney failure, blindness in adults, and amputations not related to injury.

A study released by the American Diabetes Association earlier this year estimates that diabetes cost the Nation $132 billion in health care costs last year and that health spending for people with diabetes is almost double what it would be if they did not have diabetes.

When I met with Katie yesterday, she gave me a nice photograph album telling about her family and her battle with diabetes. And I was amazed when she showed me this picture of just 1 month's supply of the medical devices and syringes and insulin that she needs to keep healthy. And she told me that it costs her family $2,000 a month for those supplies. That really hit home to me, the cost of treating people with diabetes and keeping children like Katie healthy.

The statistics are truly overwhelming, but what really prompted me to begin working on this issue was meeting more and more people like our delegates and their families today whose lives have been forever changed by diabetes. And that is why I want to say to all the children, it is so important that you traveled here to Washington today to tell your personal stories. You put the human faces on all of these statistics. You are more effective than any adult lobbyist could ever be, with the exception of, of course, Mary Tyler Moore. [Laughter.]

You help us focus on what Congress can do to better understand and ultimately conquer this terrible disease. And I know that the burden of diabetes is particularly heavy for children and young adults with type 1 or juvenile diabetes. Juvenile diabetes is the second most common chronic disease affecting children. Moreover, it is a disease that you never outgrow.

In individuals with juvenile diabetes, the body's immune system attacks the pancreas and destroys the islet cells that produce insulin. While the discovery of insulin was a landmark breakthrough in the treatment of people with diabetes, it unfortunately is not a cure. And people with juvenile diabetes face the constant threat of developing life-threatening complications as well as a dramatic reduction in their quality of life.

But thankfully, there is good news for people with diabetes. We have seen some tremendous breakthroughs in recent years in diabetes research, and I am convinced that diabetes is a disease that can be cured and will be cured.

[Applause.]

All of us have been encouraged by the development of the Edmonton Protocol, an experimental treatment developed at the University of Alberta involving the transplantation of insulin-producing pancreatic islet cells. This protocol has been hailed as the

most important advance in diabetes research since the discovery of insulin in 1921.

Of the 257 patients who have been treated, all have seen a reversal of their life-disabling hypoglycemia and 80 percent have maintained normal glucose levels without insulin shots for more than a year. Amazingly, many of the transplant recipients have even reported a reversal in some of their complications, such as improved vision and less pain from neuropathy.

Earlier this year, I joined my colleague from Washington State, Senator Patty Murray, as well as my colleague and co-Chair of the Senate Diabetes Caucus, Senator Breaux, in introducing the Pancreatic Islet Cell Transplantation Act of 2003. This will help to advance the significant research that holds the promise of a cure for more than 1 million Americans with juvenile diabetes. We now have 39 Senate cosponsors, and you can help me get even more cosponsors in your visits to Hill offices today.

Before turning to my colleagues for their opening statements, I want to welcome Representative Diana DeGette of Colorado, who I believe is here today with her daughter. Diana serves as the co-Chair, along with George Nethercutt, of the House Diabetes Caucus, and it was the House Diabetes Caucus that motivated Senator Breaux and myself to establish the Senate Diabetes Caucus. So I want to welcome the Congresswoman and her daughter, Frannie, who is a delegate to the Children's Congress, to the Committee hearing today.

Again, it is wonderful to have all the children here today. I know that your slogan is "Promise to Remember Me." I want to tell you that when I see your faces, I know all of us do promise to remember you and to fight for the research funding that will produce a cure.

I would now like to call on my colleague, Senator Pryor, for any opening remarks that he might have, and thank you for joining us today.

OPENING STATEMENT OF SENATOR PRYOR

Senator PRYOR. Thank you, Madam Chairman.

I want everybody in this room to know what a great national leader we have here for your cause. She is doing great work. Fantastic.

[Applause.]

I know that the Chairman and I share the sense that this is what being in the Senate is all about: Trying to help people out there around this country every day face their unique challenges. And certainly juvenile diabetes is one of those, and our thoughts and our prayers are with you.

One thing that I want you to know is that we on this Committee are very sensitive to your needs and very attentive to what you need. And, in fact, as the Chairman set this meeting up, she wants to talk about examining the personal toll on families; she wants to talk about financial costs to the Federal health care system; and she wants to talk about research progress toward a cure. And I tell you, she wants to continue her great leadership on this, and she is doing a fantastic job. And I just want to welcome everyone here to the Senate and to this Committee. And I want to ask the chil-

dren: Has this been a good experience for you so far in Washington? Has this been good? Good.

Well, I hope it is. And it is meaningful and it is important, and you all are making a real difference for people that have juvenile diabetes all over this country.

Now, the last thing I need to say before I step aside here is: Who is here from Arkansas? That is what I need to know. All right. Good. Great. Well, listen, maybe we will get to visit afterwards.

But thank you for coming to Washington. Your cause is very important. Mary Tyler Moore, thank you for being here. It is always an honor to see you, and thank you for your leadership on this. You do a great job to bring awareness to this and show great courage on this.

Thank you very much.

[Applause.]

Chairman COLLINS. Thank you, Senator Pryor.

Senator Lautenberg, it is a pleasure to welcome you here this morning as well.

OPENING STATEMENT OF SENATOR LAUTENBERG

Senator LAUTENBERG. Thank you very much, Madam Chairman, and I commend you for holding this hearing today on juvenile diabetes, and I welcome Mary Tyler Moore. We have seen you in so many places, but we never get tired of seeing you, and we are particularly pleased to have you here today with this group.

As the children I am sure know, when they look at me, they see a grandfather. Right? OK. Well, I have nine grandchildren, and the oldest is 9 and the youngest is 2 months. And I love them dearly, and I am always looking for some reassurance about how they feel and how they are doing.

And when I look at you, I feel similarly a love and affection for you, and I want you to be healthy, and I want to do whatever we can to make sure of that. And our Chairman, Susan Collins from Maine, deserves a vote of thanks for the courage that she has displayed, and she and Senator Murray from the State of Washington have put together a program to try and get more money to fight this disease, to fight juvenile diabetes, to see if we cannot find, if not a cure, some significant relief in the process. And it is shocking to learn that as many as a million Americans suffer from this devastating disease, and roughly 35 children will be diagnosed with juvenile diabetes each and every day.

The incidence of diabetes, type 1 and type 2, is on the rise with enormous consequences for our society. We talk about the cost, but the cost, no matter how many billions, is insignificant compared to the discomfort and the danger, the risk that children have when they get diabetes. And that is what we are about. That is what we are talking about here today. And that is why we are so glad to see each and every one of you.

Madam Chairman, I ask that my full statement be put in the record, and I would close with this: That those here, the young people who are going to tell us their story, lend encouragement for our government to spend more on research and try to find out what causes it and what we can do about it. If I would pick one of the wonderful assets, the values of this job of ours, it is that we can

sometimes do absolutely the right thing and try to help people who have contracted a disease or who are sick. Now we want to do what we can to make sure that we reduce that possibility as much as possible.

And so we send our love and encouragement to all of you, and we thank you for being here and for telling us how it is that you live your lives. It might help us get more courage and more energy about finding enough money to help you. Thank you very much.

[Applause.]

Chairman COLLINS. Thank you, Senator. Your full statement will be placed in the record.

[The prepared statement of Senator Lautenberg follows:]

PREPARED STATEMENT OF SENATOR LAUTENBERG

Madam Chairman, I commend you for holding today's hearing on Juvenile Diabetes. As many as 1 million Americans suffer from this devastating disease; roughly 35 children will be diagnosed with Juvenile diabetes each and every day.

The incidence of Diabetes—type 1 *and* type 2—is on the rise, with enormous consequences for our society. Diabetes already accounts for more than $132 billion in health care costs each year. That number will continue to rise until we can stem the tide of new cases and find better treatments.

I commend Senators Collins and Murray for introducing S. 518, a bill to promote pancreatic islet transplants so that the procedure can become standard therapy covered by insurance. Clearly, there is good reason for the people who suffer from Juvenile Diabetes and their families to have hope.

I would make one observation: This year, Congress is completing the 5-year mission to double funding for the National Institutes of Health (NIH). I was an enthusiastic supporter of that mission before I took my "sabbatical" from the Senate and am happy to support it now that I am back.

The research community has called for an 8–10 percent increase in NIH's budget for next year. But the President just wants a2.7 percent increase—that's barely enough to cover inflation.

I don't know how we can tell the witnesses gathered here for this hearing that we will have to *slow down* research.

But we *will* have to slow down research. Why? Because the President's tax cuts are causing the budget deficit to explode.

What NIH, the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK), the National Cancer Institute, and similar groups do is a pretty good example of *tax dollars at work* finding new treatments, cures, and preventions for all types of illnesses and diseases. But we are told that it's more important to *cut taxes.*

President Kennedy said, "To govern is to choose." I think we ought to *choose to invest in the research that will help our witnesses live longer and better lives.*

I want to welcome our witnesses, especially Mary Tyler Moore, who needs no introduction, and the brave boys and girls who are going to share their stories about what it is like to have Juvenile Diabetes. Thank you, Madam Chairman.

Chairman COLLINS. Senator Bennett, a pleasure to welcome you today.

OPENING STATEMENT OF SENATOR BENNETT

Senator BENNETT. Thank you very much, Madam Chairman.

I recall a hearing in this same room with Connie Mack in the chair as we began the determination on the part of the Congress to double the amount of funding for NIH over a 5-year period. And I was part of that effort. There were some in my party who, after we had done it for the first year, then the second year said to us, "Well, why do we continue to give NIH double-digit increases? Look how well they did last year, and we have got serious budget problems. Let's cut it back to a single-digit increase this year. Look how well they have done."

And we said no, we have to continue on the pattern of double-digit increases for NIH if we are going to get to the goal of doubling medical research over a 5-year period.

I am happy to say we stayed the course that was set in the hearing in this room under Senator Mack. And we did, in fact, double the amount of money going to medical research over that 5-year period.

So it is appropriate, Madam Chairman, that you are carrying on in that tradition that Senator Mack set by now addressing the question of the appropriate amount of research focused particularly on diabetes. I am happy to report that in the State of Utah, if I might get parochial—but that is what we do around here, we have at the University of Utah some of the finest research on the issue of diabetes going on anywhere in the country. It is tied to the genealogical information that the Church of Jesus Christ of Latter Day Saints maintains in Utah, because diabetes has been determined to have genetic ties. There is more information in the genealogical library that the church maintains than anyplace else in the world. So the people at the University of Utah, some of them have said to me, "I could go anywhere, I have the credentials that I would be hired by any research institution anywhere in the world, and I have chosen to come to Utah because of the genealogical information that is available, and the leg up that this gives us as we deal with diabetes."

I have a particular interest in it. My grandfather died of diabetes. So I appreciate very much the leadership that you are showing with respect to this hearing.

[Applause.]

Chairman COLLINS. Thank you very much, Senator.

We are also pleased to have with us this morning as an honorary member of the Committee for the day Senator Ben Nelson of Nebraska. He is going to be introducing two of our delegates today who will be testifying, but I also want to give him the opportunity if he would like to make any opening comments.

OPENING STATEMENT OF HON. E. BENJAMIN NELSON, A U.S. SENATOR FROM THE STATE OF NEBRASKA

Senator NELSON. Well, thank you very much, Madam Chairman, and it truly is an honor to be here today under these circumstances, recognizing the importance of the work that is about to be done and the work that will have to be done in the future.

It is my pleasure to be able to introduce the Bonness family on the second panel, and so I will have more comments at that time. But thank you very much for convening this hearing. The cause is important, and the work is equally important.

Thank you very much.

[Applause.]

Chairman COLLINS. Thank you, Senator.

Our first witness this morning is Mary Tyler Moore. I have a feeling that she needs very little introduction. Most Americans know her well from her work, her distinguished career on both television and in films and on the stage. But she also plays a very special role for everyone in this room because of her remarkably effective advocacy on behalf of individuals with juvenile diabetes.

Ms. Moore serves as the International Chairman of the Juvenile Diabetes Research Foundation, and it has been my great pleasure to work very closely with her during the last few years. Together, we have worked to almost triple funding for diabetes research since 1996. I know that is making a big difference. It would not have been possible without the effective advocacy of Mary Tyler Moore and the JDRF.

So it is a great pleasure to welcome you back to testify today, and please proceed with your statement. Welcome.

[Applause.]

TESTIMONY OF MARY TYLER MOORE,[1] INTERNATIONAL CHAIRMAN, JUVENILE DIABETES RESEARCH FOUNDATION (JDRF)

Ms. MOORE. Thank you. Thank you all for that wonderful welcome. Good morning. Before I begin my formal remarks, Senator Collins, I would like to personally thank you for your leadership and all your efforts on behalf of people with diabetes throughout our country, including conducting these hearings and co-Chairing with Senator Breaux the Senate Diabetes Caucus. With your continued support, I know we will together find a cure.

Now, please let me offer the following testimony:

Chairman Collins and Committee Members and all, I am here today as International Chairman of the Juvenile Diabetes Research Foundation. I wish I could say that I am happy to be here. But meaning no disrespect, I am definitely not. You see, I have had juvenile diabetes for more than 35 years now, and I am tired of it. I sincerely wish that I did not have to come back, year after year, to seek your help. And I do. I have to for myself, for everyone with diabetes, and most especially for the beautiful and courageous children who are here with me today.

Be certain, at JDRF we have never been more dedicated to finding a cure for diabetes and its complications, and the evidence suggests that we are truly close. Much of the progress that has led us to what we hope and believe are the final stages of our fight against diabetes is the result of your support and effort. We greatly appreciate the good partnership we have always had with Congress and every administration since our founding. We are deeply grateful for the extraordinary support you showed last year in passing the Special Juvenile Diabetes Program. But as you can see, I am here again. Despite all our accomplishments together, we must face the fact that there are still significant hurdles that we need to overcome to take the last necessary steps along our path to a cure.

Senators some of you have already met many of the 200 children, the delegates to JDRF's Third Children's Congress who are here in Washington this week. And you will be hearing from some and meeting others. You will do that later today. They are passionate and eloquent spokespeople for the need for a cure. But don't be misled by their drive, their energy, and their unwavering commitment. They—and I—struggle every minute of every day to do what happens naturally for people who don't have diabetes—that is, to achieve a balance between what I eat, the energy I expend, the

[1] The prepared statement of Ms. Moore appears in the Appendix on page 42.

amount of insulin I inject. For most of you, blood sugar balance is automatic, as automatic as breathing. But for people with juvenile diabetes, like me, it requires vigilance 24 hours a day, 7 days a week, 365 days a year.

Each of these children and I need to be a mathematician, a physician, a personal trainer, and a dietitian all rolled into one. We need to be constantly factoring and adjusting, making frequent finger sticks to check blood sugar levels, and giving ourselves multiple daily insulin injections just to stay alive. Not to live life to its fullest, mind you; just to stay alive. And it isn't easy. Even with the greatest of care and the closest of personal scrutiny, like many children and adults with juvenile diabetes, I find I am often unable to achieve good balance. My blood sugars can go dangerously low or frighteningly high. Yes, dangerous and frightening, because serious lows can lead to seizures, coma, and death. And high blood sugars can, over time, result in disabling and life-shortening complications.

Some of you may already know the startling toll diabetes takes. For example, diabetes causes over 40 percent of kidney failures in our country that require dialysis or transplantation. It is responsible for more than half of amputations not associated with trauma. It is the leading cause of blindness in adults—the leading cause. Moreover, I have seen studies that say that virtually everyone with juvenile diabetes shows evidence of heart disease by age 40—and, further, that the pre-menopausal women with juvenile diabetes have a more than 30 times greater risk of death from heart attack.

Beyond the incomprehensible personal costs, consider the economic burden that our country must bear as a result of this disease. Diabetes costs this Nation over $130 billion every year. This includes one out of every four Medicare dollars spent. Taken altogether, it should be crystal clear why it is urgent that we find a cure and find it as soon as possible.

Chairman Collins, you and your colleagues from both sides of the aisle have always welcomed us warmly during the past Children's Congresses. In our prior meetings, you have promised to remember us when making decisions about funding for juvenile diabetes research. Today, we are happy to acknowledge to all who might listen that you are indeed keeping your promise. And we thank you, not just as your constituents, but also as your partners in a shared mission to find a cure.

JDRF is working closely with the NIDDK and its Director, Dr. Allen Spiegel. Our joint task is to ensure that the dollars provided by the Special Juvenile Diabetes Program are used to fund projects that otherwise could not be done. And we are confident that these projects will focus on what is needed to rapidly acquire mission-critical knowledge, provide essential research resources, and speed the application of advances for the benefit of people with juvenile diabetes.

Madam Chairman, Senators, it is vital to remember that because children and adults with juvenile diabetes and their families never get a rest from their disease, we never rest in our efforts to find and deliver a cure. And because JDRF is a global cure enterprise, we are always looking beyond the horizon to anticipate what must be done next to achieve our ultimate goal—a world without juvenile

diabetes. Our approach has consistently focused on what is next. And let me give you an example, looking at our four steps we have taken to get to the point where we are today in islet transplantation.

Step one: In the mid-1990's, JDRF created a map of all that is known about diabetes and identified the knowledge gaps and obstacles to progress along the various paths to a cure. We use this continuously updated map to guide us in efforts to push scientific advances from the laboratory bench to the patient's bedside.

Step two: This research mapping made it clear that islet cell transplantation was a potential cure. So we are invested in creating a global network of research centers to prepare and distribute human islets for basic and clinical research.

Step three: As it became clear that research centers throughout the world were now able to test islet cell transplantation, JDRF substantially boosted our investments in research to find a way to transplant these islets without the need for toxic immunosuppressive drugs.

Step four: In 2000, when Dr. James Shapiro's group in Edmonton reported the first major critical success in islet transplantation, JDRF jumped to overcome the next obstacle confronting transplant research, and that is the inadequate supply of islets. So to create an unlimited supply of islet cells for transplantation, we are leading a global effort to support stem cell research. This is particularly necessary because each year, there are fewer than 2,000 cadaver pancreases donated. Yet well over 1 million Americans with juvenile diabetes could potentially benefit from islet cell transplantation.

Overall, we have made terrific progress. But we do continue to look into the future and ask ourselves, "What is next?" And here is what we believe must be next, to speed a cure for diabetes.

First, we need policies and regulations that encourage organ donations and promote the retrieval of additional human pancreases. As I said, supply is a major obstacle to making islet transplantation a cure for all those with diabetes who might benefit. I am grateful for the real leadership and vision that you have shown by introducing the Pancreatic Islet Cell Transplantation Act of 2003. This bill, which JDRF supports, will provide regulatory incentives for organ procurement organizations to retrieve additional pancreases. It will also test, within Medicare, insurance coverage for islet transplants for people with juvenile diabetes and kidney failure. I am hopeful that Congress will pass the legislation this year, and we are eager to work with you in achieving this goal.

Second, we need to work with the Senate and the President to do things necessary to speed progress in stem cell research and to provide ample opportunity for this research to accomplish our shared goal: Finding ways to relieve the suffering of millions of Americans. Even with increased organ procurement, we will ultimately still face a critical shortage of islet cells for transplantation. To meet this demand, I believe we need to ensure that the United States can take its proper place in the world as a leader in stem cell research and the development of human stem cell-derived therapies, including the creation of human islets for transplantation.

But, Madam Chairman, right now, due to the restrictions of the current administration policy, this is just not happening. I know the President worked hard to find a balance in his policy. He clearly recognized the great potential of stem cell-derived therapies to reduce pain and suffering of millions of people with many diseases, including juvenile diabetes. And in my heart, I know that he intended to make it easier, not more difficult, to create therapies to treat human disease. But now, nearly 2 years after his August 9, 2001, decision, researchers tell us that the progress being made in stem cell research is not as far along as it could be. The number of cell lines everyone had hoped for—there were supposed to be more than 60—turns out to be closer to 10. Of these lines, only a few are widely available for research. Perhaps more important, of those approved lines, none can be used to develop human therapies. That is right—none. The problem is that each of those cell lines were established using mouse feeder cells, and the threat of contamination makes them unsuitable for human therapies.

Further, because of the current circumstances, the best and brightest of young researchers in the United States are shying away from the field of human stem cell research. So not only do we have an insufficient number of cell lines to conduct the necessary research, we have a potentially more devastating deficiency of brain power.

Again, I am confident this was not the outcome the President intended. His staff, Secretary Thompson, and Dr. Zerhouni are all doing what they can within the current constraints. And we are pleased to be working closely with them. But at the end of the day, without some change, we may not be able to achieve our shared goals: Finding cures for juvenile diabetes and other disabling diseases as soon as possible.

Third, we need to continue to invest in developing methods to replace human islets without immunosuppression. Just 3 years after the reported success of the Edmonton Protocol, more than 250 people have undergone islet transplantation and no longer need insulin injections to survive. But the procedure is not yet safe for children and most people with diabetes. So we must sharpen our research to focus on transplantation without toxic immunosuppression, as well as redoubling our efforts to prevent diabetes and reverse or prevent its devastating complications.

Finally, because we want a cure for everyone with juvenile diabetes, including the children here today, we need to establish a framework for research oversight which ensures that the needed clinical studies are safe for the participation of children.

Madam Chairman, diabetes is an all-too-personal time bomb which can go off today, tomorrow, next year, or 10 years from now. A time bomb that affects millions, including me and the children here today. It needs to be defused. But to find a cure for diabetes and its complications, and then make these cures available to everyone who might benefit, will require that we remain vigilant in our purpose and continuously committed to asking, answering, and acting upon the "What next?" question.

So what is next for you? Please listen to the children this morning, who will tell you how they struggle with juvenile diabetes. Learn about how they bravely face its daily challenges—challenges

that no 15-year-old or 8-year-old or 2-year-old should have to endure. Feel their longing to know a day without diabetes and live the normal, carefree life of a child. Listen to the researchers as they highlight the progress made to date and the exciting opportunities we can now realize because of JDRF and NIH leadership and the extraordinary investment Congress has made in medical research. And hear firsthand from an islet transplant recipient about how spectacularly her life has changed since her procedure and how she will not rest until her young son, who also suffers from juvenile diabetes, can be cured.

Finally, please join me in making a personal promise to remember what we have learned today. Ask ourselves: What must we do next? And then commit together to do what we must to find a cure.

Thank you once again for all you have done and for the opportunity to speak with you this morning.

[Applause.]

I cannot tell you how touched I am by that reception. Thank you.

Chairman COLLINS. Well, thank you for your testimony. I think every member of this panel joins everyone in this room in remarking on your eloquence in telling your own personal story as well as your advocacy. Your willingness to share your personal story as well as your leadership at the Juvenile Diabetes Research Foundation makes a real difference. It inspires each and every one of us.

As you spoke, I could not help but remember the first time I met a family whose son had diabetes from my home State of Maine, and the little 10-year-old boy looked up at me, and he said, "I just wish that I could take one day off from my diabetes." And that is when I knew that I had to get involved. So thank you for presenting your story.

I am going to limit questions on this round so that we can hear from the children, so let me just ask you one question.

Two years ago, you came to Congress to testify at the Children's Congress. Are you more hopeful today as a result of the investment in research and the medical advances that we have seen that we are on the verge of providing a cure and better treatment for people with diabetes?

Ms. MOORE. Senator Collins, I most definitely am more enthusiastic and stronger in my belief that a cure is, figuratively, around the corner. It cannot come soon enough for all of us, I know that, but especially because of the promise of stem cell research. I think that is the big hope. I think that it will make a huge difference to the people who suffer from all kinds of diseases. And won't it be lovely to have all that money that we don't have to spend taking care of people with horrible illnesses and can spend it on things that make us a better, healthier, happier Nation.

Chairman COLLINS. Thank you.

[Applause.]

Senator Pryor.

Senator PRYOR. Thank you. I know that you are more encouraged today than you have ever been, but what do you see as the largest obstacle to finding a cure today?

Ms. MOORE. I think any roadblock that is thrown in the way of the good scientists who are working to find the cure. I think fear is a major obstacle. And from good guidance sometimes we recog-

nize fear and have to put it in its place and take the chance and move forward.

Senator PRYOR. Are you comfortable with the funding levels that NIH and others are providing for the research going on right now?

Ms. MOORE. We are very grateful for all the advances made possible by the government and by private donors who have done whatever they can to bring this to the attention of government and the people.

Senator PRYOR. I am not as familiar with the islet cell transplantation like the Chairman is here. Do I understand that there are some people who are very good candidates for that and others that maybe are not so good? Could you educate me on that very briefly?

Ms. MOORE. Well, mostly it is children who are not good candidates for it right now. That may change, but in all, the overwhelming lack of islet cells is the major problem. There are over a million people who could benefit from a pancreatic islet cell transplant, but they cannot because there are not enough of them. There just are not enough, and it costs too much. It is approximately $100,000 per operation. And the immunosuppressants that one must take in order to receive and make functioning the islet cells are a tough thing to live with. Very tough.

Senator PRYOR. Right. Thank you again for being here today.

Ms. MOORE. Thank you.

Chairman COLLINS. Thank you, Senator. Senator Bennett.

Senator BENNETT. Thank you, Madam Chairman. I have nothing to add.

Chairman COLLINS. Thank you. Senator Lautenberg.

Senator LAUTENBERG. Thank you, Madam Chairman, for holding this hearing. We can sense from the reaction of people here whose lives are affected by juvenile diabetes a sense of interest and encouragement and even gratitude for what has happened. We thank Mary Tyler Moore for her eloquent statement and for information that frankly those of us—and I include myself in this—who have been spared contact, direct contact with juvenile diabetes fail at times to understand the impact of this disease. When you talk about a child in a lifetime having 50,000 injections prospectively, it is a painful prospect. And if we could wave a magic wand, we certainly would do it.

I would ask you this, Ms. Moore: What do you think we can do on a relatively immediate basis to speed up the process for the development of islet and other technologies that we know something about?

Ms. MOORE. I think continue to fund the research, just get in back of us 100 percent, support stem cell research in particular.

Senator LAUTENBERG. How about the expansion of stem cell availability? Would that make a big difference, do you think?

Ms. MOORE. The expense of stem cell——

Senator LAUTENBERG. Expanse.

Ms. MOORE. Expanse. It is possible. It is there to be done. But we need the permission from our President to advance, to do the things that they are doing in other countries.

Senator LAUTENBERG. That would give a lot of encouragement to people, wouldn't it?

Ms. MOORE. It certainly would.

Senator LAUTENBERG. Thank you very much.
Ms. MOORE. Thank you.
[Applause.]
Chairman COLLINS. Senator Specter.

OPENING STATEMENT OF SENATOR SPECTER

Senator SPECTER. Thank you very much, Madam Chairman, and thank you for convening this hearing. And thank you, Ms. Moore, for your leadership for many years on this important subject. You have appeared in this room on a number of occasions testifying before the Subcommittee on Labor, Health and Human Services, and Education. And as a result of your efforts and the efforts of others, the funding in the National Institutes of Health has been raised for the National Institutes on Diabetes and Digestive and Kidney Diseases to $1.633 billion, and the total diabetes funding is at $845 million. That is as a result of the increases on NIH funding from $12 billion to $27.5 billion in the past several years.

The issue of fear which you commented on and the question raised by Senator Lautenberg on stem cell research is a very important one, and the reality is that the hands of the scientists are being tied or at least efforts are being made to tie their hands, and there is a lot of concern and a lack of initiative in the scientific community because of legislation passed by the House of Representatives which criminalizes research on stem cells, which some people have characterized as "therapeutic cloning."

That is a term which raises a lot of emotion, erroneously. We are all against human cloning. But when you talk about therapeutic cloning, it is really not true. The essential medical procedure is that an egg is donated, the core is taken out, and then if a woman, for example, has Parkinson's or Alzheimer's or juvenile diabetes, a skin sampling is taken, placed in the core. It is kept in a laboratory dish, and those stem cells then are consistent to be used for that patient.

The entity dies within 14 days so there is nothing cloning about it at all.

Ms. MOORE. Right.

Senator SPECTER. And I believe that it is important to use every opportunity to acquaint Americans that about 128 million are suffering from one of these maladies which might be curable by additional stem cell research. And juvenile diabetes is among them.

So thank you for all that you have done, and I thank all of you for coming to this proceeding today, especially the children, and there are many others on Capitol Hill who are dedicated to scientific research additional funding and to finding a cure for juvenile diabetes and other dreaded maladies.

Thank you, Madam Chairman.

Ms. MOORE. Senator, we thank you.
[Applause.]
Chairman COLLINS. Senator Durbin.

OPENING STATEMENT OF SENATOR DURBIN

Senator DURBIN. Thank you very much, Madam Chairman, and thank you, Mary Tyler Moore, for what you have done and for your leadership, and thanks to all of your young supporters here who

are starting to move a little bit here. They want the Senators to get moving with the questions.

I want to refer to one aspect of this. Another one of my "sheroes" in life is a lady named Connie Payton from Chicago, whose late husband, Walter Payton, really made a plea toward the end of his life for organ donation. And she has continued in that fine work, and we have engaged the National Football League to make this part of their public service. And we have focused on Thanksgiving, the great national holiday, to encourage families when they come together to spend just a few moments with one another and let other members of the family know if you want to be an organ donor.

It seems to be one of the major obstacles for organ donation, that the family members don't know what you feel in your heart about organ donation. And as I read these amazing statistics which you have brought to us about how—and, in fact, you need really two donors, do you not?

Ms. MOORE. Yes.

Senator DURBIN. For the pancreata that is necessary for this new approach. It really dramatizes the enormous demand and need for organ donors in our country as part of this effort.

And if the Chairman will give me a moment here, I would just like to do a little show of hands here, and the children are exempt from this vote. They are used to raising their hands in classrooms. But this is for all of the adults in the room, Senators and staff and audience. How many people in this room have communicated to members of their family that they would be organ donors or have signed a organ donation card? Good. This is an audience that is not typical of America because you understand this. And I hope that this hearing, among other things, spreads the word across America. We need more organ donors for so many good reasons and for these children. And I hope, Madam Chairman, that is a message that we send from this hearing as well.

Thank you very much.

[Applause.]

Ms. MOORE. Thank you so much, Senator.

Chairman COLLINS. I want to thank you very much for testifying today. Senator Nelson is going to start off with the introduction of our next panel when I bring them up here. Thank you so much, Ms. Moore, for all that you are doing. Because of your eloquent testimony and your leadership and advocacy year after year, we have been able to make a real difference in funding research for diabetes. And I know we are going to continue our great partnership, so thank you so much for being here today.

Ms. MOORE. Thank you, Madam Chairman.

[Applause.]

Chairman COLLINS. I would now like to call forward the children's panel. Our second panel of witnesses this morning consists of children who know firsthand the burden of living with diabetes. Our witnesses on this panel are Colleen Rea of Stamford, Connecticut, accompanied by her son, Dylan; Sophia Cygnarowicz of Columbia, Illinois, whom Senator Durbin may wish to introduce; Katie Halasz of Wells, Maine; Eric and Alex Bonness of Omaha, Nebraska; and LaNiece Evans-Scott of Backlick, Ohio. And we are

just delighted to have those children with us. They are all delegates to the Children's Congress, and we are going to start by having Senator Nelson introduce the Bonness children.

Senator NELSON. Well, thank you very much, Madam Chairman. It really is an honor for me to be here today to introduce some fellow Nebraskans. I would like to thank you, Madam Chairman, for not only this opportunity but for your leadership. It is very clear that your commitment is making progress possible, and we all thank you very much. I know all the families who have been touched by this disease appreciate what you are doing, and we hope that as a result of this hearing today we will be able to advance the efforts toward a cure.

I would like to start off this morning, before I introduce the two delegates, by introducing a gentleman who is well known in Nebraska, not simply as a former football player, all-American at Nebraska, and an NFL player, coached by one of our colleagues in the House, former coach but now Representative Tom Osborne, but a person who has taken this cause not only seriously but to the far reaches of our country to make sure that we are all aware. He has advanced the recognition of this disease. He has advanced the efforts to make sure that we are all working every way that we can to help this cause.

Today, he joins us as the Chair-dad of the Children's Congress, and I could list all the accomplishments on the gridiron and in the courtroom as a lawyer. But I just simply want to say to Eric Bonness, thank you very much, and please be recognized this morning.

[Applause.]

He is joined by a very able partner. Dr. Bonness, it is good to have you here as well.

[Applause.]

As we all turn our attention to the two young representatives, the two young delegates here, I think that I can speak on behalf of their parents and all of us who would say that with all the recognition and all the accomplishments of their parents, their parents and we all hope that they will be able to exceed those accomplishments in their lives ahead. I speak, of course, today of Alex and Eric Bonness. They are two of our Nebraska delegates and two of Nebraska's finest young people. Both are extraordinary young men. They were diagnosed with type 1 juvenile diabetes before they entered their teens. Eric was diagnosed when he was 10, and Alex, although he is the younger brother, he is the elder when it comes to living with his disease because he was diagnosed when he was only 4.

But for every day since those fateful days that they were diagnosed, these two have measured their blood sugar, taken medication, and, in general, have had to monitor their health in ways that most adults could not imagine, certainly with the level of care that few could match. But they, like so many others like them, have done this day in and day out because they simply have to.

I will let them fill you in on what this entails for them, but I am sure my words could never match theirs. I do want to say, though, that the kind of courage that they have shown from the time they were young children in dealing with this disease has to be an inspi-

ration for all of us, and it has to be encouragement for all of us to do everything that we can, as adults, as Members of the Congress, and as human beings.

That inspiration should lead us to work with the Juvenile Diabetes Research Foundation in finding a cure for diabetes so that Alex and Eric and all the young people in this room and all the young people out there who live with this disease every day will not have to live with it any longer. That is what our hope is all about today. That is what our dedication must bring. And I only hope that these young men who come to us today, who have had to learn words like "glaucoma," "retinal scans," and "diagnostics," when they should have only had to learn about their favorite action figures or video games, they have met the challenges of juvenile diabetes, and we need to join them in the challenge of finding a cure.

So it is an honor for me today to host Eric and Alex and their family, as well as Nebraska's other two delegates who are in town but will not be testifying, Megan Stewart and Alyxandria Harter. It is my pleasure to present Eric and Alex Bonness.

[Applause.]

Chairman COLLINS. Senator Durbin.

Senator DURBIN. Thank you very much, Madam Chairman. There are a number of Illinois children delegates here, and if they would either raise their hand or stand up, and I am going to introduce Sophia at the end here: Sean Bottorff from St. Charles, there he is; Alexandra Case of Chicago; Kevin Covarrubias of Maryville; Devan D'Silva, Arlington Heights; Michael Johnson of Evanston; and Abigail Wolter of Alton. Thank you.

And the person I would like to especially introduce has just successfully completed the first grade. She is here today from Columbia, Illinois. Sophia Cygnarowicz is here to tell us a little about her experience with juvenile diabetes. She said she would like to know what life is like without diabetes, and she would like to eat Sno-Cones whenever she wants. [Laughter.]

We are looking forward to her testimony. Thank you, Madam Chairman.

[Applause.]

Chairman COLLINS. Thank you. Senator Lautenberg.

Senator LAUTENBERG. Thank you, Madam Chairman. I want to call attention to the wonderful young people who have come from New Jersey. They don't have as long a trip geographically as some of the others, but their trip to getting here is the same perilous journey. And we want to say hello, and I will ask the same thing, that a hand be raised for Jessica Barszcz—Jessica, are you here? Yes, OK. Welcome. Kyle Gertner. Emily Greatrex. Is Emily here? Oh, a beautiful child from New Jersey. Lindsey Rosenthal. Hi, Lindsey. And Carey Towell. Carey, hi. Well, we are happy to see these youngsters and tell them that we are going to work hard to see that life gets better for them and their friends as well.

Thank you.

Chairman COLLINS. Thank you.

We are going to start with Katie Halasz today because she is from my home State and I am the Chairman. [Laughter.]

I got to meet Katie and her Mom yesterday in my office, and she gave me a photograph album illustrating what it has been like for

her since she was diagnosed. She is 16 years old. She is from Wells, Maine. This photograph album is just wonderful. It tells about what she felt. It shows what she has to do each day to monitor her blood and to give herself insulin. It was very helpful, and I really treasure it.

So, Katie, please begin. Bring the mike up close to you so we can hear you. Thank you.

TESTIMONY OF KATIE HALASZ,[1] DELEGATE, AGE 16, JDRF CHILDREN'S CONGRESS, WELLS, MAINE

Ms. HALASZ. Unlike Dylan and Sophia, I do know what it is like to live without diabetes. I dream of another day without diabetes. My name is Katie Halasz. I am 16 years old and from Wells, Maine. I want to tell you how my life changed on June 12, 1999, at 11 p.m. when I was diagnosed with juvenile diabetes.

At first, I did not know what diabetes was. The doctor told me I would have to take insulin shots the rest of my life. I did not think that diabetes would change my life that much, but, boy, was I wrong. I have to test my blood sugar and take shots all the time. It affects everything I do, even being part of the color guard for the school band is a challenge. My blood sugars often go high and result in ketones, which is poison in my body, and it can be really dangerous. When you get ketones, you cannot do any exercise. It is very hard on my team and on me when I cannot march.

School is a lot harder when you have diabetes. My school does not allow me to test my blood in the classroom. My classes are on the third floor, and the nurse's office is on the first floor. When I feel low, I have to walk down three flights of stairs, and this is very dangerous. Some of my teachers think that I leave the classroom just to get out of class. Do they think I enjoy sticking a needle in my finger? When my blood sugars are high, I cannot concentrate on my work and my vision gets blurred. My teachers do not understand. Some of them even think it is my fault that my sugars go high because they think that I eat things like candy bars. They do not understand that my sugars can go up for no apparent reason. Educating my teachers has been my biggest challenge since being diagnosed with diabetes.

Having diabetes complicates more than just school. Last year I had a cyst underneath my arm. It became infected. I went to see a surgeon once a month to have the area opened so it could be drained. My sugars were always high because of the infection, and the area would not heal because of the high sugars. Finally, I had to have surgery to remove the cyst. The doctors had to remove half the tissue from my underarm.

Senator Collins and Members of this Committee, we are here today to ask for your help in finding a cure for juvenile diabetes. Each of us wants to be able to go to school, play in the band or on sports teams, without worrying about going into a coma because of low blood sugars. Each of us wants to grow up without the daily stress of trying to treat this horrible disease and the fear of complications. We will do our part to educate policymakers about dia-

[1] The prepared statement of Ms. Halasz appears in the Appendix on page 48.

betes and raise money to support research. But we need you to be our partner in this effort. We cannot do it alone.

Senator Collins, I am glad and grateful you are my Senator. You have shown incredible dedication and leadership in our common quest for a cure. Thank you from the bottom of my heart.

[Applause.]

Chairman COLLINS. Thank you, Katie. You did a great job.

We are now going to hear from Dylan Rea, but we are actually going to hear from his mother, Colleen, since Dylan is age 4. So, Colleen, would you please proceed?

TESTIMONY OF COLLEEN REA, ON BEHALF OF HER SON, DYLAN REA,[1] DELEGATE, AGE 4, JDRF CHILDREN'S CONGRESS, STAMFORD, CONNECTICUT

Ms. REA. Good morning. My name is Colleen Rea, and I am from Stamford, Connecticut, and it is an honor to appear before you today with my 4-year-old son Dylan. Dylan and I are here today, along with all of these children, to tell you why finding a cure for juvenile diabetes is so important. You see, I know all too well about the devastation of diabetes. Diabetes has followed me and haunted me my entire life for three generations of my family.

When I was a child, I found glass syringes in my house and was told that my grandfather, who died before I was born, had diabetes. When I was a young woman, my mother called and asked me to meet her at a hospital emergency room. My mother was being admitted for the first time because of her diabetes. When I saw her, she was scared. Within 10 years and many hospital stays and operations later, I was told that my mother was dying. It took only 10 years for diabetes to kill my mother.

When my son Dylan was diagnosed with type 1 diabetes, or juvenile diabetes, at the age of 14 months old—less than 2 years after my mother had died—I was devastated. It was almost more than I could bear. I knew what diabetes had done to my grandfather, and I had seen what diabetes did to my mother.

We are very diligent in trying to care for Dylan's diabetes. But controlling blood sugar levels in a toddler is impossible because there are so many variables. There are always times when Dylan's blood sugar is dangerously high or frighteningly low, sometimes in the same day. He wears an insulin pump 24 hours a day, and we check his blood sugar at least eight times a day. And there are precious few people who are able to babysit him. My husband and I must be available 24 hours a day, 7 days a week. Diabetes never takes a break, and neither can we. We are Dylan's pancreas.

While we are concerned about Dylan's physical health, we also worry about his emotional health. Dylan may grow up to live a long life, have a great and fulfilling career, and a wife and children of his own someday. But we know that in our hearts, despite our best efforts, he may be denied all of that. Either way, he has this day and this childhood, and I want it to be wonderful.

We walk a tightrope in caring for Dylan, to help our child feel love and joy when we continually assault his body with needles and lancets. We give our child hope and faith in the face of fear and

[1] The prepared statement of Ms. Rea appears in the Appendix on page 50.

disease. We tell Dylan he is healthy but needs medicine every day, all day, to survive.

I know that a cure is possible and within our reach. I hope that it will be found soon so that Dylan and all of these children will live a long and fulfilling life. This is my greatest wish and why we are here today to ask for your help and support in our quest for a cure.

Say thank you.

Master REA. Thank you.

[Laughter/applause.]

Chairman COLLINS. Good job, Dylan. That was great.

Thank you very much, Colleen, for your very moving testimony.

We are in the middle of two roll call votes, so I am going to have Sophia testify, and then we are going to have a 15-minute recess before we come back and hear from Eric and Alex and LaNiece. Sorry about that. We cannot control the schedule.

Sophia, could you give your statement to us?

TESTIMONY OF SOPHIA CYGNAROWICZ,[1] DELEGATE, AGE 7, JDRF CHILDREN'S CONGRESS, COLUMBIA, ILLINOIS

Miss CYGNAROWICZ. Hi. My name is Sophia, and like my friend Dylan, I don't know what life is like to have a day without diabetes. I am 7 years old. I have had diabetes since I was one.

I have taken 4,380 shots of insulin and have pricked my finger over 13,000 times to test my blood sugar. I don't like it. It hurts. It is so hard to keep my blood sugar in a good range. No matter how hard I try, I still go low and high.

Low blood sugars make me very tired and cranky. I need to eat but a lot of times I don't want to. Sometimes I wake up in the middle of the night because I go low. My Mom and Dad will feed me and test my blood sugar to make sure I will be OK before I go back to sleep.

I just finished first grade. It is hard going to school when you have diabetes. We did cooking projects and had lots of parties. I watched all the other kids eat cookies and cake. I couldn't eat them, and that wasn't fair. When I feel low at school, I can't think well. My teacher gives me sugar tablets, and I walk down to the nurse's office to do a blood sugar test. A friend comes with me to make sure I get there OK. Then I have juice and crackers. It takes me a while before I get better. I don't like to miss class.

Summer is lots of fun, but not when I go out and can't stay outside and play with my friends. I have to eat at the same time every day so my blood sugar won't go too low. I have to eat even when I am not hungry.

I don't know what life is like without diabetes, but I sure would like to find out. Finding a cure is important to me because I won't have to take shots or do blood tests. Most of all, I could eat a Sno-Cone whenever I wanted to. My friends in this room and I aren't asking for much. We just want a life without diabetes.

[Applause.]

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[1] The prepared statement of Miss Cygnarowicz appears in the Appendix on page 52.

Chairman COLLINS. Thank you, Sophia. You did a wonderful job talking to us and helping us understand what it has been like for you to live with diabetes, so thank you for a great job.

We are now going to have to recess for 15 minutes, and then we will come back and hear from the three remaining children. Thank you.

[Applause.]

[Recess.]

Chairman COLLINS. The hearing will come to order.

I am very pleased now to recognize Eric Bonness for his testimony. Eric and his brother Alex are going to be testifying next. And then we will hear from LaNiece Evans-Scott, who has been very patient at the end of the table. So, Eric, would you please give your testimony.

TESTIMONY OF ERIC BONNESS,[2] DELEGATE, AGE 18, JDRF CHILDREN'S CONGRESS, OMAHA, NEBRASKA

Mr. ERIC BONNESS. Having diabetes is not something you struggle with alone. It affects your whole family. If you have diabetes, it affects everything you do. If you also have a brother with diabetes, it affects everything—times two. Our family has twice as many blood glucose kits and twice as many insulin pumps, more than $10,000 worth. We do twice as many blood sugar checks and change catheters twice as often. We have twice as many blood sugar highs and lows. We have twice the costs—economic, physical, and emotional.

My name is Eric Bonness. I am 18 years old and from Omaha, Nebraska. I was diagnosed with type 1 diabetes when I was 10, 3 years after doctors diagnosed my little brother, Alex, with diabetes. I did not have to go to the doctor's office to be told I had diabetes. I found out one morning in my bedroom after I had been up all night going to the bathroom and guzzling water. Just before dawn, I opened my eyes as my parents sat down on my bed holding my little brother's blood glucose meter. For 3 years I had seen the fear—and the tears—in the eyes of my little brother as he endured thousands of finger pokes and insulin shots. I knew I was about to get my first finger poke to test my blood sugar. I was terrified. I had always been afraid for Alex. Now I was afraid for me. The doctors said there was only a small chance I would ever get diabetes. Suddenly, statistics did not matter.

My mom poked my finger. Then my parents and I watched in silence as the seconds ticked down on the blood glucose meter to reveal my blood sugar. The numbers seems to explode off the screen at me—495. I asked my mom if I had diabetes, but I already knew the answer.

Like any brother, Alex can be a real pain. [Laughter.]

But he has always helped me with the pain of diabetes. When I was first diagnosed, Alex would get candy for me when I had a low blood sugar. He also taught me how to give myself insulin shots to bring down high blood sugars. Now that we are older, we still help each other recover from insulin reactions. We give each

[2] The prepared statement of Mr. Eric Bonness appears in the Appendix on page 54.

other test strips when one of us runs out. We even borrow the other's insulin pump when ours stops working.

It is scary enough to have diabetes myself. But it is even worse to watch my little brother suffer with diabetes. Alex sometimes has a low blood sugar and migraine headache at the same time. He becomes semiconscious, incoherent, and unable to help himself. I watch my parents struggle as they try to raise his blood sugar before he slips into a coma. We are lucky my mom is a doctor. Other families would have to go to the hospital. During these episodes, my parents give Alex an emergency IV or shot of glucagon to raise his blood sugar level. It is horrible to see diabetes make my brother so vulnerable. If diabetes is doing this to him now, even with the best available medical care, what is diabetes going to be doing to him in the future?

I am not going to wait to find out. I start college next year and I plan to go on to medical school. We have to find a cure, and soon. Diabetes is not going to kill my brother, and it is not going to kill me.

We need your vote to keep our hope alive. Thank you.

[Applause.]

Chairman COLLINS. Thank you very much. Eric, you should see your parents' faces right now. They are so proud of you, and we all are. Thank you for your testimony.

Alex, now you get to take your revenge on your brother for that "pain" comment, right?

TESTIMONY OF ALEX BONNESS,[1] DELEGATE, AGE 15, JDRF CHILDREN'S CONGRESS, OMAHA, NEBRASKA

Mr. ALEX BONNESS. My name is Alex Bonness. I am 15 years old and Eric's younger brother. I was diagnosed with type 1 diabetes when I was 4 years old. I don't remember the day I found out I had diabetes, but I do remember being really scared of the finger pokes and shots. When I was diagnosed, no one on either side of my family had type 1 diabetes, so living with it was a real big shock to us. I remember feeling lost, confused, and alone. Some nights I would throw tantrums and cry when it was time to go to bed. I never talked about why I did it. My parents thought it was because of the monster in my closet. Boy, were they wrong. I was afraid of a monster all right, but it was not in my closet. It was diabetes.

When I was 7, I felt like I was saved. That is when Eric was also diagnosed with diabetes. I know it sounds terrible to say I felt like I was saved because my brother was diagnosed with diabetes. How could such a bad thing become good? I was sad Eric had to go through so much pain, but somehow I no longer felt alone. When Eric reached out to me, I made sure I was there for him. Don't get me wrong. Eric can be a real pain. [Laughter.]

But it was important for me to be there for him.

As Eric and I have grown up together, we have always told each other we can beat diabetes. I know we can. But as I get older, my fears grow, too. When Eric hit his teenage growth spurt, I watched

[1] The prepared statement of Mr. Alex Bonness appears in the Appendix on page 56.

his uncontrollable blood sugars skyrocket to high levels because of his changing hormones. It scared me to death. I worried about him.

Now I am hitting my teenage growth spurt, and I worry about me. I have cried myself to sleep. I have also cried with my mom about what scares me most, like complications such as blindness and having my legs amputated. Mom always tries to comfort me. But she and I both know that complications could occur at any time.

For example, I have to go to the eye doctor every year. At my recent eye appointment, I sat on pins and needles with every word my eye doctor said. She saw no signs of complications—yet. On the way home, I thought about what I would have said and done if she had seen blood vessels in my retina starting to deteriorate.

I am not a little kid anymore. And I know my brother can't save me from going blind. But I know research can. And you can make that happen.

Thank you.

[Applause.]

Chairman COLLINS. Thank you.

Eric and Alex, thank you so much for your testimony. I cannot imagine how hard it must be to have one child with diabetes. To have two must be so difficult. But I am so glad you have each other and that you can help each other.

LaNiece, you have been very patient today, and I am looking forward to hearing what you have to tell us. So it is your turn now.

TESTIMONY OF LANIECE EVANS-SCOTT,[1] DELEGATE, AGE 10, JDRF CHILDREN'S CONGRESS, BACKLICK, OHIO

Miss EVANS-SCOTT. Many of the kids here today, like my friend Alex, worry about getting complications from juvenile diabetes when they get older. I am here to tell you that some of us, like me, already have serious complications from juvenile diabetes. I am LaNiece Evans-Scott from Backlick, Ohio. I am 10 years old, and I have battled juvenile diabetes my entire life.

I was diagnosed with juvenile diabetes after going into a coma when I was only 16 months old. I spent the first 5 years of my life in and out of hospitals. My mom had to learn how to give me shots and take care of me. She has not been able to work because she has to take care of me all the time. She drives me 5 hours to see a special doctor who helps me care for my diabetes.

I already have problems with my kidneys, and I take medicine every day so that my kidneys won't fail. I worry about what will happen to my kidneys and what other complications I will face as I get older if a cure is not found soon. I am also blind in one eye, not from diabetes, but I worry about what my diabetes will do to my other eye.

I have a lot of trouble in school because the teachers send me home when my blood sugar levels are bad. I am not bad. I am good. It is the diabetes that is bad. I do the best I can, but I am only a kid and diabetes is a horrible disease. I have fallen behind in school because I miss so many classes. I like school, and I also like bowling. I have a lot of friends, and I am on the bowling team.

[1] The prepared statement of Miss Evans-Scott appears in the Appendix on page 58.

I used to be shy about having juvenile diabetes, but I have learned that I must tell my story to important people like you so you know how serious diabetes is and why a cure is important. I want a cure so that I can be like my friends and go to sleepovers and birthday parties. I want a cure so I can go to school every day without worrying about being sent home. I want a cure so my mom won't worry so much about me and can go back to work.

I don't have time to wait. Please promise to remember me. Please promise to remember us. Thank you.

[Applause.]

Chairman COLLINS. Thank you, LaNiece. You did a great job helping us better understand what having diabetes has been like for you.

I understand that each of you, in fact, all of the delegates in this room to the Children's Congress were selected from more than 800 applicants on the basis of a special letter that you wrote on why getting a cure for diabetes is important to you. So I want to congratulate not only those children who testified, but every single child who is here today, because you won the right to come to Washington to help us better understand what having diabetes is like and why we need to work really hard for a cure. So congratulations to each of the children here today.

[Applause.]

Now, I am just going to ask you a couple of questions. LaNiece, we will start with you. What is the hardest thing about having diabetes for you?

Miss EVANS-SCOTT. Taking shots.

Chairman COLLINS. Taking the shots. How about you, Alex?

Mr. ALEX BONNESS. I would say putting in catheters, and I guess living with it every day, not being able to do what other kids do.

Chairman COLLINS. Eric, how about you?

Mr. ERIC BONNESS. I would have to say that no matter how careful you think you are, how much care you are taking with your diabetes, your sugars are always off. There is always something that—you can never have total control, which means you are going to end up having complications. So just the fear of not being able to fully be in control of this disease is probably the most scary thing.

Chairman COLLINS. Katie, what is the hardest thing for you?

Ms. HALASZ. I think taking shots and testing my blood all the time.

Chairman COLLINS. Sophia, how about you?

Miss CYGNAROWICZ. Taking shots and doing blood tests.

Chairman COLLINS. And doing the blood tests.

And, Colleen, I have a little different question for you. These other children, with the exception perhaps of Sophia, are old enough that they can monitor their blood sugar so that they know when they are getting into trouble to some extent, although we have learned it is hard when you reach your teenage years. How do you determine when Dylan may need your help since obviously he is so young he cannot report to you other than through the blood test?

Ms. REA. Well, his eyes. His eyes tell a lot. And if he is very high, he gets very aggressive with other children and with myself. If he is very low, he gets sleepy. And if he is tired during the day,

which he doesn't normally nap, but we do a lot of glucose testing, especially when he was first diagnosed and could not even speak. He was 14 months old. I have tested up to 18 times in 1 day.

Chairman COLLINS. Oh, wow. That has got to be so hard.

I am going to turn to my colleagues for questions, and then I am going to have one final question for you. Senator Lautenberg.

Senator LAUTENBERG. Madam Chairman, my questions were already answered by the stunning presentation made by these young people, and when I say "stunning," I am not talking about—they are all good-looking, but that is not the stunning part. The stunning part is the realization about how much more difficult life is when juvenile diabetes is present.

I have got to say for everybody here that we are so fortunate to have Susan Collins, the Senator that she is and Chairman of this Committee—by the way, "Chairman" doesn't go with female, but we know what we mean when we say "Chairman." She is the Chairman, and she is so motivated by her experiences with people who have had juvenile diabetes. And I feel similarly because when I look at you, all of you, I see my own grandchildren and what I wish for them in the years ahead. But we are lucky that we have Susan Collins here because she is on the Republican side of the ledger, I am on the Democratic side of the ledger, and the two of us are determined—we talked privately outside—to do whatever we can, and I know I include my other colleagues here as well, do whatever we can to move this process along, to make life just a little bit easier for all of you. And we hope that one day you will come here and visit and say, "What a past I have had, but I have passed it," and we thank you all.

[Applause.]

Chairman COLLINS. Thank you, Senator, for your support and your kind comments.

Senator Coleman.

OPENING STATEMENT OF SENATOR COLEMAN

Senator COLEMAN. Thank you, Chairman Collins, and I join my colleague, Senator Lautenberg, in applauding the Chairman for her tremendous leadership, and not just because she has a great heart, but she gets things done. And I am very hopeful. As we listened to these small voices, by the way, these are little voices, but they are very loud. They are very loud, and what you are saying, the witnesses, by the presence of the other kids is echoing very loudly in these halls. So you really are making a difference. And, Chairman, I thank you for putting this together and for your leadership.

I want to say to LaNiece, you are very good. And folks in this room, the parents have got to be very proud. It is hard to sit up here in front of U.S. Senators and present testimony, and the parents should be very proud.

Eric, let me ask you, how do you describe to your pals, how do you describe juvenile diabetes to kids, to your buddies?

Mr. ERIC BONNESS. I just say the only people that really understand the disease are the people who are my close friends, because in order to really understand the disease, you have to be around it all day. So, actually, my close friends understand it when they see—just by watching me test my sugar, seeing what I do with the

various readings that I get of my blood sugar. As far as other kids, they think when I wear my insulin pump that I have a pager or stuff like that.

So I can explain it to people, but in order to get a full understanding of the disease, you pretty much have to live around it.

Senator COLEMAN. Alex, the same question.

Mr. ALEX BONNESS. Yes, I agree. I think the awareness of it is very hard to get out for people to understand really what it is.

Senator COLEMAN. Do you take the time to talk to them a little about it?

Mr. ALEX BONNESS. Yes, I try to, because I get jokes about when my blood sugar is low, we are eating candy during the day. And kids have actually said to me, "Wow, I wish I had diabetes." It is kind of weird to hear them say that because they don't really understand how terrible it is.

Senator COLEMAN. LaNiece, the same question to you. How do you tell your friends? What do you say to them, and how do they react?

Miss EVANS-SCOTT. Some people think the same thing he just said. They just want diabetes because I get to eat in class. And at the beginning of the school year, me and my mom always go to the class that I am in and explain it to them. Some people don't understand it, though.

Senator COLEMAN. Katie?

Ms. HALASZ. I am actually really lucky because my friends help me take care of the disease. They make sure I always have food with me. They make me test my blood all the time and help me take my shots and stuff. So I am very fortunate with that.

Senator COLEMAN. Sophia, do you talk to your friends at all about this? And what do you tell them, and what do they say?

Miss CYGNAROWICZ. I do not really know.

Senator COLEMAN. OK. That is OK.

Colleen, in terms of other parents, do you have conversations and do they get it?

Ms. REA. Oh, they get it. I talk to every person who will stand still long enough.

[Laughter/applause.]

Senator COLEMAN. Thank you, Madam Chairman.

Chairman COLLINS. Thank you.

Senator Fitzgerald, your constituent, Sophia, has been great in helping us understand the disease.

OPENING STATEMENT OF SENATOR FITZGERALD

Senator FITZGERALD. Well, thank you, Senator Collins. And, Sophia, I want to welcome you here. I know where you are from in Illinois. You are from Columbia, and I was there not too long ago. I want to welcome you for coming all this way, and I want to welcome the other Illinois constituents who are here. I know Senator Durbin introduced them earlier.

And all of you kids, too, I was very impressed with your statements, and you should be very proud of the good work that you are doing helping to spread awareness of the difficulties associated with diabetes.

Now, Senator Coleman asked you about what the other kids were thinking, and I am just wondering. You did not quite get into this, but are any kids at school maybe mean to you or do they make fun of your diabetes? Does that happen to any of you? LaNiece, are some of the kids mean?

Miss EVANS-SCOTT. Sometimes.

Senator FITZGERALD. What do you say to them if they are mean?

Miss EVANS-SCOTT. I don't really say anything to them.

Senator FITZGERALD. Alex?

Mr. ALEX BONNESS. It is not really a disease that is—it is not physical. You cannot see it. You couldn't look at me and tell that I have diabetes. So I don't really get much trouble from friends.

Senator FITZGERALD. Did you when you were younger, maybe in second or third grade?

Mr. ALEX BONNESS. Sometimes people joke around about it, bullies just trying to be mean, called me a diabetic and stuff. I mean, it is rough, but you cannot do anything about it. So you have got to move on.

Senator FITZGERALD. Katie, are the kids pretty understanding?

Ms. HALASZ. Some of them are. I know that the parents, they don't really want me to go over to their houses because they don't want to take the responsibility. But I don't—other than that, they are fine with it.

Senator FITZGERALD. Now, if you were to stay at somebody's house overnight, you would have to be checking your blood sugar, and the parents of your friend might be worried about liability having you stay overnight.

Ms. HALASZ. Yes.

Senator FITZGERALD. How about the rest of you on the panel, are you able to stay overnight at your friends' houses?

Mr. ALEX BONNESS. Pumps help, but I have actually had—my brother talked about the migraine headaches, and at a sleepover I did have one one time. So people kind of get worried about it sometimes. I definitely don't do as many sleepovers as a lot of my friends do.

Senator FITZGERALD. The others of you, have you ever slept over at a friend's house?

Miss CYGNAROWICZ. Yes.

Senator FITZGERALD. Sophie, have you slept over at a friend's house?

Miss CYGNAROWICZ. Yes.

Senator FITZGERALD. And do you check your own blood sugar?

Miss CYGNAROWICZ. Yes.

Senator FITZGERALD. You do. OK.

Do all of you have to wake up in the middle of the night to check your blood sugar, or are you able to sleep through the night?

Mr. ALEX BONNESS. I am lucky enough that my parents actually wake up every night and check our blood sugars while we are sleeping.

Senator FITZGERALD. Is that the same with all of you?

Ms. HALASZ. I know when I am high or low, we have to wake up every couple hours to make sure we are coming down or keep going up. But, yes, there are a lot of nights that we have to check our blood in the middle of the night.

Senator FITZGERALD. How many times does your blood sugar have to be checked during the night?

Ms. HALASZ. Anywhere from two to three.

Senator FITZGERALD. Two to three times every night.

Mr. ALEX BONNESS. If you are either high or low before you go to bed. In most cases, you are usually good so you only check like one time. But in some cases, yes, two or three times.

Senator FITZGERALD. And do your parents get up and check that?

Mr. ALEX BONNESS. Yes.

Miss EVANS-SCOTT. Yes.

Senator FITZGERALD. For all of you, and do you sleep right through it?

Mr. ALEX BONNESS. Well, mostly.

Senator FITZGERALD. OK. Well, Colleen, you are the one who has to wake up then and check the blood sugar. It is a real burden on the parents, isn't it?

Ms. REA. Well, I go to bed late, and I test him before I go to bed. And if his numbers are good, because he has the insulin pump and he doesn't take a lot of insulin compared to these other children yet, I can sometimes sleep through the night. Occasionally I get to sleep through the night.

Senator FITZGERALD. Thank you so much for being here. We will all be working together to try hopefully someday years hence not to have these hearings in Washington because I am hopeful that someday we will arrive at a cure or some satisfactory solution that makes it easier to live life with diabetes. But thank you all very much for what you have done to bring awareness to people around our country on this issue. You are making a great contribution and leaving a significant mark on this country at a very early age.

So thank you all very much.

[Applause.]

Chairman COLLINS. I told you I was going to do one more question, but I changed my mind in view of the hour. You are the best panel of witnesses I have ever seen, so thank you so much.

[Applause.]

And I know I speak on behalf of every Senator who has been here today when I do promise to remember you. Thank you for being here.

[Applause.]

We are now going to move to our final panel, but before we do, the JDRF has asked me to announce that if any of the children are feeling as if your blood sugar is low right now, there is food right outside the hearing room if you need a snack. So you can feel free to go get it if you think you need a snack.

We are now going to call forth our final panel. Our final panel of the day will testify about some of the promising breakthroughs that have been made in juvenile diabetes research as well as future opportunities for research. They will tell us about the work that is being done in pancreatic islet cell transplantation, which has been hailed as the most important advance in diabetes research since the discovery of insulin.

Dr. Allen Spiegel is the Director of the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health.

Dr. Bernhard Hering is an Associate Professor of Surgery and Director of Islet Transplantation at the University of Minnesota.

And Anne Seidel of Dallas, Texas, is an actual islet cell transplant recipient, and I am so eager to hear your story.

I want to turn to Senator Coleman, because there is a distinguished witness from Minnesota here, for any additional comments that he might have.

Senator COLEMAN. Thank you, Chairman Collins, and I would just like to do a very brief introduction for Dr. Hering from Minnesota.

Minnesota has established itself as the cluster for medical research and technology, and in addition to making big contributions to the State's economy, this activity also has important benefits to our Nation's health. I was pleased to form a Medical Technology Caucus with Senator Biden, again, bipartisan. This is not a partisan issue. The health of our kids and our families are not partisan issues. It is Democrats and Republicans coming together.

I am proud to note that a large part of this activity has always centered around the University of Minnesota, particularly in dealing with the issue of islet transplantation in our transplant facility. And Dr. Hering is one of the leaders in islet transplantation. Again, as has been noted, this technology represents a major source of hope for diabetics, their families, and their friends. I share Senator Fitzgerald's hope and passion that very quickly we move forward with a cure. But the reality is that some of the advances that Dr. Hering is involved with are very important, and I appreciate, Madam Chairman, your inviting him here today to discuss the current status of this technology and the steps we next need to take.

I am proud to be a cosponsor with Chairman Collins on S. 518, the Pancreatic Islet Cell Transplantation Act. Voices are being heard, and we will work hard to make sure that we make progress in this area.

Thank you, Madam Chairman.

Chairman COLLINS. Thank you very much, Senator Coleman.

Dr. Spiegel, we will proceed with you.

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

Dr. SPIEGEL. Thank you. Chairman Collins, Senator Coleman, delegates to the JDRF Children's Congress, family members, and guests, I appreciate the opportunity to testify at this hearing on type 1 diabetes. Nothing I could say would be more eloquent than the testimony you just heard from Mary Tyler Moore, from the children and teens who told their stories, nor the testimony you will hear from Anne Seidel, an islet transplant recipient. Nonetheless, I have much to tell you about what NIH support has accomplished to date and how we plan to seize the exciting opportunities before us in type 1 diabetes research.

All this is detailed in a thick report on the special statutory funding program for type 1 diabetes, released yesterday by Secretary Thompson. The full report, as well as a slimmed-down executive

[1] The prepared statement of Dr. Spiegel appears in the Appendix on page 60.

summary, are available in hard copy and on the NIDDK website. This morning I will just offer a few examples and highlights.

First, though, on behalf of NIH, I would like to thank you and the other Members of Congress for your support of the NIH and of the special statutory funding program which has significantly augmented our regularly appropriated funds for diabetes research.

The special program has enabled the formation of unique, productive collaborations involving multiple institutes at NIH and the Centers for Disease Control, and has brought new researchers from multiple disciplines together to accelerate research on type 1 diabetes.

I would also like to acknowledge the JDRF for its vigorous support of type 1 diabetes research. The JDRF is an invaluable collaborator as the NIH continues to define specific research goals and needs in type 1 diabetes. The JDRF indeed has partnered with NIH in diabetes initiatives and has brought its international scope to bear in combating diabetes since this disease knows no geographic boundaries.

When the special funding program was increased from $30 million to $100 million per year in fiscal year 2001 and extended to 2003, we formulated an ambitious research plan with input from expert scientists and key advocacy groups such as the JDRF. Our type 1 diabetes research plan has six broad goals: To identify the genetic and environmental causes; to prevent or reverse the disease; to prevent or reduce hypoglycemia, the low blood sugar you heard so much about; to prevent or reduce complications; to attract new talent to type 1 diabetes research; and last, but certainly not least, to find a cure.

In the 2 years since I last testified before you, significant progress has been made in all these areas as reflected in just five examples.

First, basic research on diabetes complications has shown that a vitamin derivative can prevent complications in animal models and has led to clinical trials of a drug to prevent blindness. Second, a network of pediatric centers called "DirecNet" has been created with the special funds to test new technology made by two different companies for continuous, non-invasive glucose monitoring so we can develop alternatives to the multiple finger sticks we heard about from the kids this morning and that Senator Fitzgerald asked about. Third, a biotechnology drug, a monoclonal antibody, has shown promise in reversing recent onset type 1 diabetes and will be tested in a larger clinical trial supported by the special funds. Fourth, investigators have reported success in converting adult stem cells—and both mouse and human embryonic stem cells—into insulin-producing cells. Fifth, the Immune Tolerance Network, with support from the special funding program, is completing a multi-center trial of the Edmonton Protocol for islet transplantation first reported in the year 2000. An interim report released just 3 weeks ago indicated that several centers are capable of rendering greater than 60 percent of their islet transplant recipients insulin independent.

You will hear in much greater detail about islet transplantation from one of the pioneers to my left, supported by NIH, Dr. Bernhard Hering. Let me say that NIH is vigorously addressing the two

major scientific hurdles we must clear to make islet transplantation a true cure: Developing an inexhaustible supply of insulin-producing cells, and achieving immune tolerance, a state of acceptance of a transplant that no longer requires taking potentially toxic and costly immunosuppressive drugs lifelong.

For the former hurdle, the Beta Cell Biology Consortium, created with the special funds, is intensively studying all aspects of islet development so we can learn how to grow sufficient amounts for treatment. A significant portion of the special funds, recently augmented—with your leadership—by the Congress from $100 million to $150 million per year and extended from 2004 to 2008, will be devoted to research needed to make islet transplantation a widely available reality. We will also be focusing attention on so-called translational research that converts basic science advances into practical diagnostic tests, treatments, and preventive measures.

I am grateful for this opportunity to give you some examples of the progress and plans being made in type 1 diabetes research, particularly with the assistance of the special statutory funding program. We are living in a new and exciting era of scientific research that, with its rapid advancement and immense opportunities, is unprecedented. We intend to take full advantage of the new technologies and information that have emerged in this new era to realize greater progress in diabetes research.

We continue to be inspired by the dedicated efforts of patients and their families and by organizations such as the Juvenile Diabetes Research Foundation. We remain steadfast in our fight against diabetes, helping kids such as Katie Halasz right now with efforts such as our guide for school personnel, "Helping the Student with Diabetes Succeed," while ever focused on the ultimate goal—finding a cure.

We must help all the children in this room who represent the children with type 1 diabetes in this entire country. They are the reason for all of our efforts. Thank you.

[Applause.]

Chairman COLLINS. Dr. Hering.

TESTIMONY OF BERNHARD J. HERING, M.D.,[1] ASSOCIATE PROFESSOR OF SURGERY, DIRECTOR OF ISLET TRANSPLANTATION, UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINNESOTA

Dr. HERING. Chairman Collins and Senator Coleman, my name is Bernhard Hering, and I am addressing you today on behalf of my physician-scientist colleagues. Our ability to transform the landscape of juvenile diabetes in this country in the next decade depends heavily on the Federal Government's efforts. Chairman Collins, I want to applaud your efforts and those of the more than 30 Senators who have cosponsored your legislation entitled "The Pancreatic Islet Cell Transplantation Act of 2003." I believe that, if passed, this bill will empower clinical researchers to expedite the translation of islet transplant research into unsurpassed, innovative treatments for individuals with juvenile diabetes and accel-

[1] The prepared statement of Dr. Hering appears in the Appendix on page 66.

erate the integration of such treatments into health care delivery systems.

Although the research community has experimented with islet cell transplants for decades, they are now at last becoming a practical, successful, superior, and distinct therapy for patients with juvenile diabetes. This disease continues to be challenging, with significant morbidity and mortality. Diabetes is a devastating burden to patients and their families, especially when acute complications are frequent and chronic complications are advanced. In the previous panel, you heard about the daily challenges people face in living with juvenile diabetes from the most effective messengers—children who suffer each and every day with this disease.

Please allow me now to illustrate how islet transplants are unsurpassed in their potential to transform the lives of people with difficult-to-control juvenile diabetes. Lorna is a 35-year-old mother of two boys who developed diabetes at age 9. She completely lost her ability to sense low blood sugar levels, also referred to as hypoglycemia. Brain function is severely compromised during episodes of hypoglycemia, leading to confusion, distorted perception of surroundings, dizziness, odd behavior, seizure, coma, and possibly death. Lorna became incapacitated by weekly episodes of severe hypoglycemia, requiring the help of a third person and often paramedics. As a result, Lorna lost her driver's license, was laid off at work, was divorced, and was denied the right to see her boys.

In August 2000, Lorna was admitted to the General Clinical Research Center at the University of Minnesota for an islet transplant under a protocol supported by the Juvenile Diabetes Research Foundation and the NIH. She was taken to a radiology suite, where a local anesthetic was given and a catheter was placed through her skin into the portal vein of her liver. Islets isolated from a cadaver donor pancreas were resuspended in buffer, transferred to a transfusion bag, and infused over 20 minutes through the catheter into her portal vein. Infused islets were carried by her blood to smaller branches of the portal vein, where they lodged, engrafted, and resumed tightly controlled secretion of insulin in response to her blood sugar levels. The catheter was then removed, and she was discharged to go home 2 days later.

Lorna's blood sugar levels returned to normal. She was able to completely discontinue insulin injections 1 month after her islet transplant. Since her transplant, she has not experienced a single episode of severe hypoglycemia. She learned to love life again, rediscovered her ability to make contributions to our world, regained control over her destiny, received her driver's license back, found a new job, married the paramedic who had repeatedly saved her life——

[Laughter/applause.]

Dr. HERING [continuing]. While she was diabetic, closed on a new home, and was granted authorization to take care of her boys again, all in the first year after her transplant. Now, almost 3 years later, Lorna continues to be insulin independent and diabetes free. She takes immunosuppressive medications to prevent rejection of her transplanted islets. She has not experienced any severe adverse events. You will hear another remarkable success story from Anne Seidel following my testimony. Equally impressive suc-

cess stories have been reported by a few other centers in the United States, including the University of Miami, Baylor College in Houston, and the University of Pennsylvania, to name the most active and successful of centers.

For patients like Lorna, insulin is survival, but an islet transplant is return to life. Islet transplants are now a clinical reality, not just a topic for investigational research.

Let us now assume for just one moment that your 35-year-old daughter suffers from juvenile diabetes complicated by recurrent episodes of severe hypoglycemia, that she meets all accepted medical criteria for an islet transplant, that she has good health insurance, and that she wants to proceed with an islet transplant. Will she be able to undergo an islet transplant?

Most likely no. There is a severe shortage of donor organs for islet transplants. Funding in the area of clinical translation of islet transplantation has not kept pace with the science, and regulations must be changed to provide incentives for additional procurement of donor organs for islet transplantation and research. And insurance coverage of islet transplantation is currently not available, thereby largely restricting them to patients meeting the very stringent eligibility criteria of research protocols.

This disconnect between the promise of basic science versus the delivery of better health in the United States is of significant concern. Islet transplants for the treatment of diabetes are being covered by several provinces in Canada, where a landmark pilot clinical trial called the Edmonton Protocol was performed in 2000. The steadfast commitment to basic biomedical research in the United States has provided the basis for today's high success rate in reversing diabetes in human patients. It has also provided an unprecedented supply of information for further breakthroughs in clinical islet transplants. Yet islet transplants remain largely unavailable 3 years after the demonstration of proof of principle. Failure to use available science is costly and harmful. It leads to overuse of inferior care. In contrast to Canada, we fail to deliver the best care we could for patients with difficult-to-control diabetes. Health insurance companies should be on board but are not.

Both my learned opinion and my best bet are that one-third of the gifted children with juvenile diabetes with us today in this room will develop devastating, destructive, or deadly diabetes complications before they are 50 years old—unless we enhance our preclinical and clinical research agenda markedly in the next 2 years in order to realize a sizable effect within 10 years. The potential short- to mid-term impact of islet transplants on patients with juvenile diabetes prone to develop devastating complications is unmatched by any other treatment modality. The Pancreatic Islet Cell Transplantation Act of 2003 would help overcome the fragmentation and underfunding of today's clinical islet transplant infrastructure and remove major translational blocks in the implementation of islet transplants. More specifically, it would be instrumental in maximizing donor pancreas utilization, in documenting the benefits of islet transplants, in shortening the time to FDA approval of transplants of human islets, and, finally, in developing an unlimited supply of tissue for transplantation such as xenogeneic islets from animals or stem cell-derived islets.

In closing, I believe the Pancreatic Islet Cell Transplantation Act of 2003, if passed, will greatly enhance the islet transplant translational infrastructure and help it to operate much more efficiently. It will raise needed awareness, create additional momentum, send a very strong signal to all major stakeholders in health care delivery, and facilitate the expedient delivery of today's science and technology for the benefit of thousands of patients afflicted with juvenile diabetes. The bill will also help prepare the field to respond nimbly to the extraordinary advances that surely will emerge from stem cell biology and other high-impact, cell-based technologies of the future. Thus, this legislation will have implications well beyond its primary objectives.

As I look around the room at all these children who are here today to take an active role in finding a cure for juvenile diabetes, I know that the scientific community and Congress must match their passion and dedication. This will not be an easy task, but progress in science has been truly remarkable and emerging opportunities are even more extraordinary. Removing translation blocks will allow our patients to benefit from scientific breakthroughs.

We were able to put a man on the moon more than 30 years ago because we wanted it, because President Kennedy declared it possible. I know we could cure diabetes if we declared it possible.

Madam Chairman, Senator Coleman, thank you from the bottom of my pancreas.

[Laughter/applause.]

Chairman COLLINS. Thank you for your testimony. Ms. Seidel.

TESTIMONY OF ANNE SEIDEL,[1] ISLET CELL TRANSPLANT RECIPIENT, DALLAS, TEXAS

Ms. SEIDEL. Senator Collins and Members of the Committee, thank you for the opportunity to appear before you today as an example of a true success story resulting from the public-private partnership between the Juvenile Diabetes Research Foundation and the Federal Government in supporting medical research and the National Institutes of Health. I am Anne Seidel, proud mother of Charlie, 6, and Lacey, 5. I have been an active JDRF volunteer for 5 years in Dallas and nationally.

I was diagnosed with juvenile diabetes 35 years ago, at age 6. My son Charlie, now 6, was diagnosed 5 years ago. I cannot describe to you the anguish I experienced when he was diagnosed with juvenile diabetes. As a mother, your focus in life is caring for and protecting your children, but I could not protect him from this disease that was ravaging my body for over 30 years at that point.

While I focused all of my energy on caring for Charlie when he was diagnosed, diabetes was taking an enormous toll on my body. Over the years of living with diabetes, I have won the battle of near blindness and kept going. I have had nerve damage in my feet and partial paralysis of my stomach and kept going. My blood sugars would jump from being at a level of 16—so low that I was in danger of becoming unconscious—to a level of 600—which is so high that I could slip into a coma—in the course of 2 hours and then back down and back up again. This roller coaster defined

[1] The prepared statement of Ms. Seidel appears in the Appendix on page 77.

many of my days. Most days, feeling nauseated and exhausted, I had to keep going.

But the complication of my diabetes that prevented me from keeping going was when I lost my ability to feel my low blood sugars. Instead of being able to sense this and quickly take some sugar and rectify the situation, my blood sugar often kept dropping until I was unconscious, blacked out, totaling my car, or so confused that I did not know who I was, who my children were, and oftentimes not sure whose diabetes I was taking care of. I came very close several times to accidentally giving Charlie insulin that he didn't need, and the result of that could have meant his death.

About 4 years ago, I began watching—with more than a passing interest—the advancement of pancreatic islet cell transplantation. Upon investigation, the state of my diabetes matched the criteria for participating in these clinical trials. When deciding to participate in the trials, I had to come to terms with the fact that the procedure was not available for children, and because of the immunosuppressive drugs, this was not available for many. As a mother, your instincts are to take care of your children first. And after lots of introspection, I had to become OK with having the procedure because I thought in an airplane the parent must put the oxygen mask on themselves first so they can save their child, and I had to do the same with my diabetes.

After speaking with every center in the world that was conducting islet transplants, I was screened at several places and I chose to be on one list. Because of the severe shortage of pancreases in the United States and with my rare blood type, I spent over 2 years on the waiting list, hoping for the call. Every day that passed, I worried that my diabetes would worsen and that while I waited I might be prevented from receiving a transplant because of ensuing complications. I decided to increase my chances for a transplant and listed at three additional centers.

I received my transplant on February 5 and my second on April 9 of this year. Most current protocols involve two pancreases, two transplants to receive the appropriate number of islet cells. I was called to come to the Methodist Hospital in Houston, and the insulin-producing islet cells were extracted from a donor pancreas, put into an IV bag. And while this was being done, I changed into my gown and went into the radiology suite where the radiologist fed a small needle into my liver and dripped the cells into me. I was in the surgery suite for only about 20 minutes and was conscious throughout the procedure. Back in the recovery room, I looked down at my side and I said the surgeon, "You mean you just saved my life and all I have to show for it is this Band-aid?" Thirty hours after the transplant, I was home.

Since my transplant, I no longer need to take insulin. To give you a sense of how dramatically this has changed my life, in the 35 years I had juvenile diabetes, I have taken 255,500 units of insulin and have pricked my fingers 56,210 times. For the first 12 years of my diabetes, I tested my urine 21,900 times. People have asked me to describe how I feel after the transplant, and the best analogy I can think of is that I felt like I had not bathed in 35 years and somebody finally washed me off.

An amazing result of the transplant is that many of the complications that plagued my days before are now gone. The nausea, exhaustion, confusion, unconsciousness, foot pain, and a large helping of fear are now gone. Having clear thoughts, energy, not feeling fearful of endangering myself or my children has been nothing less than utopia. Diabetes doesn't define me anymore. I truly have received the gift of a lifetime.

As one of the approximately 250 people worldwide whose life has been changed through an islet transplant, I thank you from the bottom of my heart. Your commitment to the NIH, coupled with JDRF's commitment, has truly saved my life. But there is no time to sit back and congratulate ourselves because there are many more who cannot take advantage of this procedure. And I will not rest or be truly happy until Charlie and these kids and all my friends with type 1 can be cured like myself. They deserve no less. Call me demanding, but I do not like being one of so few.

It may sound strange, but diabetes has given me many opportunities in my lifetime, one of which is the privilege of being here and talking to you. I want to thank you publicly and JDRF for saving my life. A cure is within our grasp. Together, our efforts and funds must make this happen sooner than later. Thank you.

[Applause.]

Chairman COLLINS. Ms. Seidel, thank you so much for sharing your miraculous story with us. I think your story gives hope to every person in this room. And I, too, look forward to the day when there are no shortages, when insurance and Medicare cover this procedure—in fact, I am looking at introducing an amendment to have a demonstration project under Medicare to pay for the procedure. And we need to get my legislation passed to overcome some of the other barriers that Dr. Hering also outlined for us.

You have made the process sound relatively easy. But you do have to take immunosuppressive drugs, don't you?

Ms. SEIDEL. Yes.

Chairman COLLINS. Have you had any negative reaction to those or are you generally doing as well as you seem to be doing?

Ms. SEIDEL. I am doing really well. I have had very few complications from the drugs. I have experienced mouth sores, which are common side effects of the immunosuppressants, but to me, any bump in the road has been a very small price to pay for what I have received.

Chairman COLLINS. It really is wonderful. I have followed this procedure for the last couple of years and read a lot about it, but you are the first recipient whom I have had the honor to meet. It is just fabulous to hear your story today.

Ms. SEIDEL. Thank you for helping make it possible.

Chairman COLLINS. Thank you.

Dr. Hering, can you help us understand better why this procedure is not appropriate for most children right now?

Dr. HERING. At this point in time, we have to limit this procedure to a very small subgroup of patients in whom the benefits outweigh the risks associated with the use of immunosuppressive medication. And I think it would not be appropriate to consider islet transplantation at this point in time for the treatment of children because complications are possibly very harmful.

But progress has been made recently in our ability to prevent rejection, and as Dr. Spiegel pointed out, major research networks have been established recently to evaluate emerging breakthrough technologies in this direction.

The limiting factor has been to move the wonderful progress that has been made from the mouse level to the point that it can be safely evaluated in people. So we need to make this translational step and need to provide compelling evidence obtained in non-human primate studies that would justify testing in people. If we could do this and if we could really reduce the time it takes to take these steps, we could clearly capitalize on all the breakthroughs that have been reported recently.

Chairman COLLINS. Thank you for the research that you are doing.

Dr. Spiegel, thank you for giving us the broader overview of all of the promising developments in research. Every time you appear before me, I always put you on the spot, and I always feel bad about it, but I am going to do it again this year. That is, we have heard from Dr. Hering and we have heard from the Juvenile Diabetes Research Foundation that the legislation that I have introduced to try to remove some of the barriers to the procurement of more pancreases and to otherwise encourage the development of more procedures to facilitate the kind of transplant that has made such a difference to Ms. Seidel. I have introduced the Pancreatic Islet Cell Translantation Act and would really like to have the support of NIH. Can we count on the support of NIH for my legislation?

Dr. SPIEGEL. Given what a strong supporter you have been of type 1 diabetes research and of the NIH, I, of course, would like to say yes, so I hesitate to really inject this note in this wonderful hearing. You know, though, very well that in my position I really can't comment on pending legislation.

What I will say is I am happy to address any aspect of the science associated with this, and I would say that this is clearly being very carefully evaluated in the Department and elsewhere. We are obviously very motivated by the advances Dr. Hering has talked about, and we are trying with a collaborative islet transplant registry in a variety of ways to meet these goals. But I really can't comment further.

Chairman COLLINS. Well, I thought I would try.

Dr. Spiegel, in addition to the very promising developments with islet transplantation, what do you view as the single other most promising therapy on the horizon for juvenile diabetes?

Dr. SPIEGEL. Just sticking with the issue of a cure, we have the wonderful opportunity with the resources you have put at our disposal to explore at least two other alternative strategies, and these need to be explored in parallel. One is an artificial pancreas. Many of the kids you have seen—and heard from—have these pumps, and these are an improvement in terms of insulin delivery. If we could hook those up with a continuous sugar-monitoring device that is non-invasive—and these are being studied in this collaborative trial that I mentioned—we might have what is called a closed-loop system.

Again, such an artificial pancreas would never mimic perfectly what we see with the actual islets, but it would be pretty close and

could be pretty good. And if it were miniaturized, it could make a huge difference. So that is being pushed, and that is really an example also of public-private partnership, basic research done by NIH-supported investigators, including the small business set-aside—which we support, as you know—which is then picked up by industry. Two major companies are advancing this technology. They claim they are close, but we have to see the evidence.

The other issue is a complicated issue that Dr. Hering referred to—xenotransplantation, the idea, for example, of pig islets. People have taken pig insulin for years, and it works very well. It works just as well in many respects as human insulin. So, why can't we just use pig islets? There are issues about viruses that are present and, of course, transplant rejection.

There, too, we are supporting research. I want to make a point here with regard to both the immune tolerance we heard about and xenotransplantation. As important as this is for type 1 diabetes, it transcends one disease. It is important for all transplantation. There is a shortage of all these organs in terms of kidney and liver, etc. So this is very important research.

Knock-out technology, so-called, has created pigs that lack the sugar that causes hyper-acute rejection. And that is a step in the direction of making this a reality.

Chairman COLLINS. Thank you. Senator Coleman.

Senator COLEMAN. Thank you, Madam Chairman.

I was mentioning the Minnesota connection. First, I want to thank Mary Tyler Moore for her leadership, and I would be remiss in not mentioning the Minnesota connection there because she lived and worked there for many years. So we are very proud. But thank you for your strong voice here.

Another Minnesota connection are folks from Medtronic, and I don't want to pick out one company, but there is some great work going on in the biotechnology side.

Dr. Spiegel, let me ask you first, you just touched briefly upon stem cell, and, in fact, another area where the University of Minnesota is doing some breakthrough work on adult stem cells. Give me your best sense of how far down the road, if you can do that, we are from using stem cell research to make any significant advances here, either for adult or for juvenile diabetes?

Dr. SPIEGEL. Thank you, Senator Coleman. I will focus my remarks exclusively on stem cells as applied to diabetes, particularly type 1 diabetes.

Indeed, at the University of Minnesota, is a colleague of Dr. Hering's, Dr. Catherine Verfaille. She just addressed our National Advisory Council, and she is a member of our Beta Cell Biology Consortium. She is doing extraordinary work on what are called multi-potent adult progenitor cells. While she hasn't yet had definitive success in turning these into insulin-producing cells, they have been turned into liver cells and other relevant cells, and we are looking for further developments.

There have been reports of adult bone marrow-type stem cells in mouse models curing diabetes. At the same time, there have been substantial advances, as I said in my testimony, both in terms of turning mouse embryonic and human embryonic stem cells into insulin-producing cells. They don't produce as much insulin as we

would want. They are not perfect in terms of being like the real beta cells in the islets. But this is a very important step in the right direction that we are supporting heavily within the guidelines of the President's decision of August 9, 2001. We at NIH are totally committed to making this not only an acceptable but a priority area of research. And that is the message that I and Dr. James Battey, who heads the NIH Stem Cell Task Force, are putting out across the country to encourage our investigators.

Senator COLEMAN. I am familiar with Catherine's work and working with some technology companies to do the next step, and translate the research into a reality. Is the FDA process of looking at that stuff, is that set up in a way to allow us to move quickly enough to take advantage of some of these research opportunities?

Dr. SPIEGEL. To answer this would really be beyond my purview, so I hesitate to do so. What I would say is that the company, Athersys, which you are referring to, is one that has had an opportunity to present to the Stem Cell Task Force. We are really interested in public-private partnerships under Dr. Zerhouni's leadership. He has been creating a vision for the future of NIH called a roadmap, and there are many aspects of that vision which we discussed at a retreat last Friday that are relevant to this audience: Re-engineering the clinical research enterprise, facilitating harmonization with the NIH and the FDA, and public-private partnerships. These are very relevant themes.

Senator COLEMAN. Thank you very much.

Ms. Seidel, just one question. How were you chosen? You said in your testimony you fit the criteria, but how did you take advantage of or get picked for this opportunity?

Ms. SEIDEL. When the criteria was outlined by most of the centers that were doing it, Minnesota being one, the criteria included patients that were healthy otherwise, having primarily one complication which is asymptomatic, low blood sugars, meaning low blood sugars that you cannot feel to the point where that can paralyze your life from being normal in any way. And that was something that I suffered from. Otherwise, I was healthy.

Dr. Hering can tell us more, but, really, the patients that were being selected were patients that could then be quickly rendered free of those low blood sugars once they were transplanted, but whose bodies could withstand the transplantation and the immunosuppressive drugs.

Senator COLEMAN. What was your biggest fear when you decided to take advantage of the islet transplant?

Ms. SEIDEL. How long it was going to take. That was my biggest fear. I knew that we had a severe shortage of organs in the United States, and with a rare blood type, I hoped that my complications of diabetes didn't worsen while I waited.

Senator COLEMAN. How long after the surgery did you first get the sense that, wow, something has changed?

Ms. SEIDEL. Almost immediately. I felt better within a couple hours of the anesthesia wearing off.

Senator COLEMAN. Dr. Hering, how many potential patients like Ms. Seidel do you kind of wade through before you get to choose? Which has to be, by the way, a pretty daunting feeling about making those kinds of choices. I would hate to be in that position. But

what is your universe? And then ultimately how large is the patient group that benefits from this opportunity?

Dr. HERING. Thank you, Senator Coleman, for your question. When we announced our program, within a matter of a few weeks we received 2,500 applications, and it was the first challenge how to deal with those applications and how to be able to get back to patients and explain in sufficient detail why we can do it or why we cannot do it.

First and foremost, we have to protect the safety of participants. We have a long list of 40 exclusion criteria. We need to continue considering those criteria very seriously to protect the safety of participants.

I believe that of those 2,500 that contacted us initially, only 30 to 40 were identified as eligible candidates. If you ask the question how many patients in the United States at this point in time would meet criteria like Anne Seidel, I think you are talking about at least 5 percent of our population that has been diagnosed with type 1 diabetes. So you are talking about 50,000 people at this point in time.

When I look at the field of islet transplantation and cell replacement therapies today, what we do is we show the feasibility of cells to reverse diabetes. This is a completely new area in diabetes therapy that has not been available before. Everybody who wants to see can see what the implications are and future technologies are waiting to be implemented. Thus, what we do today is just a first step. We show the feasibility of all therapy, a technology that is fundamentally new and different. I think we need to keep the momentum going. Of particular importance is that we maximize donor pancreas utilization. We are not facing a true shortage. We are facing logistical problems. Within 1 year we could procure 2,000 additional donor pancreases. These organs are available, but are currently not recovered. I think your bill clearly addresses this point very directly. This example indicates that it is not only science that is limiting our ability to deliver the new technology of all therapy. We really have to identify non-scientific roadblocks and address these problems.

Senator COLEMAN. Thank you, Doctor. I again want to applaud both of you for your work and also what you are doing today to help us, I think simply better educate some folks so that in the end we can pass Chairman Collins' legislation and make a real difference in a lot of lives. So thank you very much.

Thank you, Madam Chairman.

Chairman COLLINS. Thank you, Senator.

I want to thank our panel for your expert testimony today. It was fascinating and a fitting conclusion to what has been a very moving experience for me in chairing this hearing. Thank you all so much for being with us.

I want to thank all of the witnesses who appeared today, and most of all, I want to thank the children because they are the ones who really motivate all of us to work harder in the search for the cure.

I also want to pay tribute to Mary Tyler Moore. You could not have a better adult spokesperson for this cause.

And I want to thank the Juvenile Diabetes Research Foundation. They have worked so hard to put this Children's Congress together. I am very proud to have been the co-Chair this year, and it has been a real privilege to work with a group of people who are so caring and so committed. Together, I am positive that we are making a difference every day. Thank you for being here.

The hearing record will remain open for 15 days for the submission of some additional questions that we ran out of time for and any statements. Thank you very much.

This hearing is adjourned.

[Applause.]

[Whereupon, at 1:02 p.m., the Committee was adjourned.]

APPENDIX

PREPARED STATEMENT OF SENATOR LIEBERMAN

Thank you, Madam Chairman for calling this hearing today so that we can focus on a disease that affects the daily lives of up to a million children and their parents across the country and on an organization—the Juvenile Diabetes Research Foundation—that deserves enormous credit for its global leadership in working to find a cure for this misunderstood disease.

It's such a pleasure to have this group of young, lively representatives here today who are all doing their part to raise awareness about the importance of juvenile diabetes research. Three of these young lobbyists are from my home State of Connecticut. If you'll indulge me for a moment, Madam Chairman, they are Matt Ruby, a 17-year-old from Avon, Amanda Updyke, a 14-year-old from East Lyme, and Dylan Rae, from my home town of Stamford, who will join his mom and dad in testifying today. Dylan, I know I'm a little late, but I understand you had a big day over the weekend, so, on behalf of my colleagues here today, I want to wish you a belated but hearty Happy Fourth Birthday.

As you all know too well, Type 1 diabetes affects anywhere from 500,000 to 1 million Americans, most of them children and young adults. In act, the risk of developing Type 1 diabetes is higher than the risk of developing virtually any other severe, chronic childhood disease. That's why the search for a cure is so important.

What most people don't realize is that insulin is not a cure. Type 1 diabetes needs constant attention and is often difficult to manage. And because of the threat of complications, it can reduce the quality of life and shorten the life span of those who suffer from it.

Diabetes is also one of the most expensive diseases to treat. Finding a cure not only would improve the lives of these young people with us today, it would save taxpayers millions of dollars in Medicare, Medicaid and State Children's Health Insurance Program expenses.

That's why I have proposed an American Center for Cures, an institute dedicated to finding the next generation of medicines that will enable this generation of Americans to live healthier, stronger, and longer lives. We must take some of the miraculous developments that are occurring in laboratories around American today—the Human Genome Project, stem cell research, all sorts of other pharmaceutical breakthroughs—and focus them in one place with the goal of curing some of the chronic diseases—including diabetes—that plague 100 million Americans and cost $750 billion a year to treat.

We can do this, but we can only do it with an investment of public money, attractions for private money, and a center to make this a real goal. The experts I talk to say that with research we are within reach of cures for a variety of diseases including diabetes, Alzheimers, Parkinson's, cancer and AIDS, if we really work at it.

In the meantime, we must lend our strong support to Chairman Collins' bill, the Pancreatic Islet Cell Transplantation Act, which I am pleased to co-sponsor. Among other things, this bill directs the Secretary of Health and Human Services to study and assess the value of a promising new therapy—pancreatic islet cell transplantation—whereby healthy pancreatic cells are injected into diabetics who's own pancreases have failed. It is a simple procedure, very similar to a blood transfusion, and the early results have given a lot of people hope.

When all is said and done, what we need is national leadership on this issue, national leadership to commit resources and marshal our resolve to cure this disease. This is America. In America we don't just manage problems; we solve them. That's what our country is all about. All of you have committed to a goal of curing diabetes. Today, I join you in that commitment—to banish diabetes from our lives and the lives of our loved ones forever.

Thank you, Madam Chairman.

Testimony

By

Mary Tyler Moore

New York, NY

On Behalf of the

Juvenile Diabetes Research Foundation International

"Juvenile Diabetes – Examining the Personal Toll on Families, Financial Costs to the Federal Health Care System, and Research Progress Towards a Cure"

Before the

Senate Governmental Affairs Committee

216 Hart Senate Office Building

June 24, 2003

10:00 a.m.

Good Morning. Before my formal remarks, Senator Collins, I'd like to personally thank you for your leadership and all your efforts on behalf of people with diabetes, including conducting these hearings and Co-Chairing (with Senator Breaux) the Senate Diabetes Caucus. With your continued support, I know we will, together, find a cure. Now, please allow me to offer this testimony:

Chairman Collins, Senator Lieberman, committee members. I am Mary Tyler Moore, and I'm here today as International Chairman of the Juvenile Diabetes Research Foundation. I wish I could say that I am happy to be here. But meaning no disrespect, I'm not. You see, I've had juvenile diabetes for more than 35 years now, and I'm tired of it. I sincerely wish that I didn't have to come back, year after year, to seek your help – but I do. I have to, for myself, for everyone with diabetes, and most especially for the beautiful and courageous children who are here with me today.

Be certain, at JDRF we have never been more dedicated to finding a cure for diabetes and its complications -- and the evidence suggests we are truly close. Much of the progress that has led us to what we hope and believe are the final stages of our fight against diabetes is the result of your support and effort. We greatly appreciate the good partnership we have always had with Congress and every Administration since our founding. We are incredibly grateful for the extraordinary support you all showed last year in passing the Special Juvenile Diabetes Program—the most significant legislation ever enacted relating to juvenile diabetes research. But, as you can see, I'm here again. Despite all our accomplishments together, we must face the fact that there are still significant hurdles we need to overcome to take the last necessary steps along our path to a cure.

Senators, some of you have already met many of the 200 child delegates to JDRF's 3rd Children's Congress who are here in Washington this week; you'll be hearing from some, and meeting others, later today. They are passionate and eloquent spokespeople for the need for a cure. But don't be misled by their drive, their energy, and their unwavering commitment. They – and I – struggle every minute of every day to do what happens naturally for people who don't have diabetes: achieve a balance between what I eat, what I do, and how I feel. For most of you, blood sugar balance is as automatic as breathing. But for people with juvenile diabetes, like me, it requires vigilance 24 hours per day, seven days per week, 365 days per year.

Each of these children and I need to be a mathematician, a physician, a personal trainer, and a dietician all rolled into one. We need to be constantly factoring and adjusting, making frequent finger sticks to check blood sugars, and giving ourselves multiple daily insulin injections just to stay alive. Not to live life to its fullest, mind you; just to stay alive. And God knows, it isn't easy. Even with the greatest of care and the closest of personal scrutiny, like many children and adults with juvenile diabetes, I find I am often unable to achieve good balance. My blood sugars can go dangerously low, or frighteningly high. Yes, dangerous and frightening — because serious lows can lead to seizures, coma, and death. And high blood sugars can, over time, result in disabling and life-shortening complications. Some of you may already know the startling toll diabetes

takes. For example, diabetes causes over 40% of kidney failures in our country that require dialysis or transplantation. It is responsible for more than half of amputations not associated with traumatic injuries. Is the leading cause of blindness in adults – the *leading* cause. Moreover, I've seen studies that say that virtually everyone with juvenile diabetes shows evidence of heart disease by age 40 – age 40! – and that pre-menopausal women with juvenile diabetes have a more than 30 times greater risk of death from heart attack. Beyond the incomprehensible personal costs, consider the economic burden our country must bear as a result of this disease: diabetes costs this nation over $130 billion per year. This includes one out of every four Medicare dollars spent. Taken altogether, it should be crystal clear why it is urgent that we find a cure, and find it as soon as possible.

Chairman Collins, you and your colleagues, from both sides of the aisle, have always welcomed us warmly during our past Children's Congresses. In our prior meetings, you've promised to remember us when making decisions about funding for juvenile diabetes research. Today, we are thrilled to acknowledge to all who might listen that you are, indeed, keeping your promise.

We thank you not just as your constituents, but also as your partners in a shared mission to find a cure. Reflecting our long-term commitment to partnering with government for this purpose, JDRF is working closely with the NIDDK – the lead agency responsible for investing the supplemental research dollars called for in the Special Diabetes Program --- to ensure that this funding is truly responsive to the needs of people affected by juvenile diabetes. From our discussions with Dr. Alan Spiegel, NIDDK's director and a good friend of JDRF, we are confident that these "special" dollars will be used to fund projects that otherwise could not be undertaken through the usual NIH appropriation. And we expect that these projects will focus on what's needed to rapidly acquire mission-critical knowledge, provide essential research resources, and speed the application of scientific advances for the benefit of people with juvenile diabetes.

Madame Chairman, Senators, it's vital to remember that because children and adults with juvenile diabetes and their families never get a rest from their disease, we never rest in our efforts to find and deliver them a cure. And because JDRF is truly a global cure enterprise, we are always looking beyond the horizon, to anticipate what we must do next to achieve our ultimate goal – a world without juvenile diabetes. Our approach has consistently focused on "what's next." Let me give you an example, looking at four steps we have taken to get to the point where we are today in islet transplantation:

Step one: In the mid-90s, JDRF created a map of all that is known about diabetes, and identified the knowledge gaps and obstacles to progress along the various paths to a cure. We use this continuously updated map to guide us in efforts to push scientific advances from the laboratory bench quickly to the patient's bedside.

Step two: This process made clear that islet cell transplantation is a potential cure. So we invested in creating a global network of research centers to prepare and distribute human islets for research.

Step three: As it became clear that with JDRF support, research Centers throughout the world were able to test islet cell transplantation, JDRF moved its focus ahead. We substantially boosted our investments in research aimed at the induction of immune tolerance, concentrating on finding the means to replace the need for transplant patients to take toxic immunosuppressive drugs for the rest of their lives.

Step four: In 2000, when Dr. James Shapiro's group in Edmonton reported the first major clinical success in islet transplantation, JDRF jumped to the next obstacle confronting transplant research: the minute supply of islets for transplantation. To create an unlimited supply of islet cells for transplantation, we led a global effort to support stem cell research. This is particularly necessary because each year, there are fewer than 2,000 cadaver pancreases donated. Yet well over 1 million Americans with juvenile diabetes could potentially benefit from islet transplantation.

Overall, we've made terrific progress, Madame Chairman, but we continue to look into the future and ask ourselves, "What's Next?" Here is what we believe must be next, to speed a cure for juvenile diabetes:

First, we need policies and regulations that encourage organ donations and promote the retrieval of additional human pancreases. As I said, supply is a major obstacle to making islet transplantation a cure for all those with diabetes who might benefit. I am thrilled that you have shown real leadership and vision by introducing "The Pancreatic Islet Cell Transplantation Act of 2003." This bill, which JDRF strongly supports, will provide regulatory incentives for organ procurement organizations to retrieve additional pancreases. It will also create a demonstration project within Medicare to test insurance coverage for islet transplants for people with juvenile diabetes and kidney failure. I am hopeful that Congress will pass the legislation this year, and we are eager to work with you on this.

Second, we need to work with the Senate and the President to make the policy adjustments required to be certain we can accomplish our goal and that of the President: empowering stem cell researchers to find ways to relieve the suffering of millions of Americans. Even with increased organ procurement, we will – ultimately – still face a critical shortage of islet cells for transplantation. As a result, we need to ensure that the public and private sectors have the scientific freedom and support required for the U.S. to take its proper place as the world leader in promoting stem cell research and the development of human stem cell-derived therapies.

As you know, Madame Chairman, right now, due to the restrictions of current Administration policy, this just won't happen. I know the President worked hard to find balance in this policy. He clearly recognized the great potential of stem cell-derived therapies to reduce pain and suffering of millions of people, with a host of diseases, including juvenile diabetes. And, in my heart, I know it was his intent to make it easier, not more difficult, to create therapies to treat human disease. But now, nearly two years after his August 9th, 2001 decision, researchers tell us that the progress being made in stem cell research is not as far along as it should be. The number of cell lines everyone

had hoped for – more than 60 were supposed to be available – turns out to be closer to 10. Of these lines, only a few are widely available for research. Perhaps most important, of those "approved lines" none – that's right none – can be used to develop human therapies. The problem is that each of those cell lines were established using mouse feeder cells or other non-human products; the threat of contamination makes them unusable for human therapies.

For these reasons and others, the best and the brightest of young researchers in the U.S. are shying away from the field of human stem cell research. So not only do we have an insufficient number of cell lines to conduct the necessary research, we have a potentially more devastating deficiency of brainpower.

Again, I have no doubt this was not the outcome the President intended, since if unaddressed, it certainly does not well serve the interests of the American people. Similarly, I should acknowledge that the White House, Secretary Thompson, and Dr. Zerhouni, the NIH director -- as well as other NIH directors working on the NIH stem cell task force – are all doing what they can, within the current constraints. We are working closely with them, and we are all the same page in terms of our need to focus on finding a cure as soon as possible.

Third, we need to continue to invest in developing methods to replace human islets without immunosuppression. It is nothing short of miraculous that today, just three years after the Edmonton Protocol, more than 250 people have undergone successful islet transplantation and no longer need insulin injections to survive. But the procedure is not yet safe for children and most people with diabetes. So we must sharpen our research focus on immune tolerance, as well as redouble our efforts to prevent diabetes and reverse or prevent its devastating complications.

Finally, because we want a cure for everyone with juvenile diabetes, including the children here today, we need to establish a framework for research oversight which properly balances the need to protect children from harm with the need to support the conduct of the research required to find the cure on their behalf.

Madame Chairman, diabetes is an all-too-personal time bomb, which can go off today, tomorrow, next year, or ten years from now. A time bomb that affects millions, including me and the children here today. It needs to be defused. But to find a cure for diabetes and its complications, and then make these cures available to everyone who might benefit, will require that we remain vigilant in our purpose and continuously committed to asking, answering, and acting upon the "What Next?" question.

So "What's next?" for you. Please listen to the children this morning, who'll tell you how they struggle with juvenile diabetes. Learn about how they bravely face its daily challenges – challenges no 15-year-old, or eight-year-old, or two-year-old should have to endure. Feel their longing to know a day without diabetes and live the normal, care-free life of a child. Listen to the researchers, as they highlight the progress made to date and the exciting opportunities we can now capitalize on because of JDRF and NIH leadership

– and the wonderful investment Congress has made in medical research. And hear first hand from an islet transplant recipient about how spectacularly her life has changed since her procedure – and how she won't rest until her young son who also suffers from juvenile diabetes can be cured.

Finally, please join me and JDRF in making a promise to remember what we have learned today, and as a result ask ourselves: What Next?

Thank you, once again, for all you have done, and for the opportunity to speak with you this morning.

Testimony of Katie Halasz

Unlike Dylan and Sophia, I do know what it's like to live without diabetes. I dream of another day without diabetes. My name is Katie Halasz. I am 16 years old and from Wells, ME. I want to tell you how my life changed on June 12, 1999 at 11:00 p.m. when I was diagnosed with juvenile diabetes.

At first, I didn't know what diabetes was. The doctor told me that I would have to take insulin shots the rest of my life. I didn't think that diabetes would change my life that much, but boy was I wrong! I have to test my blood sugar and take shots all the time. It affects everything I do - even being part of the color guard for the school band is a challenge. My sugar level often goes high and results in keytones that are poisons in my body that can be very dangerous. When you get keytones you can't do any exercise. It is very hard on my team and on me when I can't march.

School is a lot harder when you have diabetes. My school doesn't allow me to test my blood in the classroom. My classes are on the third floor and the nurses office is on the first floor. When I feel low I have to walk down three fights of stairs, and this is very dangerous. Some of my teachers think that I leave the classroom just to get out of class – do they think I enjoy sticking a needle in my finger?! When my blood sugars are high, I can't concentrate on my work and my vision blurs. My teachers don't understand. Some of them even think that it is my fault that my sugars go up because they think that I eat things like candy bars. They don't understand that my sugars can go up for no

apparent reason. Educating my teachers has been one of my biggest challenges since being diagnosed with diabetes.

Having diabetes complicates more than just school. Last year I had a cyst under my arm. It became infected. I went go to see a surgeon about once a month to have the area opened so it could drain. My sugars were always high because of the infection, and the infection would not heal because of the high sugars. Finally, I had to have surgery to remove the cyst. The doctors also had to remove half of the tissues in my underarm.

Senator Collins and members of this Committee, we are here today to ask for your help in finding a cure for juvenile diabetes. Each of us wants to be able to go to school, play in the band and on sports teams, without worrying about going into a coma because of a low blood sugar. Each of us wants to grow up without the daily stress of trying to treat a horrible disease and the fear of complications. We will do our part to educate policymakers about diabetes and raise money to support research. But we need you to be our partner in this effort – we can't do it alone. Senator Collins, I am glad and grateful you are my Senator. You have shown incredible dedication and leadership in our common quest for a cure. Thank you from the bottom of my heart.

Testimony of Colleen Rea

Good morning. My name is Colleen Rea. I'm from Stamford, Connecticut, and it is an honor to appear before you today with my four-year-old son Dylan. Dylan and I are here today, along with all of these children, to tell you why finding a cure for juvenile diabetes is so important. You see, I know all too well about the devastation of diabetes. Diabetes has followed me and has haunted my family for three generations.

When I was a child, I found glass syringes in my house and was told that my grandfather, who died before I was born, had diabetes. When I was a young woman, my mother called and asked me to meet her at the hospital emergency room. My mother was being admitted for the first time because of her diabetes. When I saw her, she was scared! So was I! Within ten years and many hospital stays and operations later, I was told my mother was dying. It took only ten years for diabetes to kill my mother.

When my son Dylan was diagnosed with Type 1, or juvenile, diabetes at fourteen months old - less than two years after my mother died – I was devastated. It was almost more than I could bear. I knew what diabetes had done to my grandfather. I had seen what diabetes had done to my mother.

We are very diligent in trying to treat Dylan's diabetes. But controlling blood sugar levels in a toddler is impossible because there are so many variables. There are always times when Dylan's blood sugar is dangerously high or frighteningly low. He wears an insulin pump 24 hours a day. We check his blood sugar at least eight times a

day. There are precious few who are able to babysit him. My husband and I must be available 24 hours a day, seven days a week. Diabetes never takes a break, and neither can we. We are Dylan's pancreas.

While we are concerned about Dylan's physical health, we also worry about his emotional health. Dylan may grow up, live a long life, have a great and fulfilling career, and a wife and children of his own one day. But we know in our hearts that, despite our best efforts, he may be denied all of that. Either way, he has this day and this childhood, and I want it to be wonderful.

We walk a tightrope in caring for Dylan - help our child feel love and joy when we are continually assaulting his body with needles and lancets; give our child hope and faith in the face of fear and disease; tell Dylan he is healthy but needs medicine every day, all day, to survive.

I know that a cure is possible and within reach. I hope that it will be found soon so that Dylan and all of these children will live a long and fulfilling life. This is my greatest wish and why we are here today to ask for your help and support in our quest for a cure.

Thank you.

Testimony of Sophia Cygnarowicz

Hi. My name is Sophia, and like my friend Dylan, I don't know what it is like to have a day without diabetes. I am seven years old. I have had diabetes since I was one.

I have taken four thousand, three hundred, and eighty shots of insulin and have pricked my finger over thirteen thousand times to test my blood sugar. I don't like it! It hurts! It is so hard to keep my blood sugar in a good range. No matter how hard I try I still go low and high.

Low blood sugars make me very tired and cranky. I need to eat but a lot of times I don't want to. Sometimes I wake up in the middle of the night because I go low. My mom and dad will feed me and test my blood sugar to make sure I will be o.k. before I go back to sleep.

I just finished first grade. It is hard going to school when you have diabetes. We did cooking projects and had lots of parties. I watched the other kids eat cookies and cake. I couldn't eat them, and that wasn't fair. When I feel low at school I can't think well. My teacher gives me sugar tablets and I walk to the nurses office to do a blood sugar test. A friend comes with me to make sure I get there o.k. Then I have juice and crackers. It takes me a while before I feel better. I don't like to miss class.

Summer is lots of fun, but not when I go low and can't stay outside and play with my friends. I have to eat at the same time everyday so my blood sugar won't go too low. I have to eat even when I'm not hungry.

I don't know what life is like without diabetes, but I sure would like to find out. Finding a cure is important to me because I won't have to take shots or do blood tests. Most of all, I could eat a snow cone whenever I wanted to. My friends in this room and I aren't asking for much, we just want a life without diabetes.

2003 CHILDREN'S CONGRESS

ERIC BONNESS TESTIMONY

Having diabetes is not something you struggle with alone – it affects your whole family. If you have diabetes, it affects everything you do. If you also have a brother with diabetes, it affects everything—times two. Our family has twice as many blood glucose "kits", and twice as many insulin pumps—more than ten thousand dollars worth. We do twice as many blood sugar checks, and change catheters twice as often. We have twice as many blood sugar "highs and lows". We have twice the costs——economic, physical and emotional.

My name is Eric Bonness. I am eighteen years old and from Omaha, Nebraska. I was diagnosed with type 1 diabetes when I was ten, three years after doctors diagnosed my little brother, Alex, with diabetes. I didn't have to go to the doctor's office to be told I had diabetes. I found out one morning in my bedroom after I had been up all night going to the bathroom, and guzzling water. Just before dawn, I opened my eyes as my parents sat down on my bed holding my little brother's blood glucose meter. For three years I had seen the fear—and the tears—in the eyes of my little brother as he endured thousands of finger pokes and insulin shots. I knew I was about to get my first finger poke to test my blood sugar. I was terrified. I had always been afraid for Alex. Now, I was also afraid for me. The doctors said there was only a small chance I would ever get diabetes. Suddenly, statistics didn't matter.

My mom poked my finger. Then, my parents and I watched in silence as the seconds ticked down on the blood glucose meter to reveal my blood sugar. The numbers seemed to explode off the screen at me—"495". I asked my mom if I had diabetes, but I already knew the answer.

Like any brother, Alex can be a real "pain". But he has always helped me with the "pain" of diabetes. When I was first diagnosed, Alex would get candy for me when I had a low blood sugar level. He also taught me how to give myself insulin shots to bring down high blood sugars. Now that we are older, we still help each other recover from insulin reactions. We give each other test strips when one of us runs out. We even borrow the other's insulin pump when ours stops working.

It's scary enough to have diabetes myself. But, it's even worse to watch my little brother suffer with diabetes. Alex sometimes has a low blood sugar and migraine headache at the same time. He becomes semi-conscious, incoherent and unable help himself. I watch my parents struggle as they try to raise his blood sugar before he slips into a coma. We are lucky my mom is a doctor. Other families would have to go to the hospital. During these episodes, my parents give Alex an emergency I.V.—or shot of glucagon—to raise his blood sugar level. It's horrible to see diabetes make my brother so vulnerable. If diabetes is doing this to him now, even with the best available medical care, what is diabetes going to do to him in the future?

I am not going to wait to find out. I start college next year and plan to go on to medical school. We have to find a cure—and soon. Diabetes is *not* going to kill my brother, and it's not going to kill me.

We need your vote to keep our hope alive.

Thank you.

2003 CHILDREN'S CONGRESS

ALEX BONNESS TESTIMONY

My name is Alex Bonness. I am fifteen years old and I am Eric's younger brother. I was diagnosed with Type 1 diabetes when I was four. I don't remember the day I found out I had diabetes but I do remember being really scared of the finger pokes and shots. When I was diagnosed, no one on either side of our family had Type 1 diabetes so living with it was a big shock to us. I remember feeling lost, confused, and alone. Some nights, I would throw tantrums and cry when it was time to go to bed. I never talked about why I did it. My parents thought it was because I afraid of the imaginary monster in my closet. Boy were they wrong! I was afraid of a monster alright, but it wasn't in my closet. It was diabetes.

When I was seven, I felt like I was saved. That's when Eric was also diagnosed with diabetes. I know it sounds terrible to say I felt like I was saved because my big brother was diagnosed with diabetes. How could such a bad thing become a good thing? I was sad Eric had to go through so much pain because of diabetes, but somehow I no longer felt so alone with my disease. When Eric reached out to me, I made sure I was there for him. Don't get me wrong—Eric can be a real "pain". But it was important for me to help him.

As Eric and I have grown up together, we have always told each other we can beat diabetes. I know we can. But as I get older, my fears about diabetes seem to grow too. When Eric hit his teenage growth spurt, I watched his uncontrollable blood sugars skyrocket to extremely high levels because of his changing hormones. It scared me to death. I worried about Eric.

Now, I am hitting *my* teenage growth spurt—and I worry about me. I have cried myself to sleep. I have also cried with my mom about what scares me most: going blind or having my legs amputated. Mom always tries to comfort me. But she and I both know that complications could occur at anytime.

For example, I have to go to the eye doctor every year. At my recent eye appointment, I sat on pins and needles with every word my eye doctor said. She saw no signs of complications——yet! On the way home, I thought about what I would have done if she had seen blood vessels in my retina starting to deteriorate.

I am not a little kid any more. I know my brother can't save me from going blind. But I also know that **research can! And you can make that happen!**

Thank you.

Testimony of LaNiece Evans-Scott

Many of the kids here today, like my friend Alex, worry about getting complications from juvenile diabetes when they get older. I am here to tell you that some of us, like me, already have serious complications from juvenile diabetes. I am LaNiece Evans-Scott from Backlick, Ohio. I am ten years old, and I have battled juvenile diabetes my entire life.

I was diagnosed with juvenile diabetes after going into a coma when I was only 16 months old. I spent the first five years of my life in and out of hospitals. My mom had to learn how to give me shots and to take care of me. She hasn't been able to work because she has to take care of me all of the time. She drives me five hours to see a special doctor who helps me care for my diabetes.

I already have problems with my kidneys and I take medicine every day so that my kidneys won't fail. I worry about what will happen to my kidneys and what other complications I will face as I get older if a cure isn't found soon. I am also blind in one eye – not from diabetes, but I worry about what my diabetes will do to my other eye.

I have a lot of trouble in school because the teachers send me home when my blood sugar levels are bad. I am not bad! I am good! It is the diabetes that is bad! I do the best I can, but I am only a kid and diabetes is a horrible disease. I have fallen behind in school because I miss so many classes. I like school and I also like bowling. I have a lot of friends and I am on the bowling team.

I used to be shy about having juvenile diabetes, but I have learned that I must tell my story to important people like you so you know how serious diabetes is and why a cure is important. I want a cure so that I can be like all of my friends and go to sleepovers and birthday parties. I want a cure so I can go to school every day without worrying about being sent home. I want a cure so my mom won't worry so much about me and can go back to work.

I don't have time to wait. Please promise to remember me. Promise to remember all of us. Thank you.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Juvenile Diabetes – Examining the Personal Toll on Families, Financial Costs to the Federal Health Care System, and Research Progress Toward a Cure

Witness appearing before the
Senate Committee on Governmental Affairs

Allen M. Spiegel, M..D.
Director
National Institute of Diabetes and Digestive and Kidney Diseases

June 24, 2003

DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
Statement of the Director
National Institute of Diabetes and Digestive and Kidney Diseases

Chairman Collins and Members of the Committee: As Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I appreciate the opportunity to testify at this hearing on type 1 diabetes, held in conjunction with the "Children's Congress" of the Juvenile Diabetes Research Foundation International (JDRF). On behalf of the NIDDK and the other Institutes and Centers of the National Institutes of Health (NIH), I am pleased to report that we are aggressively pursuing research on childhood diabetes and its complications. We are gaining insights into the underlying causes of disease development, working diligently toward more effective treatment and prevention strategies, and striving for a cure.

Type 1 diabetes is the form of the disease that strikes mainly in childhood and adolescence; it affects approximately one million Americans. Patients require daily insulin administration and must carefully monitor their food intake and exercise in order to manage the disease. Even with continuous and vigilant disease management, patients are still susceptible to developing serious, long-term complications. Although we have a much greater understanding of the disease than we did a decade ago, we still need to carry out both basic and clinical research to find new ways to improve the quality-of-life for type 1 diabetes patients, whether through advances in insulin delivery, islet transplantation, or other avenues. Research is the key to a cure.

The NIH is focused on six broad goals in type 1 diabetes research: (1) to understand the genetics and environmental causes of type 1 diabetes so that we can identify who is at risk for developing the disease; (2) to prevent or reverse the disease; (3) to develop cell replacement therapy as a cure for diabetes; (4) to prevent or reduce hypoglycemia (low blood sugar) which limits tight control of blood sugar; (5) to prevent or reduce complications; and (6) to attract new research talent to the field. The research we undertake to achieve these goals is supported by both our regular appropriation and by the Special Statutory Funding Program for Type 1 Diabetes Research. Research teams are vigorously studying different aspects of the disease, such as interactions between genetic and environmental factors, the development and function of the insulin-producing beta cells of the pancreas, and how the misdirection of the body's immune defense system can be corrected to spare the beta cells from immune attack. Because of the complexity of the disease, investigators with diverse expertise are attacking the disease from many different angles. Through this multifaceted approach, we can attain a comprehensive understanding of the disease process--the foundation for future advances in treatment, prevention, and approaches to a cure.

Relative to each of our six research goals, I would now like to highlight some of the specific advances and initiatives that have been made possible through the Special Funding Program. We have deployed the special funds to create unique, multidisciplinary consortia to tackle the major obstacles to developing methods to prevent and cure type 1 diabetes. These have involved not only partnerships among scientists with complementary expertise from multiple

academic institutions, but also partnerships among many of the Institutes and Centers of the NIH, the Centers for Disease Control and Prevention (CDC), the JDRF, and the American Diabetes Association (ADA). I will highlight selected examples of our major efforts. Further information and additional examples are presented in a new "Report on Progress and Opportunities" to date under the Special Funding Program, which began in fiscal year 1998 and will continue through fiscal year 2008. This important interim assessment is based on input from external scientific and lay experts, grant recipients, and NIH staff involved in the program.

Understanding the Genetics and Environmental Causes of Type 1 Diabetes

Type 1 diabetes is caused by a combination of genetic and environmental factors. Identifying these factors is key to both prevention and cure. Already we know some of the major genes that predispose patients to develop type 1 diabetes, but identification of other key genes will provide new targets for therapy. To this end, we have formed a collaboration to collect genetic material from 7,500 families in which one member has type 1 diabetes. This material will be an invaluable resource to investigators in their search for culprit genes. We know much less about the environmental factors that trigger onset of type 1 diabetes in a genetically susceptible individual. To address this question, an international consortium will use our knowledge of key genes predisposing to type 1 diabetes to identify infants at high risk for developing the disease and follow them through adolescence in a search for environmental factors that may trigger disease onset. We call this study "Triggers and Environmental Determinants of Diabetes in Youth," or "TEDDY." The Special Funding Program has also allowed us to address the important issue of whether rates of development of type 1 diabetes in America are changing over time. The NIDDK and the CDC are supporting a population-based registry to define the prevalence and incidence of diabetes in children. This project, entitled "SEARCH," will identify children with diabetes in six regions of the country and will help us understand how the disease strikes and unfolds.

Reversing or Preventing Type 1 Diabetes

To spur the testing of promising new strategies to prevent, delay, or reverse progression of type 1 diabetes, the NIDDK, in conjunction with the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), the ADA, and the JDRF, has established a clinical trial network, the "Type 1 Diabetes TrialNet," consistent with a major recommendation of the congressionally-established Diabetes Research Working Group. Teams of diabetes experts and immunologists will test promising new therapies that may preserve the ability to make insulin in those newly diagnosed with type 1 diabetes and actually prevent the development of the disease in individuals at high risk based on genetic and immunologic tests. The NIAID-led Immune Tolerance Network will partner with TrialNet in efforts to test promising interventions and strategies to prevent or reverse type 1 diabetes. An international trial addresses the role of environmental factors in the development of type 1 diabetes. The NICHD-led "Trial to Reduce the Incidence of Type 1 Diabetes in the Genetically-At-Risk," or "TRIGR," will compare the development of type 1 diabetes in infants who are weaned onto a hydrolysate of cow's milk formula *versus* standard cow's milk formula.

Developing Cell Replacement Therapy

Insulin therapy, via daily injections or a pump, is a poor substitute for the body's exquisitely precise regulation of blood glucose by insulin-producing pancreatic beta cells. In contrast to insulin administration, a real cure could emerge from cell-based therapy, such as the transplantation of insulin-producing cells. Just this month, researchers participating in the Immune Tolerance Network, led by NIAID, reported the preliminary results from a study in which the islet transplantation protocol pioneered in Edmonton, Canada, was replicated at nine sites. Although the success rates varied among the centers, this study showed that the new procedure can relieve some patients of the burden of daily insulin injections. However, the immunosuppressive drugs of the new protocol do carry significant side effects and the long-term results of the procedure have yet to be established. This confirmation of the success of the Edmonton protocol offers great hope to the diabetes community of investigators, patients, and families and will stimulate further research to improve the procedure. Nonetheless, there are still some barriers in the field of islet transplantation that could limit its widespread use in clinical application, such as: (1) inadequate supplies of islets and (2) imperfect methods to prevent transplant rejection and recurrent autoimmunity.

To make the promise of islet transplantation a reality for those with type 1 diabetes, we are accelerating research on many aspects of beta cell development and function with the goal of creating an unlimited supply of islets for transplantation. A key component of this effort is the NIDDK-sponsored Beta Cell Biology Consortium. This collaboration is providing scientists with access to information, resources, technologies, expertise, and reagents that are beyond the means of a single research effort. It represents an unprecedented effort to delineate each step in the pathway that leads to formation of beta cells with the unique capacity for appropriately regulated insulin secretion and to develop methods to create unlimited supplies of these vital cells.

We are also supporting research to develop alternatives to the lifelong immunosuppressive drug treatments that are currently required to prevent rejection of transplanted islets as well as recurrence of the autoimmunity that caused type 1 diabetes. In addition to the efforts of the Immune Tolerance Network and other NIAID-funded investigators, preclinical work is being pursued in promising animal models. The NIDDK and the NIAID, through the Autoimmunity Centers of Excellence and the Prevention Centers for Autoimmune Diseases, support multidisciplinary basic and clinical research in type 1 diabetes and other autoimmune diseases. Another research consortium is pursuing methods to induce immune tolerance to transplanted kidneys and islets in non-human primates to achieve long-term graft survival. This approach would avoid lifelong immunosuppressive therapies that can have deleterious and often life-threatening side effects.
Key new resources have been developed to spur islet transplantation research. A network of islet cell resource centers will improve methods of islet isolation and provide islets to researchers nationwide. A newly created transplant registry will collect and analyze data from all islet/beta cell transplants performed in the U.S. and Canada. This effort will expedite progress and promote safety, as this technology advances at an accelerated pace after the success of the Edmonton protocol. Through this multifaceted bench-to-bedside approach combining shared resources, collaborative fundamental basic research, preclinical

development in animal models, and multicenter clinical trials, the NIH is aggressively pursuing every avenue toward progress in islet transplantation that can directly translate into potential therapies for type 1 diabetes patients.

Reducing or Preventing Hypoglycemia in Type 1 Diabetes

Perhaps the most distressing, acute complication of type 1 diabetes is hypoglycemia, or low blood sugar. It is caused by excessive treatment with insulin relative to food intake and physical activity. The potential for hypoglycemic episodes has impeded the use of intensive insulin therapy even though major clinical trials have shown that such therapy can significantly reduce the risks of longer-term diabetic complications. Some diabetes patients are also at risk for a condition called "hypoglycemia unawareness," in which they have difficulty recognizing the symptoms of hypoglycemia and are, therefore, more vulnerable to adverse outcomes. Hypoglycemia is a particular problem in young children, who may not be able to realize and communicate their symptoms to parents. For these reasons, we have made a greater understanding of hypoglycemia and new approaches to mitigate this problem a key goal to be pursued through the Special Funding Program, and have established research programs to address these important issues.

We have established a network, called "DirecNet" (led by NICHD), to test recently-developed glucose sensors in children with type 1 diabetes to determine their value in reducing the risk of hypoglycemia. Already, DirecNet has compared two new devices, which had not been previously tested in children. These approaches--as well as the support of basic and clinical studies of hypoglycemic complications, and glucose-sensing and insulin-delivery technologies--are all directed toward improved management of the disease.

Preventing or Reducing the Complications of Type 1 Diabetes

The complications of diabetes affect virtually every system of the body. Diabetes increases the risk of blindness, kidney failure, chronic wounds and skin ulcers, nerve pain and other neurological problems, lower limb amputation, heart disease and heart attacks, stroke, high blood pressure, gum disease, and pregnancy-related problems. Diabetes and its complications can shorten average life expectancy by up to 15 years. Costs to the nation are in excess of $130 billion annually in health-related expenditures. The NIDDK continues to foster, through the Special Statutory Funding Program for Type 1I Diabetes Research and through our regular appropriation, exciting new opportunities for the research community to intensify the study of many diabetic complications. A particular focus of the program has been on the development of tools needed to enhance clinical research, such as the development of biomarkers which can predict the development of complications and can serve as outcome measures allowing clinical trials to be conducted more efficiently and less expensively. Another focus has been on the development of animal models that faithfully replicate development of complications of diabetes in humans. These models are essential for preclinical drug development.

In addition to clinical studies, basic research is under way to identify the genes that may increase a person's susceptibility to developing the eye and kidney complications of diabetes. Identifying the genetic basis of these complications will reveal new targets for therapy.

Attracting New Talent to Research on Type 1 Diabetes

Type 1 diabetes research spans an extraordinarily broad range of scientific disciplines. For this reason, a cadre of exceptionally talented and dedicated researchers is needed to bring expertise to bear on understanding, treating, preventing, and curing type 1 diabetes. As more research is being done in the laboratory, or "bench," there is a need to rapidly move those results into the clinic, or "bedside," to directly benefit patients. For this reason, the NIH is sponsoring "bench-to-bedside" initiatives, which form partnerships among basic and clinical scientists. In addition, we are supporting the research training and career development of pediatric endocrinologists. Due to heavy clinical demands, it is especially challenging for pediatric endocrinologists involved in diabetes care to also pursue research careers, yet their clinical expertise is invaluable to type 1 diabetes research. The NIDDK, in collaboration with the ADA and the JDRF, is supporting research training and career development programs in pediatric endocrinology at institutions whose environments, mentors, and programs should make them particularly effective in enhancing the number of independent investigators who can contribute to research in this area.

I am grateful to share with you these few highlights of the Special Statutory Funding Program for Type 1 Diabetes Research. With the recent completion of the Human Genome Project, we are living in a new and exciting era of scientific research. We intend to take full advantage of the new technologies and information that have emerged to realize greater progress in diabetes research. Diabetes is a devastating illness for patients and their families, especially when it strikes in infancy, childhood, or adolescence. We continue to be inspired by the dedicated efforts of patients and their families, by organizations such as the Juvenile Diabetes Research Foundation International. We are thankful for the full range of appropriations for type 1 diabetes research. We continue to be vigilant in our fight against diabetes so that we can help all the children in this room; they are the real motivation behind all of our efforts. I am pleased to answer any questions you may have.

Juvenile Diabetes –
Examining the Personal Toll on Families,
Financial Costs to the Federal Health Care System,
and Research Progress Towards a Cure

Testimony
on

Research Opportunities in Pancreatic Islet Transplantation
and Thoughts on
"The Pancreatic Islet Cell Transplantation Act of 2003" (S.518)

Presented by

Bernhard J. Hering, M.D.

Eunice L. Dwan Chair in Diabetes Research
Director, Islet Transplantation, University of Minnesota
Co-Director, Juvenile Diabetes Research Foundation Center for Islet Transplantation
at the University of Minnesota and University of California at San Francisco
Co-Director, NIH Immune Tolerance Network Islet Transplant Subgroup
Medical Director, NIH Collaborative Islet Transplant Registry
President, Cell Transplant Society

Before the

UNITED STATES SENATE
COMMITTEE ON
GOVERNMENTAL AFFAIRS

June 24, 2003

Chairman Collins and members of the Committee on Governmental Affairs,

My name is Bernhard J. Hering. I am the Director of Islet Transplantation and holder of the Eunice L. Dwan Chair in Diabetes Research at the University of Minnesota, and Co-Director of the Juvenile Diabetes Research Foundation (JDRF) Center for Islet Transplantation at the University of Minnesota and the University of California at San Francisco. I currently serve as Co-Director of the NIH Immune Tolerance Network Islet Transplant Subgroup, as Medical Director of the NIH Collaborative Islet Transplant Registry, and as President of the Cell Transplant Society.

I am addressing you today on behalf of my physician-scientist colleagues. Our ability to transform the landscape of juvenile diabetes in the US in the next decade depends heavily on the federal government's efforts. Chairman Collins, I want to applaud your efforts and those of the more than thirty Senators who have Co-sponsored your legislation entitled "The Pancreatic Islet Cell Transplantation Act of 2003 (S.518)". I believe that, if passed, this bill will empower clinical researchers to expedite the translation of islet transplant research into unsurpassed, innovative treatments for individuals with juvenile diabetes and accelerate the integration of such treatments into health care delivery systems.

Although the research community has experimented with islet cell transplants for decades, they are now, at last, becoming a practical, successful, superior, and distinct therapy for patients with juvenile diabetes. This disease continues to be challenging;

with significant morbidity and major socioeconomic impact. Diabetes is a devastating burden to patients and their families, especially when acute complications are frequent and chronic complications are advanced. In the previous panel, you heard about the daily challenges people face in living with juvenile diabetes from the most effective messengers – children who suffer each and every day with this disease.

I would like to provide you with a better understanding of the science behind juvenile diabetes. Islets are clusters of insulin-producing cells located in the pancreas (Fig. 1). They make up only 1% to 2% of the total pancreas. In someone with juvenile diabetes, all insulin-producing cells are destroyed. The cells are attacked by the person's own immune system. In some patients, despite multiple daily insulin injections, frequent needle sticks for blood sugar self-measurements, and many lifestyle restrictions, blood sugar levels become erratic. The levels change rapidly from extremely high to dangerously low. This lack in control leads to acute complications, such as seizures and coma, and to chronic complications such as blindness, kidney failure, heart attack, and stroke.

Figure 1. Human islets isolated from a donor pancreas

Please allow me to illustrate how islet transplants are unsurpassed in their potential to transform the lives of people with difficult-to-control juvenile diabetes. Lorna (who gave permission to share some of her story) is a 35-year old mother of 2 boys who developed diabetes at age 9. She completely lost her ability to sense low blood sugar levels (also referred to as hypoglycemia). Brain function is severely compromised by hypoglycemia,

leading to confusion, distorted perception of surroundings, dizziness, odd behavior, seizure, coma, and possibly death. Lorna became incapacitated by weekly episodes of severe, life-threatening hypoglycemia, requiring the help of a third person and often paramedics. As a result, Lorna lost her driver's license, was laid off at work, was divorced, and was denied the right to see her boys.

In August of 2000, Lorna was admitted to the General Clinical Research Center at the University of Minnesota for an islet transplant under a protocol supported by the Juvenile Diabetes Research Foundation. She was taken to a radiology suite, where a local anesthetic was given and a catheter was placed (under ultrasound guidance) through her skin into the portal vein of her liver. Islets isolated from a cadaver donor pancreas were resuspended in buffer, transferred to a transfusion bag, and infused over 20 min through the catheter into her portal vein (Fig. 2). Infused islets were then carried by her blood to smaller branches of the portal vein, where they lodged, engrafted, and resumed tightly controlled secretion of insulin in response to her blood sugar levels. The catheter was then removed and she was discharged to home 2 days later.

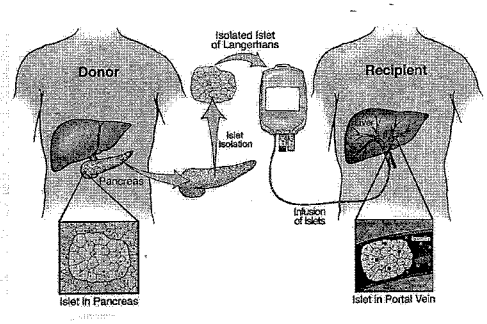

Figure 2. Islet transplantation procedure: After recovery of a donor pancreas, about 500,000 of the 1 million islets can be retrieved. Those islets are subjected to quality control while being cultured for two days. Islet preparations meeting release criteria are slowly infused into the portal vein of the recipient, similar to a blood transfusion. Islets follow the bloodstream and lodge in small branches within the liver, where they resume producing insulin.

Lorna's blood sugar levels returned to normal (Fig 3). She was able to completely discontinue insulin injections 1 month after her islet transplant. Since her islet transplant, she has not experienced a single episode of severe hypoglycemia. She learned to love life again, rediscovered her ability to make contributions to the world, regained control over her destiny, received her driver's license back, found a new job, married a paramedic who had repeatedly saved her life while she was diabetic, closed on a new home, and was granted authorization to take care of her boys again - all in the first year after her transplant. Now, almost 3 years after her islet transplant, Lorna continues to be insulin-independent. She still takes immunosuppressive medications to prevent rejection of her transplanted islets. But she has not experienced any severe adverse events. You will hear another remarkable success story from Anne Seidel following my testimony.

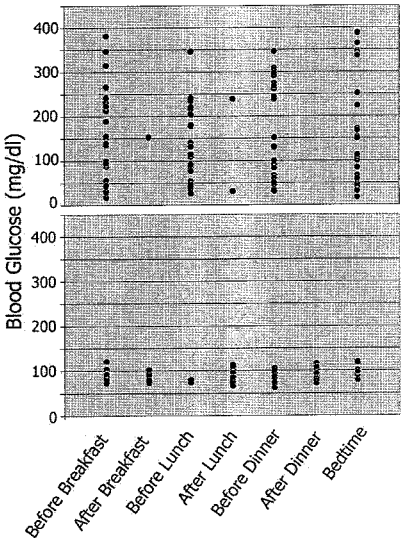

Figure 3. Blood glucose control during the month before islet transplantation (upper panel) and after islet transplantation and discontinuation of insulin injections (lower panel). Normal range is 70-120.

For patients like Lorna, insulin is survival, and an islet transplant is return to life. We have since performed islet transplants in 17 additional recipients at my Center. Diabetes was completely reversed for all but 2 of them and major complications were not encountered. Islet transplants should be considered for treating diabetes in selected patients. Islet transplants are now a clinical reality, not just a topic for experimental research.

Let us now assume for one moment that someone has a 35-year-old daughter who suffers from juvenile diabetes complicated by recurrent episodes of severe hypoglycemia, that she meets all accepted medical criteria for an islet transplant, that she has a good health insurance plan, and that she wants to proceed with an islet transplant. Will she be able to undergo an islet transplant?

Most likely no. There is a severe shortage of pancreata for islet transplants; funding in this area has not kept pace with the science; and regulations must be changed to provide incentives for additional procurement of pancreata for islet transplantation and research. And insurance coverage of islet transplantation is currently not available, thereby largely restricting them to patients meeting the very stringent eligibility criteria of research protocols.

Currently, I estimate that NIH grants will cover a mere 20 to 40 islet transplants in the US over the next 12 months. And even then, coverage would be sadly incomplete, leaving the patient and the clinical investigator with the burden of substantial uncovered

expenses, such as the costs for immunosuppressive medications required beyond the study period, the costs for donor pancreas acquisition and transportation, and the costs for additional personnel in order to be in compliance with increasingly complex regulations that have turned what should be patient-oriented research into a morass of hard-to-follow, often unnecessary rules (1).

This disconnect between the promise of basic science versus the delivery of better health in the US is of significant concern. Islet transplants for the treatment of diabetes are being covered by several provinces in Canada, where a landmark pilot clinical trial called the Edmonton Protocol was performed in 2000 (2). The steadfast commitment to basic biomedical research in the US has provided the basis for today's high success rate in reversing diabetes in human patients; it has also provided an unprecedented supply of information for further breakthroughs in clinical islet transplants. Yet, islet transplants remain largely unavailable 3 years after the demonstration of proof-of-principle. Failure to use available science is costly and harmful (3); it leads to overuse of inferior care. In contrast to Canada, we fail to deliver the best care we could for patients with difficult-to-control juvenile diabetes.

Both my learned opinion and my best bet are that one third of the gifted children with juvenile diabetes in this room will develop devastating, destructive, or deadly diabetes complications before they are 50 years old (4) -unless we enhance our preclinical and clinical research agenda markedly in the next 2 years (in order to realize a sizeable effect within 10 years). The potential short- to mid-term impact of islet transplants on

patients with juvenile diabetes prone to develop devastating complications is unmatched by any other treatment modality. "The Pancreatic Islet Cell Transplantation Act of 2003" would remove major translational blocks in the implementation of islet transplants. This bill, if passed, would lead to substantial improvements in the clinical research infrastructure and send a strong signal to all major stakeholders in health care delivery.

I want to take this opportunity to offer my highest compliments to you, Senator Collins, for authoring this bill. It addresses areas of major importance in the transition of islet transplants from clinical research to clinical care. I will make 3 suggestions.

First, it will be important to invite the active participation of all major stakeholders in islet transplant research. Addressing all concerns and legitimate requests of participating patients must be encouraged in the most proactive fashion. I also encourage inviting, via appropriate incentives, the active participation of diabetes care centers in recipient recruitment and posttransplant care. Their active participation could lead to the perception of collaborating diabetologists as transplant diabetologists. We also need to create incentives for involving other major stakeholders, such as academic health centers, the pharmaceutical and biotech industry, and health care payers. We need to overcome the fragmentation and underfunding of today's clinical islet transplant research infrastructure. We need to coordinate our research agenda around those institutions that are committed and best suited to contribute. We need to address the educational needs of payers: they stand to gain substantially from progress in the field and could prove instrumental in reducing the second translational block from clinical

studies into medical practice. We should give consideration to the foundation of a Translational Islet Transplant Network (TITN) to prioritize, coordinate, and conduct research efforts in preclinical and clinical islet transplants.

Second, the proposed 5-year demonstration project in islet transplant recipients with end-stage kidney failure will undoubtedly provide further insights into the risks and benefits of islet transplants in this subgroup of patients. It is important to emphasize that outcomes in this recipient group with advanced diabetes complications are likely to be fundamentally different from outcomes in preemptive islet transplants performed for the purpose of preventing irreversible complications. In particular, health care decision making for the latter group must therefore not await the final analysis of the 5-year demonstration project in islet recipients with end-stage kidney failure.

Finally, I urge the Committee to review the adequacy of Federal research funding for translational research of emerging concepts and strategies in the preclinical nonhuman primate islet transplant model. Removing this translational block will position established clinical research networks (e.g., Immune Tolerance Network) to capitalize much faster on the extraordinary opportunities that are increasingly presented by ongoing basic research investment. Documenting safety and efficacy of emerging concepts in preclinical nonhuman primate models is considered a prerequisite before embarking on clinical trials. Increased resource allocation should be considered for evaluating approaches that facilitate minimization of recipient immunosuppression (including innovative islet pretreatment strategies) and for developing strategies aimed at

increasing the supply of islet tissue suitable for transplant (including pig islet xenografts and living donor islet allografts).

In closing, I believe your bill will greatly enhance the islet transplant translational infrastructure and help it to operate much more efficiently. It will raise awareness; create additional momentum; and facilitate the expedient delivery of today's science and technology for the benefit of thousands of patients afflicted with juvenile diabetes. The bill will also help prepare the field to respond nimbly to the extraordinary advances that surely will emerge from stem cell biology and other high-impact, cell-based technologies of the future. Thus, this legislation will have implications well beyond its primary objectives.

As I look around the room at all of these children who are here today to take an active role in finding a cure for juvenile diabetes, I know that the scientific community and Congress must match their passion and dedication. This will not be an easy task, but progress in science has been amazing and emerging opportunities are extraordinary. Removing translational blocks (5) will allow us to reach our shared goal of a cure.

Thank you from the bottom of my pancreas (6).

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Testimony of Anne Seidel

Senator Collins and members of the Committee, thank you for the opportunity to appear before you today as an example of a true success story; a story resulting from a strong public-private partnership between the JDRF and the Federal government in supporting medical research and the NIH. I am Anne Seidel, the proud mom of six-year-old Charlie and five year old Lacey. I have been an active JDRF volunteer in Texas and nationally for the past five years.

I was diagnosed with juvenile diabetes 35 years ago at age 6. My son Charlie, now six, was diagnosed five years ago. I cannot describe to you the anguish I experienced when he was diagnosed with juvenile diabetes. As a mother, your focus in life is caring for and protecting your children, and yet I was unable to protect him from a disease that had been ravaging my body for nearly 30 years.

While I focused all of my energy on caring for Charlie after he was diagnosed, diabetes was taking an enormous toll on my body. Over the years of living with diabetes, I have won the battle of near blindness and kept going; I have had nerve damage in my feet and partial paralysis of my stomach and kept going. My blood sugars would jump from being at a level of 16 – so low that I was in danger of becoming unconscious – to a level of 600 – which is so high that I could slip into a coma -in the course of two hours, then back down and back up. This roller coaster defined many of my days. Most days, feeling nauseated and exhausted, I kept on going.

But the complication of my diabetes that prevented me from keeping on going was losing my ability to feel when my blood sugars went severely low. Instead of being able to sense this and to quickly ingest sugar for a quick recovery, my blood sugar would keep dropping until I was unconscious, blacked-out, totaled my car, or was so confused that I didn't know who I was, who my kids were, or whose diabetes I was trying to treat. Several times, so confused with a low blood sugar, I came very close to mistakenly giving Charlie extra insulin when he didn't need it. The result of that could have been his death.

About 4 years ago, I began watching – with more than a passing interest – the advancement of pancreatic islet cell transplantation. Upon investigation, the state of my diabetes matched the criteria for participating in the clinical trials. When deciding to participate in the trials, I had to come to terms with the fact that the procedure was not being offered to children because of the immunosuppressive drugs that the patient must take following the transplant. As a mother, your instinct is to help your child first. After lots of introspection, I concluded that it was ok for the parent to put on the plane's oxygen mask first so that they could save their child, and I must do the same with my diabetes.

After speaking with every center in the world that was conducting islet transplants, I was screened at several places and I chose one list on which to be listed. Because of the

severe shortage of pancreases in the U.S., and with my rare blood type, I spent over two years on the list waiting and hoping for the call. Each day that passed, I worried that my diabetes would worsen while I waited which might prevent me from participating in the trial. I decided to increase my chances for a transplant and I listed at three additional centers.

I received my transplant on February 5th and my second on April 9, 2003. Most of the current protocols involve two transplants to receive the appropriate number of islet cells. I was called to come to The Methodist Hospital in Houston, and the insulin-producing islet cells were extracted from a donor pancreas and put into an IV bag. While this was being done, I changed into my gown, the radiologist fed a small needle into a vein in my liver, and the cells dripped into me. I was in the surgery suite for a total of 20 minutes, and I was conscious throughout the procedure. Back in the recovery room, I looked down at my side and said to the surgeon, "You just saved my life and all I have to show for it is this regular size band-aid?!" 30 hours after the transplant, I was sent home.

Since my transplant, I no longer need to take insulin. To give you a sense of how dramatically this has changed my life, in the 35 years that I have had juvenile diabetes, I have taken 255,500 units of insulin and have pricked my fingers 56,210 times. For the first 12 years that I had juvenile diabetes, I tested my urine 21,900 times! People have asked me to describe how I feel since my transplant, and the best analogy I can think of is that I feel like I had not bathed in 35 years and that someone finally washed me clean.

Another amazing result of the transplant is that many of the complications that plagued my days before the transplant are now gone. The nausea, exhaustion, confusion, unconsciousness, foot pain, and a large helping of fear are all gone. Having energy, clear thoughts, not feeling fearful of endangering my children or anyone else has been nothing less than utopia. Diabetes doesn't define me anymore – I truly have received the gift of a lifetime.

As one of the approximately 250 people whose life has been changed through an islet cell transplant, I thank you from the bottom of my heart. Your commitment to the NIH, coupled with JDRF's commitment, has truly saved my life. But there is no time to sit back and congratulate ourselves because there are many more who cannot take advantage of this procedure. And I will not rest until my son Charlie, the hundreds of innocent children who you see before you today, and the over one million people who suffer from this disease can also be cured. They deserve no less. Call me demanding, but I do not relish being one of the few who have been saved.

It may sound strange, but diabetes has given me many gifts and opportunities – one of which is the privilege of appearing before you today to publicly thank you and JDRF for making my transplant possible. A cure is within our grasp, and together we will find it.

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FOR THE

COMMITTEE ON GOVERNMENTAL AFFAIRS

UNITED STATES SENATE

June 24, 2003

Dear Chairwoman Collins, and Members of the Committee:

Thank you for holding the hearing on "Juvenile Diabetes: Examining the Personal Toll on Families, Financial Costs to the Federal Health Care System, and Research Progress Toward a Cure". We appreciate the opportunity to present our statement for the record.

Type I Diabetes is among the most frequent autoimmune disorders in the pediatric population affecting 1 out 360 children. The trigger of the autoimmune destruction of the pancreatic cells producing insulin is still unclear mainly because the environmental triggers that induce this damage are unknown. Conversely, the environmental trigger (gluten containing grains) that causes celiac disease, another autoimmune disorder that affects as many as 1 out of 133 children and adults worldwide, is well known. Therefore, an effective treatment is available.

Type I Diabetic children are at a much higher risk to have celiac disease as compared to the general population. There is now growing evidence that this coexistence is not merely due to common genetic predisposition, rather untreated celiac disease can lead to Type I Diabetes.

Therefore, an increased awareness of celiac disease and an aggressive screening campaign to identify celiac disease patients at their early clinical stage will represent an unparalleled strategy to prevent Type I Diabetes in a subset of children that will develop this devastating condition. It should also be stressed that the lifestyle of children affected by both Type I Diabetes and Celiac Disease is much more complicated than children affected by either one of these conditions. Glucose control, the treatment costs, the clinical and management challenges are definitely much more complicated in children suffering from both conditions.

Recent studies conducted at the Center for Celiac Research (CFCR) at the University of Maryland shed some light on the rationale for this coexistence. It is now well established that it is in the interplay between environmental factors and specific susceptibility genes that dictate the immune response for the onset of autoimmune diseases. This interplay can only occur if the intestinal barrier that represents the limiting step for passage of environmental triggers into the body is jeopardized. Zonulin, a molecule recently discovered at the CFCR is the gatekeeper that controls this passage. It is now clear that both Celiac Disease and Type I Diabetes are characterized by a leaky gut as the consequence of an aberrant production of zonulin. This information will be instrumental to develop new preventive and treatment strategies to tackle these devastating conditions.

Thank you for giving us the opportunity to provide this statement.

ATTACHMENT—Lancet. 2000 Apr 29;355(9214):1518-9. Zonulin, a newly discovered modulator of intestinal permeability, and its expression in coeliac disease. Fasano A, Not T, Wang W, Uzzau S, Berti I, Tommasini A, Goldblum SE.

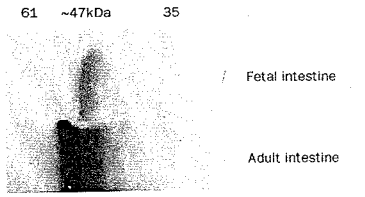

Figure 1: **Immunoscreening of human intestinal tissues with affinity-purified polyclonal anti-ZOT antibodies**

Proteins in tissue lysates of human fetal and adult intestine were subjected to sequential purification steps, resolved by sodium dodecylsulphate polyacrylamide gel electrophoresis, transferred onto polyvinylidene difluoride membranes, and probed with affinity-purified anti-ZOT antibodies. A single protein was purified that migrated with an apparent relative molecular mass of about 47 kDa and immunoreacted with anti-ZOT antibodies.

Zonulin, a newly discovered modulator of intestinal permeability, and its expression in coeliac disease

Alessio Fasano, Tarcisio Not, Wenle Wang, Sergio Uzzau, Irene Berti, Alberto Tommasini, Simeon E Goldblum

We identified zonulin, a novel human protein analogue to the *Vibrio cholerae* derived Zonula occludens toxin, which induces tight junction disassembly and a subsequent increase in intestinal permeability in non-human primate intestinal epithelia. Zonulin expression was raised in intestinal tissues during the acute phase of coeliac disease, a clinical condition in which tight junctions are opened and permeability is increased.

We have shown that zonula occludens toxin (ZOT), a protein elaborated by *Vibrio cholerae*, reversibly regulates the permeability of tight junctions.[1] ZOT interacts with a specific surface receptor[1] with subsequent protein kinase C α-dependent polymerisation of actin microfilaments strategically localised to regulate the paracellular pathway. On the basis of this observation, we investigated whether ZOT might mimic an endogenous modulator of tight junctions. We also postulated that ZOT and its putative eukaryotic analogue could be structurally and immunologically related.

Accordingly, specific anti-ZOT antibodies and an ex vivo intestinal permeability assay[1] were used in combination to screen for one or more human intestinal ZOT analogues. Non-primate intestinal tissues were used as an indicator system to identify and purify this analogue. Fetal and adult tissues were obtained from the brain and tissue bank for developmental disorders at the University of Maryland. A single protein (that we named zonulin) with a molecular weight of about 47 kDa was purified to homogeneity from both adult and fetal intestine (figure 1). To establish whether zonulin preparation was biologically active, it was tested on Rhesus monkey intestine with an *ex vivo* assay.[1] Intestinal tissues from the same animal with similar baseline tissue resistances were simultaneously exposed to either zonulin or media alone. Zonulin reversibly increased the monkey intestinal permeability compared with the media control in both jejunum (mean 35·0 [SE 1·8]% *vs* 3·0 [1·5]% permeability increment; $p<0·0001$) and ileum (26·0 [5·6] *vs* 4·9 [1·5] permeability increment), but not in the colon (1·3 [0·6] *vs* 1·1 [0·5] permeability increment, $p=0·37$, Student's *t* test). This increased permeability allowed the transepithelial passage of insulin, a macromolecule normally not absorbed when given orally.[2]

To establish whether zonulin is perturbed during coeliac disease, a condition in which tight junctions are opened through an as yet undefined mechanism,[3] intestinal tissues were obtained from seven patients with active coeliac disease and six controls and probed for zonulin with anti-ZOT antibodies. Immunofluorescence analysis of coeliac disease tissues showed enhanced zonulin expression within the intestinal submucosa with a characteristic reticular pattern that was consistently absent in control tissues. Quantitative immunoblotting of intestinal tissue lysates from patients with active coeliac disease confirmed higher zonulin protein concentrations than in control tissues (figure 2).

Since intestinal zonulin expression was increased during the acute phase of coeliac disease, when tight junctions are opened, this suggests a causal role of this endogenous mediator in

Figure 2: **Zonulin protein in intestinal tissues from coeliac disease patients and controls**

The increased expression of zonulin in intestinal tissues from coeliac patients was confirmed by western analysis. The amount of zonulin normalised to the total protein content in the tissues analysed was about 3-fold higher in intestinal specimens from patients with coeliac disease than in control tissues. These blots are representative of six specimens.

coeliac disease pathogenesis. Further, this increased expression of zonulin in the face of tight junctions disassembly might allow zonulin presentation to the submucosal gut immune system. Accordingly, we used a ZOT-based ELISA to detect antibodies to zonulin in the serum samples of patients with coeliac disease and controls. Anti-zonulin IgG was not higher in patients with coeliac disease than controls. By contrast, anti-zonulin IgA was raised in the serum samples of 25 of 117 (21%) patients with coeliac disease during the acute phase of the disease but in none of the 30 patients in remission ($p<0·0001$). Only nine of 163 (6%) healthy controls had a minimally but significantly increased anti-zonulin IgA titre ($p<0·0001$). The incidence of anti-zonulin antibodies during the acute phase of coeliac disease is consistent with the incidence of other auto-antibodies described in coeliac disease.[4] In seven patients with coeliac disease followed longitudinally, the raised anti-zonulin IgA returned to normal after 3–6 months symptomless remission on a gluten-free diet.

It has been recently reported that untreated coeliac disease predisposes to autoimmune disorders such as insulin-dependent diabetes mellitus, Hashimoto's thyroiditis, autoimmune hepatitis, and connective tissue diseases.[4] Perhaps zonulin opens small intestinal tight junctions during the early stage of coeliac disease and allows entry of putative allergens into the intestinal submucosa, in which an autoimmune response is elicited. In a spontaneous diabetic rat model, β-islet cell destruction and other autoimmune features develop only 3–4 weeks after the rise in gastrointestinal paracellular permeability.[5] Notably, these permeability changes always precede the autoimmune process.[5] Further, the barrier dysfunction is restricted to the small intestine,[5] paralleling the regional distribution of the zonulin regulatory system within the gastrointestinal tract.[1] Our findings that enhanced intestinal permeability in this diabetic rat model was associated with increased concentration of intraluminal zonulin (unpublished) further supports the pathogenic role for this protein at the onset of autoimmune disorders, such as diabetes mellitus and coeliac disease.

Our results support the idea that zonulin participates in the physiological regulation of intercellular tight junctions in the small intestine. Dysregulation of this conceptual zonulin model might contribute to the perturbation of the intestinal barrier functions, leading to the passage of environmental antigens involved in the pathogenesis of coeliac disease and related autoimmune disorders.

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