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DIABETES RESEARCH: IMPROVING LIVES ON THE PATH TO A CURE

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C O N T E N T S

DIABETES RESEARCH: IMPROVING LIVES ON THE PATH TO A CURE

WEDNESDAY, JULY 15, 2015

U.S. SENATE,
SPECIAL COMMITTEE ON AGING,
Washington, DC.

The Committee met, pursuant to notice, at 1:37 p.m., Room G50, Dirksen Senate Office Building, Hon. Susan M. Collins, Chairman of the Committee, presiding.

Present: Senators Collins, Perdue, Tillis, McCaskill, Casey, Whitehouse, Donnelly, Warren, and Kaine.

Also present: Senator Shaheen.

OPENING STATEMENT OF SENATOR SUSAN M. COLLINS, CHAIRMAN

The CHAIRMAN. Thank you. Good afternoon. This hearing will come to order.

First, let me thank everyone for gathering earlier than we had anticipated. Due to votes being scheduled on the Senate floor, we wanted to make sure that our young people who are here today and are the focus of this hearing did not have to sit for a very long time while members of this Committee went to vote.

We are holding today's hearing in conjunction with the JDRF 2015 Children's Congress to examine how diabetes affects people of all ages, with a special focus on Americans with Type I diabetes and their families.

This is the eighth consecutive Children's Congress that I have chaired. It has been such a privilege to work with JDRF, the families, the young people from all across the country whose commitment to finding a cure is inspiring.

I want to welcome our distinguished panel of witnesses and the more than 160 delegates to the Children's Congress who have traveled to Washington from every State in the country and from around the world to tell us in Congress just what it is like to have diabetes, how serious it is, and why it is so important that Congress fund the research necessary to discover a cure.

I want to give a special welcome to the two delegates from Maine, Isabelle Levesque of Arundel and Mark Hurlbert from Harrington. Also here is Kate Hall, a remarkable young woman from Casco, Maine, who was diagnosed with Type I when she was ten. An outstanding athlete, Kate recently broke a 39-year-old national high school record in the long jump. She jumped an astonishing 22 feet, five inches.

As the founder of the Senate Diabetes Caucus, I have learned a lot over the years about the difficulties and heartache that this disease causes for so many American families as they await a cure. Diabetes is a lifelong condition that does not discriminate. It affects people of every age, race, and nationality. Moreover, diabetes costs the United States an estimated $245 billion a year, a cost that is projected to more than double by the year 2020. It also accounts for one out of three Medicare dollars. In fact, medical costs for Americans with diabetes are more than double those incurred by individuals without diabetes.

These statistics are certainly overwhelming, but what really motivated me to devote so much energy and time to this cause is meeting more and more families like our delegates today, whose lives have been forever changed by diabetes. That is why it is so important that you have traveled to Washington today to tell your personal stories. You put a human face on the statistics.

Since we founded the Senate Diabetes Caucus, funding for diabetes research has more than tripled, from $310 million in 1997 to well over a billion dollars this year. As a consequence, we have seen some encouraging breakthroughs and are on the threshold of a number of new discoveries. Advances in technology, like continuous glucose monitors, are helping patients control their blood glucose levels, which is key to preventing diabetes complications. We are also moving closer and closer to our goal of an artificial pancreas, which would revolutionize diabetes care.

While today's hearing is being held in conjunction with the JDRF Children's Congress, the fact is that 85 percent of those living with Type I diabetes are adults, and many of them are seniors. I was surprised and troubled to learn that insulin-dependent Medicare beneficiaries are being denied coverage for continuous glucose monitors. As a consequence, we are seeing situations similar to what we saw with the insulin pumps in the late 1990's, where individuals with Type I diabetes have had their coverage for their monitors on their private insurance, only to lose that coverage when they age into Medicare. Even though 95 percent of private insurers cover continuous glucose monitors, Medicare does not, and that is why I have joined Senator Shaheen, the Co-Chair of the Senate Diabetes Caucus, in introducing legislation to require Medicare to cover this important device.

While we are making progress in the battle against diabetes, this is no time to take our foot off the accelerator. Earlier this year, we were able to pass legislation to extend the Special Diabetes Program for two more years, through September 2017. This provides an additional $150 million a year for Type I diabetes research over and above the regular appropriations for diabetes research at the National Institutes of Health. I am hopeful that this afternoon's hearing will help to generate even more support in Congress to extend this important program into the future.

In closing, let me just say, in the years that I have worked on this issue, I have been so impressed with the changes in technology and the differences that they have made to the lives of people living with Type I diabetes, and it never fails to inspire me when I see all the young people of all ages from all around the country

who come to Washington to share their stories with us, so thank you so much for being here with us today.

Senator McCaskill.

OPENING STATEMENT OF SENATOR CLAIRE MCCASKILL, RANKING MEMBER

Senator MCCASKILL. Thank you, Senator Collins.

In the interest of time, because we obviously have votes and we are doing this early because of that, I am not going to give my formal opening statement, but if you would indulge me for a minute, you guys look so awesome. I am not used to looking out——

[Applause.]

This is a hearing room that we usually use for Armed Services hearings, and I am on the Armed Services Committee, and typically, I am looking out at the audience and it is a bunch of, you know, dear people who are wonderful leaders and heroes, but they are kind of stiff people in uniforms, and so, I have got to get a picture of this for Instagram, okay?

I am so proud of all of you, and I am looking at all of you in blue, because you are learning firsthand that you can make a difference, and you are here in Washington because this is your government and your government needs to listen to you about what you are living with and what your needs are and the incredible gaping hole we have in this country. I am fortunate to serve with Senator Collins, because she and I agree on this, that we have to invest in medical research. It has to be something that drives our commitment as a Nation, that we are a beacon to the world on medical research.

I will only do a couple of shout-outs. Obviously, I want to shout out to Amelia Cooper, who is going to testify today. She is from Kansas City. She is probably a Royals fan. I am a Cardinals fan. We learn to love each other because it is all one State. She is not a typical 15-year-old, however. Amelia is a world traveler, having visited 35 countries, a cross-country skier, a half-marathon finisher, and a published author, and a person living with Type I diabetes, and we are proud to have you here, Amelia.

I also want to give a shout-out to someone from my alma mater, Dr. Zaghouani. He has too many accomplishments as a pediatrician for me to begin to talk. He is a Chair in Pediatrics at the University of Missouri School of Medicine in Columbia with amazing credentials, and thank you for your work.

Then finally, I want to recognize the fact that your CEO of JDRF is, in fact, from St. Louis, so we have evened out, Amelia. I bet he is a Cardinals fan, so we are kind of book-ended here, so St. Louis is very—has a very active chapter, and, frankly, a lot of you all across my State who have made me know for many years that this is something we all need to stay focused on.

Thank you all for being here, and most of all, thank you, Madam Chairman, for calling this important hearing, and the Chairman's commitment to this for many years is unmatched, and I am very proud to be Ranking on her Committee and I am very proud of the work she has done in this area, so thank you all.

The CHAIRMAN. Thank you very much, Senator, and I just want to echo what you said. This is not our typical hearing——

Senator MCCASKILL. No, no.

The CHAIRMAN [continuing]. and it is a great one—not to say that we do not have wonderful hearings all the time.

Senator MCCASKILL. We are going to get in trouble here——

The CHAIRMAN. I know.

Senator MCCASKILL [continuing]. before this is over.

The CHAIRMAN. You are right.

We will now turn directly to our panel of witnesses. It is my great pleasure to introduce Isabelle Levesque from Arundel, Maine. Isabelle was diagnosed with Type I diabetes at the age of two. She is an extraordinarily active girl who enjoys reading, arts and crafts, playing soccer and softball, camping, fishing, and music.

Senator McCaskill has already introduced our second witness, Amelia Cooper.

Third, we will hear from Kate Hall. Kate has become quite a star in the State of Maine. As I mentioned in my opening statement, she recently broke a 39-year-old national high school long jump record with an astonishing jump of twenty-two feet, five inches.

Senator Donnelly, I had to have her show me just how long that was.

She was diagnosed with Type I diabetes at age ten, but she is yet another shining example of someone who has not let this lifelong disease stop any of her goals or ambitions.

We are next going to hear from Bob Amato, and I am going to be turning to Senator Whitehouse to introduce Bob. Senator Whitehouse.

Senator WHITEHOUSE. Thank you, Chairman. It is a pleasure to be here. This is the most inappropriate Aging Committee hearing I have ever seen, and it is terrific to see this blue sea of young faces.

I want to express my appreciation to Jordan Delisle of Rhode Island, who came and advocated this morning in my office and did a wonderful job. She is here with her mom, Loriann.

I want to recognize, as Senator McCaskill did, the leadership that Chairman Collins has shown on this issue for a long time. There is an enormous amount of support in this room for the continuous glucose monitoring, and the bill to make that a part of Medicare is Senator Collins. She has led a letter to the Appropriations Committee to support diabetes research, and we are all happy to be Senator Collins' wingmen on this issue—wingmen and wingwomen, if that is a word, on this issue.

I get the pleasure of introducing a panelist here today, Bob Amato of Rhode Island. Just like some of the other witnesses who Chairman Collins has already introduced, Bob was diagnosed with Type I diabetes at a very young age. The difference is that he has been living with the diabetes for 67 years. Bob refused to accept that having——

[applause].

Even back then, Bob refused to accept that having Type I diabetes meant that he could not lead an active life. He became a runner and eventually the track coach at Providence College in Rhode Island. In fact, Bob was admitted into the Providence College Athletic Hall of Fame in 2009. He was one of the most successful coaches in the history of Providence College, finishing with an as-

tounding career record of 162 wins, 14 losses, and one tie. I am very pleased that Bob could be here today to share the successes and the challenges that he has experienced living with Type I diabetes.

Bob, to you and your family, welcome. We look forward to hearing about your experiences.

Thank you, Madam Chair.

The CHAIRMAN. Thank you.

Senator DONNELLY. Madam Chair, I have a question.

The CHAIRMAN. Yes.

Senator DONNELLY. Would the former track coach of Providence College like to offer a track scholarship to the young girl sitting next to you?

The CHAIRMAN. I think he is too late. Believe me, that occurred to me, whether I should seat them next to each other or not.

Senator DONNELLY. PC is a great college.

Chairman COLLINS. After we hear from the coach, we will hear from Dr. Griffin Rodgers, the Director of the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health. It is a great honor, Doctor, to welcome you back. You have testified at our previous hearings and it is always so interesting to hear your update on the research and the technology, so thank you for joining us again this year.

Finally, we will hear from Dr. Habib Zaghouani, and Senator McCaskill has already introduced him.

I do want to acknowledge Senator Shaheen, who has joined us. She is the Co-Chair of the Senate Diabetes Caucus. She has a granddaughter with Type I, and I believe her granddaughter and daughter are going to be with us today, too, so welcome.

Senator SHAHEEN. Thank you.

The CHAIRMAN. We will start with our first witness now, and that is going to be Isabelle, so Isabelle, please begin your testimony, and thank you so much for coming from Maine to be with us today.

STATEMENT OF ISABELLE LEVESQUE, AGE TEN, ARUNDEL, MAINE, DIAGNOSED WITH TYPE I DIABETES AT AGE TWO

Ms. LEVESQUE. Thank you, Chairman Collins and Senator McCaskill, for inviting me to testify today. My name is Isabelle Levesque. I am 10 years old and live in Arundel, Maine.

I was diagnosed with Type I diabetes, or T1D, when I was two years old. My diagnosis was the start of a very different childhood. My mom and dad began a routine of ten to twelve finger pricks and six insulin shots each day to keep my blood sugar in a healthy range. As of today, I have pricked my finger over 28,000 times, changed my pump site over 1,400 times, and changed my sensor over 400 times. Can you imagine having to stick a needle into your skin 30,000 times in just eight short years?

My family says that I am a happy child, but it is hard when you have to deal with diabetes everyday. Type I diabetes is something you can never stop thinking about. I constantly have to put my life on pause to test my blood sugar. This can happen at any time—during my favorite movie, at school, when I am swimming, or in the middle of a soccer or softball game. Sometimes I even have to

come out of a game to recover from a low blood sugar when I feel my team needs me the most. It is so frustrating. Cold weather activities are difficult, as well, because I do not always feel my low blood sugars when playing in the snow. I have been as low as 26 and did not even know it until my parents had me check.

I am here as a JDRF Children's Congress delegate because I need your help. I want to see a cure for diabetes in my lifetime, and all of my friends here today do, too. My family and I have spent the last eight years fighting for it and we need Congress to continue fighting with us by funding research through the Special Diabetes Program.

My family and I work hard to raise funds for T1D research and to teach my community about the difficult disease. We do our part. My walk team, Strides for Isabelle, has been the top fundraising team in Maine for five out of the last seven years. I am proud to say that we have raised over $100,000. Also, last summer, I helped organize a concert which I played my guitar in to increase my community's understanding of the impact of diabetes.

The money we have raised has gone toward research into new treatments for Type I diabetes, and hopefully, we will one day find a cure. From this research has come technology that has made it easier to live with diabetes. One technology I use to track and manage my blood sugar is called a continuous glucose monitor, or CGM. I have been wearing a CGM since I was three years old. Before I had a CGM, it was really hard for my mom and dad to know if my blood sugar was high or low, so they pricked my finger constantly throughout the day and used a test strip to check. For a three-year-old, and even now, this CGM has made a huge difference. Although this device has helped me to stay healthy, there is much more to be done and a cure is still needed.

When I grow up, I want to be a teacher. To help make this dream of mine be a reality, it is important that Congress continue supporting T1D research. Thank you.

The CHAIRMAN. Thank you very much. That was perfect. You did a great job.

Amelia.

STATEMENT OF AMELIA COOPER, AGE FIFTEEN, KANSAS CITY, MISSOURI, DIAGNOSED WITH TYPE I DIABETES AT AGE TWELVE

Ms. COOPER. Thank you, Chairman Collins, Ranking Member McCaskill, and members of the Committee for inviting me to testify today. My name is Amelia Cooper and I was diagnosed with Type I diabetes, or T1D, three years ago, at age twelve.

As you all know, the teenage years can be a little rough, with pressures to fit in, figure things out, and find your way. At a time when many of my peers are worrying about their hair, clothes, and social schedule, I must focus my attentions on things vital to my health. Each day, I have to carefully monitor and manage my blood glucose level, which is not easy, since exercise, diet, and many other factors all have an impact.

Despite these serious challenges, I have many reasons to be grateful. Thankfully, I was diagnosed with T1D after Frederick Banting discovered insulin. Thankfully, I was diagnosed with T1D

after insulin pumps and continuous glucose monitors were invented. Thankfully, I have learned how to manage my diabetes without allowing it to manage me, even though it is not always easy.

It is only through a very strict blood sugar management routine and advancements in diabetes treatments and devices that I have been able to live my life to the fullest.

Thirty-five: The number of countries I have visited, and still counting. Thirteen-point-one: The number of miles in a half-marathon. I have completed two so far. Ten: The number of things I wish my parents knew when I was diagnosed with T1D. I wrote this article as a published author in the blog diaTribe. Four-plus: The number of years after college that it takes to become a doctor, like my Dad, who I look up to. That is my dream job. One, as in Type I, the number associated with my disease. I am hopeful through Congress's support we will move from Type I to Type None.

Through advances in medicine, my life has gotten easier, healthier, and safer. I use an insulin pump and a continuous glucose monitor and I am well aware that these advancements took much time, research, and funding to become a reality.

While I have never participated in a formal clinical trial, I am very excited about a recent research project that I conducted. I have always been curious as to how and why my blood sugars are so irregular when I ski. Changes in altitude and prolonged activity can be very hard on blood sugar control, and after researching the topic, I realized there was an opportunity to design a study to evaluate the changes my body experiences when I ski compared to my friends without diabetes.

The results, which showed that—wait. Sorry. The results, which were presented at this summer's American Diabetes Association meeting in Boston, showed that despite strenuous activity, altitude caused an increased demand for insulin by more than a third. Most importantly, I showed that my blood sugars could be in the same range as my friends with careful monitoring and planning of my carbohydrates and insulin requirements. The use of a continuous glucose monitor was especially helpful in preventing hypoglycemia and ensuring safe blood sugars prior to riding a chairlift or skiing.

My project obviously does not compare to those responsible for the significant progress being made for the life-changing treatments for T1D, projects on beta cell encapsulation and artificial pancreas technology, treatments I hope to have available in the years to come, but my project does represent my strong desire to make an impact. I am not someone who can just stand by when there is so much to be done to improve my quality of life and that of all of my friends before you today.

In closing, I ask for your support in this fight to cure diabetes. Thank you, Chairman Collins, Ranking Member McCaskill, and members of the Committee for your time today.

Senator WHITEHOUSE. Madam Chairman, before we go on to the next witness, may I ask unanimous consent that the record of this hearing reflect something that the people behind Amelia might not have seen, which is that throughout her testimony, she virtually

never looked down at her notes, which is far better than most adults——

Senator MCCASKILL. I just hope she does not run against me. I am in trouble if that happens.

The CHAIRMAN. That really was extraordinary testimony and we thank you so much for being here today.

Now, we are going to turn to another extraordinary young woman, Kate Hall.

STATEMENT OF KATE HALL, RECENT HIGH SCHOOL GRADUATE AND TRACK AND FIELD ATHLETE, CASCO, MAINE

Ms. HALL. Good afternoon. My name is Kate Hall and I am from Casco, Maine. Thank you, Chairman Collins, Ranking Member McCaskill, and members of the Committee for the honor of being here today to speak about my experience living with Type I diabetes and Type I diabetes as an athlete.

I was diagnosed with Type I diabetes when I was 10 years old. At first, it seemed as if I would never understand every little detail that was involved in having diabetes. I had to adjust to taking shots of insulin, checking my blood sugar several times a day, learning how to count carbs in everything I ate, and learning how to deal with high and low blood sugars correctly.

However, the thing that stood out to me the most was being benched during my first soccer game after my diagnosis. That really made me realize that diabetes was not going to ever stop me from doing the things I loved most. I thought, I am not sitting out on anything ever again if I can help it. I am figuring this thing out.

Type I diabetes is challenging, particularly when it comes to what I love doing most, track and field. The events I compete in, the long jump and the short sprints, require rigorous daily training, but for me, because I live with Type I diabetes, keeping my blood sugar in a healthy range as much as possible is just as important a part of my training and success as anything else I can do to prepare for competitions.

Managing my diabetes can be really hard at times, and I realize I cannot figure everything out on my own. I need help from doctors, my parents, diabetes technology, and researchers.

Being a competitive track and field athlete, there are many tiny details involved that people have to do in order to get the best results possible. Some of these things include staying hydrated, eating well, sleeping well, training the right way, and warming up correctly to prevent injury. Not only do I have to do all of these things, but making sure my blood sugar is at a good level is another thing to add to that list.

Whenever I am training or competing, I have to take my blood sugar several times before I run in order to make sure it will not go high or low. If it is high or low, I need to quickly do what I need to do to get it to that perfect level so it does not negatively affect me. During my training or competition, I try to check my blood sugar every half-hour to ensure a high or low blood sugar will not affect my performances.

If my blood sugars do become too high or low, which has happened several times, my pH level changes and I occasionally get muscle cramps. These muscle cramps are very painful and prevent

me from competing the rest of the day or even the rest of the week. When this happens, it is extremely frustrating to think that my diabetes is preventing me from doing what I love the most, even when I try my hardest to control it.

I wear an insulin pump and was using a continuous glucose monitor until we changed health insurance companies. With most private health insurers covering CGMs these days, I am hopeful that my current plan will update its policy so I can use a CGM again. These devices help me spend more of my day in a healthy blood sugar range and also helps me focus on training and competing.

Thankfully, new technology, diabetes management devices, and also the support of my family and health care team have allowed me to pursue my passion and become a world ranked junior athlete. I was able to end my high school long jump career this year by breaking a 39-year-old national high school record with a jump of twenty-two feet, five inches, at the New Balance Nationals last month. My jump also broke the U.S. junior record set in 1982 and surpassed the automatic qualifying standard for the 2016 Olympic trials. I also finished third in the 100-meter event with a time of 11.37 seconds.

My dream is to one day represent the United States at the Olympics. This fall, I will begin training at Iowa State, and although I will be far from home and working with a new team of coaches, one key part of my life remains unchanged, the challenges of managing my Type I diabetes every single day.

Technology is important, but those of us with Type I diabetes need more. We need the scientists to help us figure out even better treatments and a cure for this disease. That is why my family and I are grateful for the funding that Congress has provided for Type I diabetes research.

Chairman Collins, we thank you for your leadership. All of us with Type I diabetes are counting on Congress to help us figure it out. Thank you.

The CHAIRMAN. Thank you. Kate, I just want to say personally how proud I am of you. It was just thrilling to hear of your success and setting new records, and to do so while coping with a very complicated illness is even more impressive.

Ms. HALL. Thank you.

The CHAIRMAN. Most of all, you really inspire all of the children who are here today to know that they, too, can achieve their dreams, so thank you for coming.

Ms. HALL. Thank you.

The CHAIRMAN. Mr. Amato, welcome.

STATEMENT OF ROBERT S. AMATO, FORMER RUNNER AND COACH, MEMBER OF PROVIDENCE COLLEGE ATHLETIC HALL OF FAME, JOHNSTON, RHODE ISLAND

Mr. AMATO. Chairman Collins, Ranking Member McCaskill, members of the Committee, thank you very much for this opportunity to speak before you. My name is Bob Amato and I am from Johnston, Rhode Island.

When I was first diagnosed with Type I diabetes, It was 67 years ago, I was approximately seven years old. Thinking at that time were that people such as you guys were not able to compete. No athletics. No gym. That was difficult. I did not accept that, and I

sought some guidance from Joslin, the Elliott P. Joslin Clinic, and again, some guidance from my parents, and I was able to prove that particular concept a fallacy, a fallacy to the point where in 2009 I was entered into the Providence College Hall of Fame for Athletics for both the running, my running accomplishments, and accomplishments as a coach.

As a coach, I had the privilege of coaching two world champions, 16 Division I All Americans. Our teams competed and won 16 New England Championships. My coaching colleagues selected me to the Coach of the Year 15 different times. That was what I would hope for when I was told it could not be done.

I was able to find success despite the daily challenges of diabetes because I always used—now this is important, the term—the latest technology, the latest technology. Now, you have got to picture that when I first came down with diabetes, the needles—are you ready for this one—the needles were metal. We had to sharpen them on a stone. The syringes were glass. Blood—testing urine was the method of determining blood glucose, and now, we are up to the insulin pump and the technology is just fantastic.

About 15 years ago, I began to realize that the normal low blood sugar warnings were no longer happening. All of you know that when you have a low blood sugar, you are either a little bit tired or you are a little shaky or things happen that are not normal, but at this point in my diabetes career, after 67 years, those body signals are gone, and that provides me with some pretty big dangers.

I needed to find a way to manage that situation. I was fortunate that the JDRF funded research program using the continuous glucose monitors, the CGMs, took place in Boston, and I was one of the first to start in on that, and we spent about a year with that program. It was great. I went from not realizing what was going on with regards to insulin reactions, as we used to call them, low blood sugars, hypoglycemia—you guys are all familiar with that—to now knowing ahead of time what to do and how to correct it. It also enabled me to control my diabetes better, which, again, is very, very important, so a new technology helped me with a situation that was really dangerous.

As a result of the JDRF study and other studies, the CGMs were endorsed by leading clinics throughout the country, the Endocrine Society, the American Diabetes Association, the American Association of Clinical Endocrinologists. I do not know what they are. They are great organizations, I know, but we cannot relate to them, but what I can say is that almost every insurance agency—almost every one—is now on board.

There is still a tragedy, and that tragedy is Medicare will not cover these things. I appealed to Medicare over a period of four solid years. The folder that I have is thicker than this. However—however—I received notice that, last November, that it was okay. The judge found in my favor. Well, I had the pleasure of coaching, again, as I said, two world champions. The feeling I had at those two world champions' successes was exactly the same when they told me, we find in favor of you, but that was not all the difficulty. Two months later, they took it back. They said no, and I was heartbroken, but I have not given up. I have not given up, and that is

what I hope you guys will do as you are going through school, high school, later on in college, and so forth. Do not quit.

Now that I depend on Medicare for my diabetes, the CGMs that could save my life—almost saved my life when I was wearing them, numerous times—and again, as I say, I will not accept the CMS's decision—those are the administrators of the Medicare program. The CGM can mean literally a difference between life and death. I am going to explain one instance.

Now, you have got to remember, we are trying to show the technology has helped me for 67 years to be healthy and strong and successful, and now, they have taken that technology away. I was driving on the interstate between Boston and Rhode Island when, not knowing, a reaction, low blood sugar occurred. My car started to move back and forth on the highway. I did not realize that. An 18-wheeler did realize it, truck. He saw what was happening and he took and pushed my car off the road into the median. When the technicians took my blood sugar, it was extremely low. That gentleman saved my life.

That did not have to happen. That did not have to happen. I could have been—the CGM is what I am trying to get at. If that was—if I had had that, I would have known ahead of time and things would have been taken care of. I could have taken care of it.

Now, about a month ago, I had a chance—things have been difficult now that we are back out of the situation. About a month ago, I had a chance to go back to visit Providence College. I went up there alone.

The CHAIRMAN. Mr. Amato, I hate to cut you off, because your story is——

Mr. AMATO. No, that is fine.

The CHAIRMAN [continuing]. absolutely fascinating. I am just worried because of the vote scheduling.

Mr. AMATO. I understand.

The CHAIRMAN. If I could ask you to wrap up, that would be great.

Mr. AMATO. Well, Chairman Collins, I would like to thank you, thank you for the opportunity of just being here and pleading for this particular situation, and I hope that the vote that will be taken and those that have been on assignment with you will continue, and if anyone has any questions, and I know you do not have the time for this, but if you do have questions, please be free to contact me and I would be glad to talk with you.

Thank you.

The CHAIRMAN. Thank you so much. Thank you for your compelling testimony.

Dr. Rodgers, it is great to have you back.

STATEMENT OF GRIFFIN P. RODGERS, M.D., DIRECTOR, NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASE, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, BEHTESDA, MARYLAND

Dr. RODGERS. It is good to be back. Chairman Collins, Senator McCaskill, and members of the Committee, thank you for this invitation to testify today.

Type I diabetes is a lifelong disease that affects Americans of all ages, including seniors, and on behalf of the National Institutes of Health, I am pleased to report that our research investment continues to improve the lives of people with Type I diabetes. Through coordinated efforts with our research partners, the JDRF and the ADA, as well as with the support of the recently renewed special statutory funding program for Type I diabetes, we are helping children sitting here today and all people with Type I diabetes live healthier lives and longer lives.

I am pleased to report that since I testified before you, this Committee, just two years ago, we have made significant scientific advances that are putting us closer to reaching our ultimate goal of preventing, treating, and ultimately curing Type I diabetes and its complications, and with the renewal of the Special Diabetes Program through Fiscal Year 2017 that you alluded to, we are also looking forward to taking advantage of future opportunities that I would like to briefly describe for you today.

Before I highlight some of these advances, I want to certainly acknowledge the important contribution that my fellow witnesses have made, and I want to thank you for your personal testimony that you are not letting Type I diabetes define you as a person, and I am pleased to share the table with Dr. Zaghouani, who, I am sure, shares the research goals of preventing, treating, and ultimately curing Type I diabetes. I would also like to thank all of those here today representing Americans of all ages with Type I diabetes.

I am happy to report that the outlook of people with Type I diabetes is better than ever. People with the disease have new and emerging technologies and treatments to help them manage their disease, and because of research conducted by NIDDK's landmark Diabetes Control and Complication Trial, or DCCT, and its follow-up study called EDIC, we know that early and intensive blood sugar control is key to reducing the risk of the devastating complications of the disease.

Just this year, for example, we learned from the DCCT EDIC that people with Type II diabetes who intensively controlled their blood sugar levels early in their disease are more likely to live longer than those who do not, and further emphasizing the importance of early and intensive blood sugar control.

However, as everyone here today knows, controlling blood sugar is easier said than done. It is extremely challenging and burdensome, and it also is limited by the potential for acute episodes of hypoglycemia or dangerously low blood sugars. A promising approach to overcoming this barrier is the artificial pancreas, which is a device that can sense blood sugar levels and automatically administer insulin.

I am pleased to report that with the Special Diabetes Program support, there has been tremendous progress in this area just last year, with researchers testing portable cellphone-based devices in real world settings. For example, in one setting, the use of an automated bihormonal bionic pancreas for five days and five nights by adults and adolescents led to lower mean blood sugar levels and reduced episodes of hypoglycemia.

Another study found that in adolescents' unsupervised overnight use of artificial pancreas for 21 nights led to improved blood sugar controls during the day and the night and reduced the number of episodes of this nighttime hypoglycemia, and because of the tremendous progress artificial pancreas technology holds, great promise in the near term approaching to help manage Type I diabetes while improving their health.

However, it is not a cure. Replacing or restoring the function of the beta cells would be the biological cure. In another area under vigorous investigation, one strategy to replace these beta cells is via islet transplantation. Our collaborative islet transplant registry has shown both safety and efficacy outcomes that have improved from the year 2007 to 2010, compared to, for example, 1999 to 2006.

Additional research progress areas have been made, both by NIDDK and the NIAID co-led Clinical Islet Transplant Consortium. They have completed a pivotal trial, a Phase three trial, and have reached another end point in a second Phase three trial, and we really look forward for these exciting results to be submitted to the FDA toward licensing pancreative islet product for transplantation.

Now, a current barrier for using islet transplantation is the scarcity of donor islets for transplantation, and here again, another major advance to overcome this difficulty has been recently reported by reporters in the NIDDK's Beta Cell Biology Consortium, who have achieved a longstanding goal of Type I diabetes research. They have discovered a way to create large numbers of these glucose responsive insulin producing beta cells, and we think with further research, such cells could possibly be used for transplantation to restore insulin producing capacity in patients with Type I diabetes.

NIH has also made important strides in research to combat diabetes complications. For example, a recent trial conducted by the National Eye Institute's Diabetic Retinopathy Clinical Research Network compared three drugs with widely differing costs for treating diabetic eye disease. The results show that in people with mild eye, or mild vision loss, all three drugs were equally effective. These results can inform clinical decisions and lead to more personalized treatment for diabetic eye disease while having significant cost implications, and importantly, the drugs were found to improve vision, which could certainly make a difference in the quality of life that people with diabetes share.

One other point I want to make is that the NIDDK and the CDC have developed a Search for Diabetes in the Youth study as a result of these special diabetes funds, and this search program has shown that Type I diabetes in people under the age of 20 has risen by 21 percent—the incidence has risen by 21 percent—during the years 2001 to 2009. These data suggest that there are some environmental factors, or factor or factors, that is contributing to disease risk, and our study of the Environmental Determinants of Diabetes of the Youth, or our TEDDY study, which is now following 6,000 kids from birth until the age of 15, we hope will very soon get a handle on what these environmental risk factors are.

I know that the time is limited, so let me just end there and just say to Chairman Collins and Senator McCaskill and members of the Committee, thank you for this opportunity to testify before you today. The NIH is grateful for your continued support of Congress, for our public and private partners, and for the unwavering efforts of the clinical study volunteers. We look forward to continuing our vigorous support of research to build-upon our recent scientific advances toward the goal of allowing people of all ages with Type I diabetes to live long and healthy lives, free of the burden of this disease.

Thank you for your attention, and I certainly look forward to answering any questions that you might have.

The CHAIRMAN. Thank you very much, Doctor.

Dr. Habib, as I am going to call you.

STATEMENT OF HABIB ZAGHOUANI, PH.D., J. LAVENIA EDWARDS CHAIR IN PEDIATRICS, AND PROFESSOR, DEPARTMENT OF MOLECULAR MICROBIOLOGY AND IMMUNOLOGY, DEPARTMENT OF CHILD HEALTH AND DEPARTMENT OF NEUROLOGY, UNIVERSITY OF MISSOURI SCHOOL OF MEDICINE, COLUMBIA, MISSOURI

Dr. ZAGHOUANI. Chairman Collins, Ranking Member McCaskill, and members of the Special Committee, I am delighted to be here, and I think the speech I am going to give is more educational and hopefully to convince you how to invest in research more and more so we can get the cure and get these children become Type None, Amelia, not Type I.

All right, so Matthew, can I have the first slide. Thank you, so please, if you focus on the slide, the poster, so Type I diabetes is an autoimmune disease. What that means is that the immune system, which is there to protect us from infection, from cancer and other diseases, in fact, make mistakes and then attack the beta cells, so the bugs are the immune system, and the flowers, the dead flowers, are the beta cells, and so, when the immune system, or the bugs, attack the flowers, or the beta cells, they die. There is no more insulin and, therefore, sugar cannot be taken for the cells. The cells cannot have energy. Therefore, they cannot function.

We started by looking at how to get the bugs away so that they do not attack the beta cells so that we can get insulin again, and when we did that, we succeeded when we tried to get the immune system away before the mice developed Type I diabetes, but we failed when we tried when diabetes is established.

We had to use a little bit of thinking. In humans, the diabetes is diagnosed when it is established, so we had to establish a technology or an approach that can reverse the diabetes, and when we looked harder, we understood that the immune system, when it attacks the beta cells, it also attacks the blood vessels that connect the beta cells to the rest of the body, so they can no longer distribute the insulin or it cannot get things to them to produce insulin. The blood vessels here are represented by a pipe, and if you look at the pipe, it is broken, so it is leaking.

In order to fix the disease—next slide, please, so the thought was, in order to fix the disease and to cure it, you cannot just eliminate the bugs. You have to fix the pipes, and so, if you eliminate the bugs with a drug and you fix the pipe with stem cells,

then you can get the flower to flower again and produce insulin and cure the disease, and this is the experiment we set to test, and we did. Next slide, please.

What we did here is we have a sick mouse in the upper panel, left side, and so we are going to treat it or give it a drug to eliminate the immune system that attacks the beta cells, and we gave it adult stem cells that we can get from the blood or the bone marrow, and watch what happened to the mouse, and surprisingly, what we found—that is a schematic representation. It is a mouse from the Internet. We made the mouse happy. It is back on its scooter.

I am hoping—I am hoping that we can get you all back on your scooters and your skis and your everything.

Thank you, so that is—two more minutes, thank you—for me.

We looked at the pancreas, a specific islet. Now, we are looking at the lower panel, the little dots. If you see, there is a brown dot in the diabetic mouse. That is the only leftover beta cells producing insulin. It is very little. You can barely see it. After we gave it this treatment, look how the insulin became—the islet became full of insulin, and that is what we want to do. That is what the experiment is aimed at.

We were able to cure Type I diabetes. You would not need to give yourself insulin anymore if this pans out and if we have funding and research to continue and develop programs that will take us there, so that is the science part of it. You can remove that.

What I want to say here is I have been doing research for 20 years on Type I diabetes and I have been making progress, and now that we are getting closer to really make the difference, I find myself really in trouble funding-wise. I have to spend 70 percent of my time writing grants, and so far this year, I have not been successful. I would rather spend my time doing the research rather than writing grants, and writing again the same thing, and writing again the same thing, and get nothing.

My advice or opinion is that, Chairman Collins, you made the statement, you said, we keep pushing the accelerator. Well, Chairman Collins, Senator McCaskill, Senators, keep pushing that accelerator. You will not get a police ticket. You will get a cure for Type I diabetes.

The CHAIRMAN. Thank you very much.

Thank you all for your excellent testimony.

Isabelle, you talked about that you have worn a continuous glucose monitor since you were very young, since, I think, age three. Does it send a signal to your parents on their phone or in some other way if your blood sugar is getting too low?

Ms. LEVESQUE. It does not matter if my blood sugar is high or low, or no matter, like, what my blood sugar is saying. I have a little iPhone in my bag and my CGM reads there, and then my iPhone sends all my numbers to my parents, so even if they are, like, across the globe, like, they can still see my numbers.

The CHAIRMAN. That is great, and it shows how important it is, as Mr. Amato says. It is truly a life-saver.

Kate, you talked about your family changing health care plans and then you lost coverage for your CGM, is that right?

Ms. HALL. Yes.

The CHAIRMAN. I want you to know that we are working very hard with your insurer and we have got some people for you to call, and I am hoping we can get that situation taken care of——

Ms. HALL. Thank you so much.

The CHAIRMAN [continuing]. for you.

Ms. HALL. Thank you.

The CHAIRMAN. Can you describe the difference for you between having a CGM and not having one?

Ms. HALL. Yes. I mean, it makes a big difference, in general, but especially with competing, I need to know what my blood sugars are every single moment, because it can go low in, like, 10 minutes without even me realizing, so usually, like, either one of my parents or my trainer will be able to see what my blood sugars are the whole time that I am competing, and if it says that I am going low, then I can make the adjustment before it goes low so I will not have those muscle cramps, and it makes a huge difference, so it has been tough not having it recently, so, hopefully, it works out.

The CHAIRMAN. Thank you.

Dr. Rodgers, did Medicare officials at CMS consult with you before they made the decision to not have coverage for CGMs for Medicare beneficiaries?

Dr. RODGERS. Chairman, I am unaware of any CMS officials contacting us on that—on this. I am in agreement with the comment that former Commissioner Hamburg of the FDA made that, really, as agencies, we should work together on this entire scheme.

Very recently, we held a Diabetes Interagency Coordinating Committee, which NIDDK chairs, and we presented information about glucose monitoring, particularly in older adults, and the proposals that came out of that meeting were presented to a group of experts and they uniformly agreed that this is really a high area for research priority, and so, they think that this is very important to move forward with.

The CHAIRMAN. Thank you. I think it is absolutely incredible that Medicare officials did not consult with you, the foremost expert that we have at NIH overseeing this research, nor did they consult with the FDA, which approved the device, before deciding that it was just a precautionary or safety device and, therefore, was considered non-medical.

Mr. Amato, it sounds like it certainly was medical for you and literally a life-saver. Would you agree with that?

Mr. AMATO. Absolutely. Yes, Senator Collins. Yes, I would have to agree with that, and I saw those two terms, "precautionary" and "medically necessary" over and over again. It is still not believed to be medically necessary, at least in the data that has been sent to me, so we will just keep our fingers crossed that we can convince them.

The CHAIRMAN. Well, as I mentioned in my opening statement, Senator Shaheen and I have a bill to mandate the coverage and we will—I cannot speak for my colleagues, but I am pretty sure we will all be pushing very hard on that.

Finally, Amelia, you said in your testimony that there were ten things that you wished your parents had known when you were diagnosed. I am almost out of time, but could you tell me the top thing that you wish your parents had known?

Ms. COOPER. I think that the top thing that I wish they had known is that when I go low, I get upset or angry or something, but then every time I got angry or upset or something, they automatically jumped to the conclusion that I was low, and after a while, it got kind of annoying.

The CHAIRMAN. Thank you very much.

Senator McCaskill.

Senator MCCASKILL. You needed them to know that you could just be angry.

Ms. COOPER. Yes.

Senator MCCASKILL. Having children, I certainly understand that.

Let me start with Dr. Zaghouani. In your testimony, you talk about the need to involve pharmaceutical companies in clinical Type I diabetes research. Is there any way at the Federal level, is there anything that we could do to encourage that kind of collaboration?

Dr. ZAGHOUANI. I think you can. The pharmaceutical companies, they take risk when they test a drug or do a clinical trial, and when they succeed, they make money, but I understand—ten years ago, I understand Merck spent $400 million to generic one drug. I do not know if that is still true now, so there is a lot of risk. I think if the government can help create an incentive for them to take that risk, I think that will push us forward toward a cure.

Senator MCCASKILL. Dr. Rodgers, we know that research dollars are scarce. NIH has been living under a dark cloud now for several years because of our cutting back on funding to NIH, and it is my understanding that there is an effort to ameliorate that somewhat this year. We still are not going to get back to the kind of increases that I think we need to be embracing to stay in our dominant position in terms of medical research around the world.

Does NIH and NIDDK—how do you decide what research studies that you fund, and are you giving priority to clinical studies that have a better chance of translational impact both in terms of quality of life for people like the young people in front of me and for the Federal Government saving money, for example? I mean, all you have got to do is turn on cable TV—not for Type I, but for Type II. There is no question that glucose monitoring is one of the drivers of our debt at this point because of the costs of monitoring, and all the ads for buying monitoring machines that is all being paid for by the Federal Government.

Dr. RODGERS. Well, Senator McCaskill, you raise a very important point, and certainly the prevalence, the burden of the disease, the number of people affected, but also the expert input that we get, the unique scientific opportunities that we may have at a particular time, all factor into the types of trials that we conduct, when we conduct them, how expensive they are.

There are other aspects sort of in your question that there are potential opportunities, for example, that one would think the private sector would be more involved in, related to a question that was just mentioned.

For example, the special diabetes statutory funding has allowed us, for example, to work with our sister organization, the National Eye Institute, to conduct a study of three commonly used drugs for

the treatment of one of the major complications, diabetic eye disease, and for example, this network—of these particular treatments that I had mentioned during my testimony, one costs about $2,000 per injection, one costs $1,200 per injection, and one costs $70 per injection, and these were given to people that had mild vision loss, over half of whom enrolled in this trial, and it is important to indicate that all of the results were quite substantial in terms of the improvement, but all three of these drugs had nearly equivalent effects.

Now, obviously, because of the financial aspects of this—this is not a particular study quite likely that a private sector pharmaceutical company would be likely to fund, but it is a kind of thing related to the question that you asked——

Senator MCCASKILL. Right, so let us go all in on the $70, right

Dr. RODGERS [continuing]. or therapies——

Senator MCCASKILL. Yes.

Dr. RODGERS. I want to caveat, though, it is for people with mild disease.

One other example, again, because of the Special Diabetes Program, we are actually able to now fund a trial called Prevention of End-Stage Renal Disease, or Renal Loss, or the PERL trial, using a fairly safe and quite effective drug called allopurinol. It is actually now a frequently used drug for the treatment of gout, because there is fairly good indication that this may prevent the progression of kidney damage to end-stage renal disease in which patients would, of course, have to undergo Medicare coverage.

If we are able to show in this trial that this safe and now generic drug can effectively prevent the disease in Type I diabetes, it will likely save tremendous amounts of funds moving forward, and it may have application in the broader setting, Type II diabetes, where the complications are quite similar.

Senator MCCASKILL. Thank you very much.

Dr. RODGERS. Thank you.

Senator MCCASKILL. Thank you, Madam Chairman.

The CHAIRMAN. Thank you.

Senator Tillis.

Senator TILLIS. Thank you, Madam Chair.

Thank you all for being here and for your testimony and for your advocacy on the Hill. I had an opportunity today to meet with some North Carolinians. I do not know—I see Rachel up here in front, and Trinity down there, and Turner. I know the others are in the room. I think on behalf of all North Carolinians, we appreciate you all wearing Tar Heel blue today.

I want to—Mr. Amato, you mentioned something that, as I was speaking with my guests in my office, when we look at the need to provide coverage for CGM, I think we have to take a look at benefits in economic terms that, I think, far outweigh the cost, because when we look at your situation—in fact, Stella—Ms. Cole, I think, is her last name, mother of Stella, a young girl, four-year-old, I think, who was in my office today—she was just relating a story about an automobile accident that occurred, and actually, her car was damaged as a result of someone who was obviously in circumstances similar to what you described.

I think as we go forward and we build support for coverage for CGM, we really need to articulate a lot of the hidden costs that probably are not being taken into account that in my mind far outweigh the cost of actually providing the device, not the least—the greatest benefit, obviously, is for Rachel's mother to be able to track her while she is playing volleyball, and Kate, similar to you, know whether or not she has a situation she needs to deal with, but also because I think it makes great fiscal sense, so I look forward to moving forward and supporting efforts to do that.

Kate, I also want to pick on you for a minute. I hear that when you set the juniors record for long jump, you were down in North Carolina.

Ms. HALL. Yes.

Senator TILLIS. Just something in the air down there. You ought to consider coming back, but can you tell me again about some of your experiences where in real time the device has had an impact on you personally?

Ms. HALL. Yes. Well, I first got it a couple of years ago and right from when I got it, I noticed a huge difference, and then it really helped me control my blood sugars, and not only that, just, especially when competing, it really, really, really helped me, the CGM. It just—it tells me when it is going high or low and I can keep it with me all the time, so instead of having to check my blood sugar every half-hour at a meet, I can just look at that and know where it is heading and grab something to eat real quick, or give insulin, and I do not get any muscle cramps and it helps me immediately, so it is very, very helpful.

Senator TILLIS. Thank you.

Dr. Rodgers, I know with the younger generation, Isabelle was very matter-of-factly talking about the integration with her iPhone, the ability to broadcast her levels real time to her parents, but what sorts of challenges do we have with seniors also taking advantage of this, and what kind of adoption rates do we see among seniors versus the more youthful population we have present today?

Dr. RODGERS. The adoption of these new technologies are certainly that seniors are embracing, perhaps not at the level that we see in the younger generations. I would say with the CGM in particular, there is a fair amount of data to recognize that hypoglycemia, very low blood sugar levels, among people 65 or older with Type I diabetes is a previously substantial unrecognized problem in terms of how often it occurs. It seems to be a major contributor to emergency room visits, for example, and when you mention the hidden costs, when comparing costs, imagine what the cost is having to return to emergency rooms repeatedly versus the costs of that type of care.

Having said that, though, I mean, this is one of these areas, and again, with the Special Diabetes Program, we recognize that we have to bring new talent into this field, not only in making these technologies more miniaturized and easier to use, but we have also been bringing in people with knowledge of behavioral science, because it is one thing to have the technology, but to get the people to use it may provide its own challenges, and to get it being used more effectively, for example, particularly with older individuals

who may be suffering with visual problems, with hearing loss, et cetera.

Senator TILLIS. Well, thank you.

Dr. RODGERS. These are issues that we are working on.

Senator TILLIS. My time is up, but one thing I would really, Madam Chair, I would like to spend some time on, or if the information is available, get access to it, but I really think to build our case for providing coverage for CGM that a look at the fully burdened cost of not doing it is critically important.

When you think about seniors' care, it is particularly—so, my mother is 82. She lives alone. She does not have diabetes, but I do know of many seniors that are living independently, and the likelihood that they can continue to live independently if they happen to have diabetes can be not only the monitoring that they themselves could see, but a family member or caregiver that may not be resident but be in a position to provide care, and when you take a look at possibly the level of additional cost by not being able to live independently, or the emergency room and other complications that could result by not having active monitoring, I think that you can really see the basis for building a compelling case for coverage.

Thank you.

The CHAIRMAN. Thank you, Senator Tillis.

Senator Donnelly.

Senator DONNELLY. Thank you, Madam Chair, and thank you to all of you for being here. I would like to mention my Hoosiers who are here with me from Indiana, Christian Allen, Aidan Sullivan, Soren Horvath.

To Kate, you will find on your way back from Iowa to Maine that you drive through Indiana along the way.

I have a home-cooked meal ready for you when you come back through Indiana.

Charlie Kimball, who came in third in the Indy 500, lost by maybe a car-length, Charlie Kimball is a Type I diabetic who drove that race car for 500 miles in 100-degree weather and did an extraordinary job, and one other thing, Madam Chair, I wanted to let you know a young man from my home town, his name is Gabe Martinez, and Gabe has had Type I since he was very, very young, and about two years ago, I told Gabe, I said, we will cure Type I diabetes—he is a huge Cubs fan—and, I said, we will cure Type I diabetes before the Cubs win the World Series.

His father said, "You have to do a lot better than that for us."

To all of you—Dr. Rodgers and Dr. Zaghouani—Dr. Zaghouani, how do we protect those islet cells from the immune system when we put those islet cells back into the body to go to work?

Dr. ZAGHOUANI. No, there is no transplantation of exogenous islet cells. It is the flowers themselves, that they have their own seeds. They rejuvenate again.

Senator DONNELLY. You are bringing the islet cells that are already in your body——

Dr. ZAGHOUANI. Back—yes.

Senator DONNELLY. Okay. How do we keep those cells from being attacked by the immune system?

Dr. ZAGHOUANI. Outstanding question, so you have juvenile kids and one of them develops the disease and the other one does not,

and the reason for that is because there are environmental factors that applied for one, not for the others, so in order for the disease to happen, you have those environmental factors to be there. It is like a hurricane in the ocean. You have thousands of events that happen and they have to come together for the hurricane to occur. The same thing with islets, so once you fix them in the same person, unless you have those all events, or environmental factors happen again, you do not need, basically, to do anything for the immune system.

Senator DONNELLY. So is this something that you——

Dr. ZAGHOUANI. This is my opinion.

Senator DONNELLY. How would you get it rejuvenated again? Is it an injection or——

Dr. ZAGHOUANI. No, there are seeds.

Senator DONNELLY. Okay.

Dr. ZAGHOUANI. Once you fix the blood vessels, I think, and you eliminate the immune system that attacked the beta cells, the seeds, or the stem cells, endogenous stem cells, not the ones that we give—the ones we give are for blood vessels—those, they will regrow and mature and——

Senator DONNELLY. If we do that, that would enable all of these youngsters to go to Type None.

Dr. ZAGHOUANI. That is what I hope.

Senator DONNELLY. How long do you think that is until it would be able to be on the market?

Dr. ZAGHOUANI. If you put the money——

Senator DONNELLY. I am not looking for a guarantee. I am just looking for a neighborhood.

Dr. ZAGHOUANI. Well, my answer is, the more money you put, the faster it goes.

Senator DONNELLY. There you go, so then, how much will it cost to get it done next week?

We are incredibly grateful for that effort and we will make sure that the funding is there for you to keep this moving along.

Dr. Rodgers, I want to note that behind you are a whole bunch of your team from the NIH, and I would like them to stand up, who have done such an extraordinary job in doing the research over the years.

Dr. Rodgers, what is the most pressing thing you need from Congress right now? Obviously, funds. What kind of funds do you need to get this to a place where we do not have another Child's Congress, or the Child's Congress two years from now is a celebration of having found a cure?

Dr. RODGERS. Well, I think, as Dr. Zaghouani mentioned, certainly, we have a lot of very good investigators with a lot of very good ideas, and that, unfortunately, at the present level of funding, we are only able to entertain and successfully fund maybe one in five or perhaps one in six of those. We think there is certainly room for other outstanding ideas, and because, obviously, in this particular case, we want to be thinking about a multi-prong approach.

We want to be able to develop new sources of cells to implant. We want to, at the same time, because we know so much about the genetics and who is susceptible to developing this, we want to continue to determine what that environmental factor is that has in-

creased the incidence by 21 percent in a short period of time. We now the genes have not changed. It must be something in the environment. If we can find what it is in the environment, if it is an infectious agent, we can develop a vaccine. If it is some that could either protect against developing the disease or it can actually cause the disease. If it is something in the diet, then dietary modification could be in effect.

For people who have the existing disease, we want to—is in their early stages of autoimmunity, we want to selectively try to turn and reverse that autoimmune disease and use fairly selective manners, which you have heard from Dr. Zaghouani, not completely wiping out the immune system, because it is there for a reason, but selectively going at the cells that are attacking those beta cells. This is what we are learning, especially with the addition of this Special Diabetes Program.

For people that have the existing disease for longer periods of time, we want them to live a more comfortable life, so to try to prevent them from developing the complications.

Senator DONNELLY. Thanks.

Mr. Amato, you are an inspiration to all of us, and to you young kids, we hope to beat this thing so when you are Mr. Amato's age, this is just a memory from long, long ago.

Thank you, Madam Chair.

The CHAIRMAN. Thank you.

It is a great pleasure to call upon Senator Shaheen, the Co-Chair of the Diabetes Caucus.

Senator SHAHEEN. Thank you very much, Chair Collins, both for your leadership as Chair of the Diabetes Caucus and for the work that you are doing on this Committee, and thank you for letting me squat at this hearing, because I am not normally a member of this Committee, but I very much appreciate being able to be here.

I want to thank all of you delegates who are part of the Children's Congress, because you are absolutely the best advocates for helping all of us who want to see a cure for diabetes and want to see the best new treatments available.

I want to recognize Skye Archibald and her family from Exeter, New Hampshire, who is here as part of the Congress, and also Senator Collins was kind enough to recognize my daughter and granddaughter, Stefany and Elle Shaheen, who have been very much a part of the Children's Congress in the past, who are here today with their diabetes service dog Coach, and to all of you who have testified, thank you very much for your work and for your willingness to share your stories today.

You know, Mr. Amato, I cannot agree more with what Senator Collins and Senator Tillis said about the importance, not just of making sure that Medicare funds the CGM because it is the right thing to do, but it is the economic thing to do, and I just want to quote from a study that was done called, "Diabetes Research and the Public Good" by two economists, and it points out that diabetes cost the United States $245 billion in 2012, and that cost is expected to double by the year 2020. Medicare costs from diabetes were $104 billion in 2012 and they are projected to increase to $226 billion by 2020.

The increased costs are attributable in a large way to diabetes' role as the leading cause of kidney failure, adult blindness, non-traumatic amputations, and nerve damage, stroke, and heart attacks, and those things happen because people do not get the treatment that they need, and a CGM is part of that treatment. There is no doubt that we should fund that, and hopefully, with everybody's help here, we can get that legislation passed to make that happen.

Dr. Rodgers, I wanted to ask you, you and Dr. Zaghouani talked about a number of the promising research that is going on to address diabetes. I wonder if you could speak to what you think is the most promising immediate breakthrough that we are looking at that will make a difference in treatment.

Dr. RODGERS. Well, I think prevention certainly is a major part of that.

Senator SHAHEEN. Or prevention.

Dr. RODGERS. Yes. Yes, and I view this in terms of prevention of either preventing people who are genetically susceptible to this disease from developing it based upon what I mentioned before and this TEDDY study, the Environmental Determinants of Diabetes of the Youth, is likely to answer that. In the intermediate term—this is a 15—this is a study of kids from birth to the age of 15, but we already are developing important knowledge from that study.

Preventing people who have those genes and who have actually begun to show signs of autoimmunity, our TrialNet study is beginning to use certain types of drugs to actually reverse that autoimmune process to allow those beta cells to last longer, and we know the longer they last, the less likely it is that individuals with Type I diabetes will develop serious complications.

For the people with the diabetes, this artificial pancreas that is linking the insulin infusion with continuous glucose monitoring, brought together by some sort of, I should not say—some sort of computer device, typically on phones now, on portable phones, is really the best technology, because we know keeping the blood sugar in line is really the best way to prevent these complications.

As I mentioned, just in the last two years, we have had such great success at this that it is quite likely, working with our friends at the FDA, that many of these devices will be approved, and so that is really, in the short term, I think, the likelihood for the best success with the largest impact.

Senator SHAHEEN. Thank you very much.

I am almost out of time, but I wonder if I could get Amelia and Isabelle to tell me, what is the best advice that you would give to someone who has just been diagnosed with Type I.

Ms. COOPER. Well, the advice that I would give is to educate your friends and family members as quickly as you can about your disease, because if you get them involved, it takes the pressure off and it just—it is better for your safety and your mental health.

Senator SHAHEEN. Thank you.

How about you, Isabelle.

Ms. LEVESQUE. I would say that, like, keep trying to raise money and make sure, like, no one stops you from doing anything just because you have Type I diabetes. Always, like, do what you dream of.

Senator SHAHEEN. That is great advice.

Thank you, Madam Chair.

The CHAIRMAN. Okay, Senator Casey, try to top that.

Senator CASEY. I will not even try, but thanks so much, everyone, for being here. We should have more hearings like this where we not only have testimony, but also questions and then audience participation and reaction. That is pretty rare, so we are grateful.

I wanted to give a shout-out to some Pennsylvanians that I met with earlier today, Ethan Howard from Wayne, Pennsylvania, Evan Wickersham from West Chester, Julia O'Leary from Lancaster, Kathryn Talerico from Pittsburgh, and Madyson Huston from Waterford. Can you give them a round of applause.

We had some pictures, and because they were so mobilized and so effective and such good advocates, I figured they could come back here and solve our appropriations problems and work on foreign policy, whatever, so we are grateful for that.

I first want to apologize for being late and missing a good bit of the testimony, but we are grateful to have this chance to talk for a minute. I will not be long, because I was late.

I wanted to make sure. Sometimes, we have an exhaustive discussion of a topic, and often Senators can leave here without getting a to-do list, or at least one that is emblazoned in our minds, and I just wanted to ask, before we get to our younger witnesses on the left side of the table—my left, your right—but, Doctor, I just wanted to go back to you. What would you hope, if you had a short list, what would you hope that the Congress would do, not only in the near term, but, say, over the next couple of years, in terms of short-term assignments and longer-term commitments, as well.

Dr. RODGERS. Well, Senator Casey, I want to say that I am very grateful for all of the support that Congress has actually given to the NIH and identifying biomedical research as an area, moving forward, that is of great interest. As I mentioned earlier, we have such great ideas out there, but unfortunately in recent years have not been able to have the opportunity to bring in as many new ideas and investigators as we certainly would like, so in the short term, again, I want to thank you for the support that we have learned about and we hope that as that progresses forward, that I will be happy in two years to report to you what has happened with that incremental support that we have received.

We in NIDDK really want to focus on all aspects of this, from prevention, to early intervention, to making certain that the primary and secondary complications are considered, because it really is the secondary complications—the eye disease, the kidney disease, the non-traumatic amputations, the neuropathy—that is really contributing greatly to the cost, that $245 million, that Senator Shaheen referenced. That is really driving the cost of this, both for our young as well as our older population, and so, we are keenly aware of that and we are really targeting our efforts in all of these categories.

Senator CASEY. For anyone else, we only have about a minute and a half, but I want to make sure you had a moment. Anyone else on the panel who——

Dr. ZAGHOUANI. I think my answer is very short, the same I gave to Senator Donnelly, is funding.

Senator CASEY. Mm-hmm.

Dr. ZAGHOUANI. Funding, and funding again.

Senator CASEY. That is an important to-do list, part of a to-do list.

Dr. ZAGHOUANI. Yes.

Senator CASEY. Well, before—I know I am almost out of time, but Isabelle, I wanted to ask you about how your friends have helped you throughout the early years of your life when you have the challenge of not just getting through school, but also dealing with a significant health challenge. Can you describe how your friends have helped you?

Ms. LEVESQUE. My friends are, like, very helpful. When I was in preschool and kindergarten, my Mom came in and she helped me explain to the class, like, why I was always, like, getting pulled aside, so they were not getting confused, so now, they, like, know that I have it and they are very, like, helpful, because, like, sometimes, my pump rings and they go and tell the teacher and they say, "Oh, Isabelle's pump is ringing. I think she needs to go to the nurse," so, they are very, like, helpful.

Senator CASEY. Well, I am going to give applause to your friends. How about that.

Thank you.

The CHAIRMAN. Thank you.

Senator Warren.

Senator WARREN. Thank you very much, Senator Collins.

Like Senator Casey, I apologize for being late. We are kind of running multiple things at once, but I had to come and join this group again this year and to say a special thank you to Senator Collins for pulling us all together. This is really a terrific annual event.

I also want to say a special shout-out, since we are all getting to do that, to Jeffrey D'Angelo from Plymouth, Massachusetts. Where are you, Jeffrey? I cannot see in this sea of blue. Good to see you, Jeffrey. All right.

We have all been talking about the cost of diabetes. Type I diabetes, it imposes, obviously, a terrible personal cost on our kids, on our families, and the financial costs are staggering. Nearly 40 percent of families with diabetic children experience financial strain, and care for Type I diabetes costs our health system an estimated $15 billion a year.

I want to start on the cost question from a different direction. Dr. Rodgers, if we could delay the onset or reduce the severity of Type I diabetes so that millions of Americans could stop buying insulin, glucose monitors, test strips, if we could stop paying the costs of doctors' visits, to emergency rooms, about what do you estimate we could save every year?

Dr. RODGERS. Well, Senator Warren, there is no doubt that if we could prevent diabetes from occurring and reduce the severity of the disease, that would result in a tremendous cost savings, and I think organizations like the JDRF have actually cost estimated what that would result in, at 10 percent or at 20 percent.

The NIH has not made any of those cost estimates, to my knowledge. What I can tell you, though, and as I referred to before, a major cost is associated with these secondary complications—the

eye disease, the kidney disease, the non-traumatic amputations, and we think that certainly with—we have already, and I mentioned previously some of the benefits that we see in terms of cost effectiveness in the treatment of these secondary complications. One could potentially do estimations on those, but I do not have, sitting here today, a good estimate to tell you how much precisely we could——

Senator WARREN. Okay. I take it, though, based on some of the estimates that JDRF have given us, a 10-percent reduction would be about $3 billion. In other words, a lot of money that we are talking about here, and when you combine it with the devastating human cost, you think it would be a no-brainer to invest more money in research on diabetes.

Let us pin this down just a little bit more. Dr. Rodgers, you direct the National Institute of Diabetes and Digestive and Kidney Disease, so how much money do you have for your work compared, and inflation adjusted, with what you had 10 years ago?

Dr. RODGERS. That is a question that—if one were to include, in addition to our regular appropriations, as well as the Special Diabetes Program appropriations, because of inflation, NIDDK has lost about 24 percent in our buying power over that——

Senator WARREN. Here we are, we see the costs imposed, and yet you have got, effectively, about 24 percent less money to work with than you had 10 years ago for the kind of research that you are doing, and as we know, you are not alone. NIH funding overall is down 25 percent since 2003. That means for NIH we are investing about $12.5 billion less in medical research this year than if we had just kept up with inflation over the last decade.

Now, last week, the House passed the 21st Century Cures Act, which includes the Cures Innovation Fund that is meant to give NIH about $1.9 billion per year for the next five years. Now, that does not fill a $12.5 billion hole, but it certainly is something.

Here is what I am concerned about in this bill. I am concerned the NIH may not even get that much. Before this bill passed the House, a section requiring the appropriators to continue to fund the NIH at current levels was taken out. This is called a maintenance of effort provision, and without it, there is nothing to stop Congress from cutting the NIH's—adding $1.9 billion at the top, but cutting $1.9 billion from their base budget, or for that matter, cutting $2 billion from their budget, or $4 billion from their budget in order to try to cut government spending overall, and if that happened, NIH's budget would not actually increase at all, even when the $1.9 billion from the Cures Innovation Fund is added on top.

Let me ask you, Dr. Zaghouani, if the result of the 21st Century Cures bill is a new fund that gets great fanfare but does not actually result in any additional money for NIH, does that help the research community?

Dr. ZAGHOUANI. Actually, I began to downsize my laboratory because I could not get the appropriate funding to maintain. I was speaking with the Director of NIH, Dr. Rodgers, and I need to have three R01 grants, three grants, about $2 million apiece, every five years, so altogether, in order to maintain my operation going, so because I could not do it for the last two years, I have started downsizing, so downsizing is not only the economics for the people,

it is the research that now is going to be stopping. We cannot make progress, and there is one more problem. While doing this research is I am training people to take over when I am out. I can no longer train those people anymore, so we are hurting ourselves at many, many different points.

Senator WARREN. What you are saying is you cannot maintain, in fact, you are cutting back, certainly not in a position to grow the research. Families struggling with diabetes, with Parkinson's, with Alzheimer's, other serious conditions, deserve more than lip service from Congress. They deserve real increases in funding on medical research, and that is what we need to do.

I introduced a Medical Innovation Act that could boost the NIH budget by 20 percent. It is not enough, but it is a start. I hope Senate colleagues will join me in this effort, or improve the 21st Century Cures bill so that it is really about additional money, or bring other ideas to the table for more money for medical research. If we are serious about saving lives through research and saving money, then Congress has to step up and make a real commitment of real dollars.

Thank you, Madam Chairman.

The CHAIRMAN. Thank you.

I want to thank all of our witnesses today, and particularly the delegates who have come from every State in the Union and across the globe to make the case for more support for diabetes funding. That is a shared goal of everyone in this Committee.

I would point out that it is because of the efforts of families all across this country whose children have juvenile diabetes, or Type I diabetes, that we have been able to triple the funding for diabetes research since 1997, when we first started the Diabetes Caucus, and I can see Dr. Rodgers nodding in agreement. I am proud of the fact that we have extended the Special Diabetes Program, which focuses on Type I and on diabetes among Native American populations, that we have been able to extend that important program.

We could not have done those spending increases that are so vital to progress without the help of the people in this room, the people who have testified, the children who have testified previously at our Children's Congresses in past year, and without the advocacy of the JDRF, the American Diabetes Association, and other groups, so we really have come a long, long ways, and that is why we have the technology that we do.

Mary Tyler Moore for many, many years always came to our hearings to review the progress and talk about her own life living with Type I diabetes. She was not able to be here this year, but she is certainly in the thoughts of many of us. She once told me that you have to be a mathematician, a physician, a personal trainer, and a dietician all rolled into one to keep your diabetes under control, and I think there is a lot of truth in that.

Fortunately today, we also have some wonderful advances in technology, and we are going to keep pushing for that as well as a change in Medicare policy so that when Mr. Amato—when the young people here become Mr. Amato's age, they are not going to have the fight that he has had to get the coverage for the CGM, and we are going to make sure that that happens.

My thanks to the more than 160 delegates and all of their families, because, after all, it does take the entire family, who have traveled to Washington to tell your stories. You are the ones who really make a difference by putting a human face on this diabetes.

I want to thank everyone at JDRF for your help in organizing this, the NIH, Dr. Zaghouani for coming, as well, Mr. Amato, but most of all, our three young people on the panel, Isabelle, Amelia, and Kate. It was wonderful to have you here in Washington.

Committee members will have until Friday, July 24, to submit any additional materials or questions for the record.

I want to thank all the members of the panel who have been here today and all of you for sitting so patiently so long. I know that that can be a trial, so thank you, and let us end this hearing in an unconventional way, by giving a round of applause to all the delegates who are here.

[Whereupon, at 3:24 p.m., the Committee was adjourned.]

APPENDIX

Prepared Witness Statements

Testimony of Isabelle Levesque

Age 10, JDRF Children's Congress Delegate

From Arundel, Maine

At the Hearing entitled:

"Diabetes Research: Improving Lives on the Path to a Cure"

Wednesday, July 15th, 2015, at 2:15 p.m.

Before the

United States Senate Special Committee on Aging

Dirksen Senate Office Building, Room G-50

Washington, D.C.

Thank you Chairman Collins and Senator McCaskill for inviting me to testify today. My name is Isabelle Levesque; I am ten years old and live in Arundel, Maine.

I was diagnosed with type 1 diabetes, or T1D, when I was two years old.

My diagnosis was the start of a very different childhood. My mom and dad began a routine of ten to twelve finger pricks and six insulin shots each day, to keep my blood sugar in a healthy range. As of today, I have pricked my finger over 28,000 times, changed my pump site over 1,400 times and changed my sensor over 400 times. Can you imagine having to stick a needle into your skin 30,000 times in just 8 short years?

My family says that I am a happy child, but it's hard when you have to deal with diabetes every day. Type 1 diabetes is something you can never stop thinking about. I constantly have to put my life on pause to test my blood sugar. This can happen at any time: during my favorite movie, at school, when I'm swimming, or in the middle of a soccer or softball game. Sometimes, I even have to come out of a game to recover from low blood sugar, when I feel my team needs me the most, it is so frustrating! Cold weather activities are difficult as well because I don't always feel my low blood sugars when playing in the snow. I have been as low as 26 and didn't even know it until my parents had me check.

I'm here as a JDRF Children's Congress Delegate because I need your help. I want to see a cure for diabetes in my lifetime, and all of my friends here today do too. My family and I have spent the last eight years fighting for it, and we need Congress to continue fighting with us by funding research through the Special Diabetes Program (SDP).

My family and I work hard to raise funds for T1D research and to teach my community about this difficult disease. We do our part. My walk team, Strides for Isabelle, has been the top fundraising team in Maine for five out of the last seven years. I am proud to say we have raised over $100,000. Also, last summer, I helped organize a concert, which I played my guitar in, to increase my community's understanding of the impact of diabetes.

The money we've raised has gone towards research into new treatments for type 1 diabetes, and hopefully will one day find a cure.

From this research has come technology that has made it easier to live with diabetes. One technology I use to track and manage my blood sugar is called a continuous glucose monitor, or CGM. I've been wearing a CGM since I was three years old.

Before I had a CGM, it was really hard for my mom and dad to know if my blood sugar was high or low, so they pricked my finger constantly throughout the day and used a test strip to check. For a three-year-old, and even now, the CGM has made a huge difference.

Although this device has helped me to stay healthy, there is so much more to be done, and a cure is still needed.

When I grow up, I want to be a teacher. To help make this dream of mine a reality, it's important that Congress continues supporting T1D research.

Thank you.

Testimony of Amelia Cooper

Age 15, JDRF Children's Congress Delegate

From Kansas City, Missouri

At the Hearing entitled:

"Diabetes Research: Improving Lives on the Path to a Cure"

Wednesday, July 15th, 2015, at 2:15 p.m.

Before the

United States Senate Special Committee on Aging

Dirksen Senate Office Building, Room G-50

Washington, D.C.

Thank you Chairman Collins, Ranking Member McCaskill, and Members of the Committee, for inviting me to testify today. My name is Amelia Cooper, and I was diagnosed with type 1 diabetes (T1D) three years ago, at age 12.

As you all know, the teenage years can be a little rough, with pressures to fit in, figure things out and find your way. At a time when many of my peers are worrying about their hair, clothes, and social calendar, I must focus my attention on things vital to my health. Each day, I have to carefully monitor and manage my blood glucose level, which isn't easy since exercise, hormones, diet, and many other factors all have an impact.

Despite these serious challenges, I have many reasons to be grateful. Thankfully, I was diagnosed with T1D after Frederick Banting discovered insulin. Thankfully, I was diagnosed with T1D after insulin pumps and continuous glucose monitors were invented. Thankfully, I have learned to manage my diabetes without allowing it to manage me – even though it is not always easy.

It is only through a very strict blood sugar management routine, and advancements in diabetes treatments and devices, that I have been able to live my life to the fullest.

42 – The number of countries I have visited. And still counting.

13.1 – The number of miles in a half-marathon. I have completed two so far.

10 – The number of things I wish my parents knew when I was diagnosed with T1D. I wrote this list as a published author in the blog diaTribe.

4 plus – The number of years after college it takes to become a doctor – like my dad, who I look up to. That's my dream job.

1 – As in type 1, the number associated with my disease. I am hopeful through Congress' support we will move from type 1 to type none.

Through advances in medicine my life has gotten easier, healthier and safer. I use an insulin pump and a continuous glucose monitor (show both here), but I am well aware that those advancements took much time, research, and funding to become a reality.

While I have never participated in a formal clinical trial, I am very excited about a recent research project that I conducted last year. I have always been curious about how and why my blood sugar levels are so erratic when I ski. Changes in altitude and prolonged activity can be very hard on blood sugar control, and after researching the topic, I realized that there was an opportunity to design a study to evaluate the changes my body experiences while skiing, compared to those without diabetes. The results, which I presented at this summer's American Diabetes Association (ADA) meeting in Boston, showed that despite strenuous activity, altitude caused an increased demand for insulin by more than a third. Most importantly, I showed that my blood sugars could be in the same range as my friends with careful monitoring and planning of my carbohydrates and insulin requirements. The use of a continuous glucose monitor was especially helpful in preventing hypoglycemia and ensuring safe blood sugar levels prior to riding a chairlift or skiing.

My project obviously does not compare to those responsible for the significant progress being made towards life-changing treatments for T1D. Projects on beta cell encapsulation and artificial pancreas technology – treatments I hope to have available in the coming years. But my project does represent my strong desire to make an impact.

I am not someone that can just stand-by when there is so much that can be done to improve my quality of life and that of all my friends here before you today.

In closing, I ask for your support in this fight to find a cure for diabetes.

Thank you, Chairman Collins, Ranking Member McCaskill and Members of the Committee, for your time today.

Testimony of Kate Hall

From Casco, Maine

At the Hearing entitled:

"Diabetes Research: Improving Lives on the Path to a Cure"

Wednesday, July 15th, 2015, at 2:15 p.m.

Before the

United States Senate Special Committee on Aging

Dirksen Senate Office Building, Room G-50

Washington, D.C.

Good afternoon. My name is Kate Hall and I am from Casco, Maine. Thank you, Chairman Collins, Ranking Member McCaskill and Members of the Committee, for the honor of being here today to speak about my experience living with type 1 diabetes or T1D as an athlete.

I was diagnosed with type 1 diabetes when I was ten years old. At first it seemed as if I would never understand every little, tiny detail that was involved in having diabetes. I had to adjust to taking shots of insulin, checking my blood sugar several times a day, learning how to count carbohydrates in everything I ate, and learning how to deal with high and low blood sugars correctly. However, the thing that stood out to me the most was being benched during my first soccer game after my diagnosis. That really made me realize that diabetes wasn't going to ever stop me from doing the things I loved most. I thought, "I am not sitting out on anything ever again if I can help it. I am figuring this thing out."

Type 1 diabetes is challenging, particularly when it comes to what I love doing most – track and field. The events I compete in, the long jump and the short sprints, require rigorous, daily training. But for me, because I live with T1D, keeping my blood sugar in a healthy range as much as possible is just as important a part of my training and success as anything else I can do to prepare for competitions. Managing my diabetes can be really hard at times, and I've realized I can't figure everything out on my own. I need help from doctors, my parents, diabetes technologies, and researchers.

Being a competitive track and field athlete, there are many tiny details involved that people have to do in order to get the best results possible. Some of these things include staying hydrated, eating well, sleeping well, training the right way, and warming up correctly to prevent injury. Not only do I have to do all of these things, but making sure my blood sugar is at a good level is another thing to add to the list. Whenever I am training or competing I have to take my blood sugar several times before I run in order to make sure it won't go high or low. If it is high or low, I need to quickly do what I need to do to get it to that perfect level so it doesn't negatively affect me. During my training or competition, I try to check my blood sugar every half hour to ensure a high or low blood sugar will not affect my performances. If my blood sugars do become too high or low, which has happened several times, my PH level changes and I occasionally get muscle cramps. These muscles cramps are very painful and prevent me from competing the rest of the day or even week. When this happens, it is extremely frustrating to think that my diabetes is preventing me from doing what I love the most even when I try my hardest to control it.

I wear an insulin pump and was using a continuous glucose monitor until we changed health insurance companies. With most private health insurers covering CGMs these days, I am hopeful that my current plan will update its policy so I can use a CGM again. These devices help me spend more of my day in a healthy blood sugar range, and also help me focus on training and competing.

Thankfully, new technology, diabetes management devices, and also the support of my family and my healthcare team, have allowed me to pursue my passion and become a world-ranked junior athlete. I was able to end my high school long jump career this year by breaking a 39-year old national high school record with a jump of 22 feet, 5 inches at the New Balance Nationals last month. My jump also broke the U.S. junior record set in 1982 and surpassed the automatic qualifying standard for the 2016 Olympic trials. I also finished third in the 100 meter event with a time of 11.37 seconds.

My dream is to one day represent the United States at the Olympics. This fall, I'll begin training at Iowa State, and although I'll be far from home and working with a new team of coaches – one key part of my life remains unchanged: the challenges of managing my type 1 diabetes every day.

Technologies are important, but those of us with T1D need more. We need the scientists to help us figure out even better treatments and a cure for this disease. That's why my family and I are grateful for the funding that Congress has provided for type 1 diabetes research. Chairman Collins, we thank you for your leadership. All of us with T1D are counting on Congress to help us figure it out.

Thank you.

Testimony of Robert S. Amato

From Johnston, Rhode Island

At the Hearing entitled:

"Diabetes Research: Improving Lives on the Path to a Cure"

Wednesday, July 15th, 2015, at 2:15 p.m.

Before the

United States Senate Special Committee on Aging

Dirksen Senate Office Building, Room G-50

Washington, D.C.

Chairman Collins, Ranking Member McCaskill and Members of the Committee, thank you for the opportunity to testify before you today. My name is Bob Amato and I am from Johnston, Rhode Island.

When I was first diagnosed with type 1 diabetes sixty-seven years ago at the age of seven, the thinking was that people like me should not participate in sports or lead an active life. This seemed unreasonable to me and with the guidance of the many physicians at the Joslin Diabetes Center, along with my family, I was able to prove this concept to be a fallacy. In 2009, I was entered into the Athletic Hall of Fame at Providence College because of my accomplishments as a runner and coach. As a coach, I had the privilege of guiding a runner to two consecutive World Championships, the team to 16 New England championships, and 23 athletes were selected as Division 1 All Americans. My coaching colleagues selected me as "University Division 1 Coach of the Year" 15 times.

I was able to find success despite the daily challenges of diabetes because I always used the latest technology to help me better control my diabetes and keep myself healthy. However, at the present time, I am hindered from continuing my successful and active lifestyle. About 15 years ago, I began to realize that the normal warning signs for hypoglycemia – or low blood sugar – were diminishing. Previously, as my blood sugar neared a dangerous low level, I would experience dizziness, sweating and shakiness, which would give me the time to eat or drink something to prevent me from passing out, having a seizure or worse. With hypoglycemia unawareness, I started experiencing many close calls and my quality of life was beginning to suffer. I needed a better way to manage my diabetes.

I was fortunate to participate in a JDRF-funded research study using a continuous glucose monitor, or CGM, which measures blood sugar in real time and alarms when blood sugar levels are about to go too high or low. The difference was life changing. The CGM provided not only an essential early signaling of a low blood sugar but essential data to help me better control my diabetes overall.

As a result of the JDRF study and other studies, the use of CGMs has been endorsed by the leading clinical societies involved in treating people with diabetes – the Endocrine Society, the American Diabetes Association and the American Association of Clinical Endocrinologists. Even private insurers recognize the importance of this technology. In fact today, over 95 percent of private plans cover CGMs for people with type 1 diabetes.

But here's the tragedy – Medicare does not cover this life-saving device so I had to stop using the CGM after the study and my serious hypoglycemic events returned. For the past 4 years, I have been appealing the decisions of Medicare in an effort to get coverage. In 2014, an Administrative Law Judge ruled in my favor, but the Medicare Appeals Council rejected the ruling, and I am yet again left without coverage for this device.

Now that I depend on Medicare for my diabetes care, the CGM that has saved my life countless times has been taken from me. I cannot and will not accept CMS' decision, for me or for all the seniors with type 1 diabetes who depend on this device.

The CGM can mean - literally - the difference between life and death. I was once on an interstate when my blood sugar plunged without me noticing, and I began driving erratically.

Fortunately, an 18-wheeler intentionally crashed into the side of my car to push me off the highway. No one was injured, and that truck driver possibly saved my life and that of others. A CGM would have alerted me well before this precipitous drop in blood sugar and the accident would have been avoided.

I had a chance to visit Providence College recently, and I stopped in at the Hall of Fame to see the plaque I received several years ago. I remembered the excitement of recruiting athletes in Ireland, England, Scotland, and all parts of the United States. I remembered the World Championship in Ireland when runners from the Providence College team were represented on the Irish national team, the English national team and the American national team. I also remembered this as a time in my life when I was able to travel the world because managing my diabetes wasn't so incredibly difficult.

I loved coaching. It gave me so much – including a livelihood that allowed me to pay my share in to Medicare. It is so disappointing and unnecessary, that at this stage of my life, I am almost incapable of doing very much at all. The CGM would allow me to be active again, yet without it, I can only go a short distance from my home unless my wife or a friend is with me. This is not how I want to spend the rest of my life. It's an injustice that needs to be rectified.

Chairman Collins, thank you for recognizing the importance of this issue and for introducing S. 804, the Medicare CGM Access Act of 2015, which would ensure that Medicare covers CGMs for seniors like me. I would also like to thank the others on the panel who have signed on as cosponsors and urge those of you who have yet to cosponsor to support this effort. Congress is doing an outstanding job of providing funds to advance type 1 diabetes research; however, the benefits of these advances will be limited unless there is coverage.

Thank you for the opportunity to testify. I am happy to answer any questions you may have.

Testimony
Before the
Special Committee on Aging
United States Senate

Diabetes Research: Improving Lives on the Path to a Cure

Statement of
Griffin P. Rodgers, M.D., M.A.C.P.
Director
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
U.S. Department of Health and Human Services

National Institutes of Health

For Release on Delivery
Expected at 2:00 p.m.
Wednesday, July 15, 2015

Chairman Collins, Senator McCaskill, and Members of the Committee, as Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I thank you for your invitation to testify at this hearing on type 1 diabetes. On behalf of the NIDDK and the other Institutes and Centers of the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services (HHS), I am pleased to report on significant recent scientific advances and future research opportunities in type 1 diabetes and its complications.

Long recognizing the importance of diabetes research toward improving the health of people affected by the disease, the NIH has invested over $1 billion a year in diabetes research in each of the last several years. This investment has been complemented by the support and efforts of our research partners—academic institutions, the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and charitable and patient advocacy groups such as JDRF (formerly the Juvenile Diabetes Research Foundation), the Leona M. and Harry B. Helmsley Charitable Trust, and the American Diabetes Association (ADA). These partners share our goals of preventing, treating, and ultimately curing type 1 diabetes. Through the invaluable support of the Congress and the Administration, through collaborative and coordinated research efforts, through the hard work of our researchers, and through the dedication and generosity of our clinical trial volunteers, we have made important strides toward these goals. I am pleased to be here today to describe recent scientific advances and future opportunities in type 1 diabetes research, including research supported by the recently renewed Special Statutory Funding Program for Type 1 Diabetes Research (Special Diabetes Program). With the Special Program now funded through Fiscal Year 2017, we look forward to taking advantage of the opportunities I'll describe to you today.

Type 1 diabetes primarily strikes children and adolescents, but it can begin at any age. It is a lifelong disease that affects Americans of all ages, including seniors. Type 1 diabetes is an autoimmune disease, in which the body's immune system launches a misguided attack and destroys the insulin-producing beta cells found in clusters called islets within the pancreas. Insulin is a hormone that helps the body regulate glucose levels in the blood. Because their body no longer produces insulin, people with type 1 diabetes—or the parents of young children with the disease—must do the work of the lost beta cells. Thus, the children here today and people of all ages with the disease must closely monitor food intake and physical activity levels, monitor blood glucose levels many times each day and night, and administer insulin through injections or an insulin pump. This is an enormous and constant burden on them and their families, and greatly affects quality of life. Despite their vigilance, they remain susceptible to dangerous and frightening episodes of hypoglycemia (low blood glucose) and to developing long-term complications affecting their eyes, kidneys, nerves, heart, and other organs. Thus, it is imperative to pursue research to identify prevention strategies and improved treatments, while striving for a cure.

IMPROVING THE OUTLOOK FOR PEOPLE WITH TYPE 1 DIABETES

Research has had a dramatic and beneficial impact on the health and quality of life of people with type 1 diabetes. A major contributor to this success is information that has been garnered by the NIDDK's landmark Diabetes Control and Complications Trial (DCCT) and its follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC). DCCT, which began in 1983, compared the effect of intensive blood glucose control versus what was conventional care at that time on the long-term health of people with type 1 diabetes. DCCT

demonstrated that intensive blood glucose control, beginning as soon as possible after diagnosis, prevented or delayed the development of complications of the eyes, kidneys, and nerves. After DCCT ended, the EDIC study—which began in 1994 and is still ongoing—followed the original DCCT participants and demonstrated enduring protective effects of intensive glucose control on eye, kidney, nerve, and heart complications. These results have transformed clinical care for people with type 1 diabetes, with doctors now recommending that people with the disease practice intensive control as early in the course of the disease as safely possible.

However, despite unequivocal evidence of the benefit of intensive glucose control, many people—especially teens—are not able to achieve the intensive control that researchers helped DCCT participants achieve. Even DCCT participants themselves could not maintain this control after the trial ended and they were not receiving diabetes treatment from the research staff. Data from children participating in the SEARCH for Diabetes in Youth study (SEARCH), which is funded by the NIDDK and CDC's Division of Diabetes Translation, show that one out of five teenagers with type 1 diabetes have hemoglobin A1c (HbA1c) levels—a measurement of blood glucose levels over time—above 9.5 percent, which is higher than the recommended level of less than 7.5 percent. Teenagers' mean HbA1c level is also closer to that achieved by the conventional than the intensive control group in DCCT, indicating that achieving the recommended intensive glucose control and attaining its long-term protective effects is particularly challenging in this age group. Thus, new approaches to improve glucose control are urgently needed.

Even though it has been over 30 years since DCCT began, critical insights continue to emerge. Recent results from DCCT/EDIC show that people with type 1 diabetes who intensively control their blood glucose levels early in the disease are likely to live longer than those who do

not. Higher average blood glucose levels and increased protein in the urine—a marker of diabetic kidney disease—were the major risk factors for death.[1] These results emphasize the importance of early and intensive blood glucose control. They also demonstrate the fruits of a long-term research investment—the NIDDK has supported DCCT/EDIC for over 30 years, and translation of these insights into long term outcomes would not have been available without sustained support. Additionally, many current studies supported by the NIDDK, such as development of artificial pancreas technologies and clinical trials of agents to preserve beta cell function, stem from DCCT/EDIC research showing that controlling blood glucose levels is key to maintaining long-term health. Thus, results from DCCT/EDIC have been transformative and far-reaching.

Because type 1 diabetes is a complex disease involving many different organ systems, propelling research progress involves partnerships among scientists with diverse backgrounds and expertise. NIH has also valued its partnerships with academic institutions, with other HHS agencies, and with patient advocacy groups such as JDRF and ADA. These partnerships have allowed us to work together toward common goals and reduce duplication. Our most important research partners are people with or at risk for type 1 diabetes who participate in clinical research studies. We are inspired by their commitment, not only for themselves and their families, but for future generations who may benefit from findings stemming from these research studies.

Toward the goals of preventing, treating, and curing type 1 diabetes and its complications, the NIH vigorously supports research focusing on all stages of the disease: to prevent the autoimmune attack before it starts; to stop the autoimmune attack early in the course of disease to protect remaining beta cells; to improve blood glucose control in people with established disease; to restore beta cell function in people with significant beta cell loss; and to

[1] http://www.ncbi.nlm.nih.gov/pubmed/25562265

prevent, treat, and reverse complications. I am pleased to share with you some of the exciting recent advances in type 1 diabetes research, many of which were reported in just the last year.

UNDERSTANDING THE CAUSES OF TYPE 1 DIABETES TOWARD DISEASE PREVENTION

To achieve our goal of preventing type 1 diabetes, it is imperative to understand the underlying causes of the disease. A person's risk for developing type 1 diabetes involves both genetic and environmental factors, and many genes contribute to disease risk. Thus, research on genetic and environmental contributors is critical toward developing prevention strategies.

In recent years, we have made significant progress in understanding genetic contributors to type 1 diabetes. About a decade ago, only a few culprit genes had been identified. Now, because of the NIDDK's Type 1 Diabetes Genetics Consortium and other groups, we know over 50 genes or genetic regions that contribute to disease risk. This represents about 80 percent of the genetic contributions to disease, making type 1 diabetes one of the few polygenic diseases (in which many genes are involved) for which most of the genetic susceptibility has been identified.

The NIDDK is building on this progress by supporting research to pinpoint the genes within these regions that could be influencing disease. We also support research to understand the function of identified genes to determine how they may be involved in disease, which could point to new targets for prevention or treatment. For example, NIDDK-supported researchers studied one of these genes, called *Clec16a*, whose function was previously unknown. They found that it encodes a protein involved in quality control of mitochondria, the cell's "power plants." Over time, mitochondria may develop problems, requiring recycling and replacement. Using mice, researchers found that reducing the amount of Clec16a protein caused too-frequent

mitochondrial recycling. Moreover, beta cells that lack Clec16a are less able to process energy and produce less insulin in response to rising blood glucose than normal beta cells do. Notably, people with a common mutation of *CLEC16a* that is linked to type 1 diabetes also have lower levels of Clec16a protein and poorer insulin response than people with other variants of the gene, suggesting the protein's role in humans is similar to its role in mice. Further research could determine whether modulating the mitochondrial recycling program helps prevent the disease.[2]

However, genetics does not represent the full picture. The CDC and NIDDK co-led SEARCH for Diabetes in Youth study reported the first national surveillance data on childhood diabetes and found that the prevalence of type 1 diabetes in people under age 20 rose by 21 percent between 2001 and 2009, and that the disease is also an increasing burden in minority youth.[3] Rising rates of type 1 diabetes suggest that there is an unknown factor—or factors—in the environment that interacts with genetic risk to trigger disease onset or protect against it. Identifying these factors—such as infectious agents, dietary factors, or some other agent—is critical to understanding the disease process and to developing prevention strategies. Toward these goals, the NIDDK supports an ambitious, long-term clinical research study called The Environmental Determinants of Diabetes in the Young, or TEDDY. After screening over 425,000 newborns, TEDDY is currently following over 6,000 of them at high genetic risk of type 1 diabetes until they are 15 years old. During that time, researchers and devoted parents regularly collect information about the children's diet, allergies, illnesses, and other environmental exposures. Over 2.7 million biological samples have been collected to date. These samples are a treasure trove of information that is now being analyzed with state-of-the-art genomic, metabolomic, and proteomic technologies to uncover possible environmental triggers

[2] http://www.ncbi.nlm.nih.gov/pubmed/24949970
[3] http://www.ncbi.nlm.nih.gov/pubmed/24794371

and protective factors. The TEDDY study represents an unparalleled resource that can give unique insight into type 1 diabetes and children's health.

TEDDY is also giving us knowledge about other autoimmune diseases, such as celiac disease (gluten intolerance), which shares some genetic risk factors with type 1 diabetes and often occurs in the same individuals. TEDDY recently found that more than one quarter of children with two copies of a high-risk variant in a specific group of genes develop an early sign of celiac disease by age 5—results that could have future implications for celiac disease screening in young children.[4]

TESTING STRATEGIES TO STOP THE AUTOIMMUNE ATTACK AND PRESERVE BETA CELLS

After a person is diagnosed with type 1 diabetes, it is critical to preserve remaining beta cells to maintain some insulin production and achieve good blood glucose control, which research has shown could improve long-term health. NIDDK's Type 1 Diabetes TrialNet and the National Institute of Allergy and Infectious Diseases' (NIAID's) Immune Tolerance Network have both tested agents in people with newly diagnosed type 1 diabetes to determine if they could halt or slow the autoimmune attack and protect remaining beta cells. Some agents have shown promise, including the drug abatacept and the anti-CD3 monoclonal antibody teplizumab. TrialNet is building on these results in newly diagnosed patients and now supports clinical trials testing whether these agents could prevent type 1 diabetes in relatives of people with the disease. The ability to conduct such prevention trials is based on research showing that blood tests can accurately identify relatives of people with type 1 diabetes who are at high or moderate risk of developing the disease within five years.

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[4] http://www.ncbi.nlm.nih.gov/pubmed/24988556

Looking forward, TrialNet is uniquely positioned to test new and emerging prevention approaches that may stem from studies such as TEDDY. Additionally, the ability to screen people for risk of type 1 diabetes with a blood test allows us to identify those who could benefit from a prevention strategy if one emerges; the NIDDK also supports research by small businesses to improve predictive tests to be used in clinical trials, as well as for use in a public health setting once prevention approaches are identified. Thus, the Special Diabetes Program has enabled the creation of a unique research pipeline with goals of discovering strategies to protect beta cells, testing those strategies in people, and identifying those who could benefit from effective strategies on a larger public health scale.

DEVELOPING TECHNOLOGIES TO IMPROVE GLUCOSE CONTROL

The results of the DCCT/EDIC studies that I described earlier show the importance of early and intensive blood glucose control to patients' long-term health. However, type 1 diabetes is an extremely burdensome disease to manage for even the most vigilant of patients, and intensive therapy brings with it the potential for acute episodes of hypoglycemia. Nocturnal hypoglycemia, an imbalance of glucose supply and relative oversupply of insulin during the night, can be a worrisome side effect in children on intensive insulin therapy. Thus, it is difficult for people to achieve recommended levels of blood glucose control using current management approaches. Recent research has shown other alarming effects of elevated blood glucose levels: scientists in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development-led Diabetes Research in Children Network (DirecNet) found that young children with long-term high blood glucose levels are more likely to have slower brain growth. Researchers did not find significant cognitive differences between healthy children and those

with type 1 diabetes, but longer-term studies could shed light on whether differences exist.[5] Thus, research findings continue to emphasize the need to develop improved technologies to help people with type 1 diabetes and their families manage their disease and keep blood glucose levels in a healthy range, while reducing the risk of hypoglycemia.

One extremely promising technology to achieve these goals is an "artificial pancreas," which is a device that fully automates blood glucose sensing and insulin administration. Such a device has three components: a glucose-sensing component that measures blood glucose levels and sends information to a computer; an insulin delivery device; and a computer that calculates the amount of insulin needed and thereby "closes the loop" between glucose sensing and insulin delivery. In other words, this technology is designed to do the work of the pancreas with minimal human input.

The NIDDK is working closely with our partners, including the FDA and JDRF, to develop artificial pancreas technology, and I am pleased to report that there has been significant recent progress. Until recently, artificial pancreas clinical trials took place in hospital settings and used laptop computers to run the technology, restricting the activities of participants. Recent trials have built on the success of the inpatient trials, testing ambulatory devices in real-world settings. For example, NIDDK-supported researchers tested a wearable, automated, bihormonal "bionic" pancreas—one that releases both insulin and its counteracting hormone, glucagon—in adults and adolescents with type 1 diabetes. The adults wore this cell-phone controlled device for five days and nights and were unrestricted in their activities—they ate in restaurants, exercised at gyms, and stayed in a hotel, while being accompanied by study staff for their safety. The adolescents wore the same device at diabetes summer camp, also being closely monitored while participating freely in all camp activities. In both trials, compared to usual care of insulin

[5] http://www.ncbi.nlm.nih.gov/pubmed/25488901

pump therapy, participants had lower mean glucose levels and reduced episodes of hypoglycemia. In fact, the bionic pancreas allowed nearly all participants to achieve recommended levels of blood glucose control.[6]

In another study, researchers tested unsupervised overnight home use of a closed-loop system in adolescents with type 1 diabetes for 21 nights. During the day, participants used standard glucose sensor and pump therapy and did normal activities. At night, they used the closed-loop system, controlling it on their own, with minimal supervision on only the first night. Results showed that closed-loop control at night improved participants' glucose control during the day and night and reduced the number of episodes of nighttime hypoglycemia.[7]

Progress is also being made testing the next generation of low-glucose suspend devices—an important component of artificial pancreas technologies. The first-generation device, approved by the FDA in September 2013, suspends the delivery of insulin when glucose levels reach a preset threshold. The next generation device predicts when this level will be reached and preemptively suspends insulin delivery. A recent NIDDK-supported study tested a predictive device over 42 nights in people with type 1 diabetes in their homes. The results showed that, compared to control nights, nighttime hypoglycemia was reduced by over 70 percent when participants used the predictive device.[8] Nighttime hours are particularly worrisome for people with type 1 diabetes and their parents. Thus, the reductions in nocturnal hypoglycemia seen in recent studies suggest that new devices have the promise to lead to real and immediate benefits.

To build on these and other advances, the NIDDK plans to support advanced clinical trials on artificial pancreas technology that are expected to generate data able to address safety and efficacy requirements by regulatory agencies regarding the clinical testing of these systems.

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[6] http://www.ncbi.nlm.nih.gov/pubmed/24931572
[7] http://www.ncbi.nlm.nih.gov/pubmed/24757227
[8] http://www.ncbi.nlm.nih.gov/pubmed/24804697

We also support research being conducted by small businesses to develop innovative technologies that may improve key components of and thus advance progress toward an artificial pancreas, as well as research conducted by academic medical centers studying physiological and behavioral factors. Partnerships between bioengineers designing these devices, clinicians, and behavioral scientists are key to make artificial pancreas use easier, so that as new technologies become available, patients and families can use them. With continued research, artificial pancreas technology can become a reality for people with type 1 diabetes.

RESTORING BETA CELL FUNCTION

Although the development of artificial pancreas technology represents an important and near-term approach to reduce the burden of managing type 1 diabetes while improving patients' health, it is not a cure. Thus, another major goal of NIH-supported type 1 diabetes research is to identify ways to replace lost beta cells and restore insulin production, which would represent a biological cure for the disease. One way to restore the ability to produce insulin is to replace beta cells through islet transplantation. The current procedure involves purifying islets from a donor pancreas and transplanting them into a person with type 1 diabetes. Research has shown that islet transplantation is highly successful in reversing hypoglycemia unawareness, a devastating complication of type 1 diabetes in which people do not recognize dangerously low blood glucose levels, making everyday tasks, like driving, a danger.

The NIDDK and NIAID co-led Clinical Islet Transplantation Consortium (CITC) has been conducting clinical and mechanistic studies in islet transplantation, with or without accompanying kidney transplantation, to make islet transplantation safer and more effective. The islet alone pivotal, Phase III islet transplantation trial has been completed and the islet after

kidney phase III trial has reached its primary endpoint. The Collaborative Islet Transplant Registry (CITR) has shown that both efficacy and safety outcome measures have improved in the 2007-2010 period compared to those from 1999-2006. Both the CITC and CITR's results showed that islet transplantation continues to show improved long-term benefits including insulin independence, improved indications of normal or near-normal blood glucose levels over time, and sustained marked decrease in severe hypoglycemic episodes. I'm pleased to report that the CITC will be submitting a report to the FDA based on these exciting results, toward licensing a pancreatic islet product for transplantation.

One barrier to islet transplantation is the scarcity of donor islets for transplant. A major advance from researchers in the NIDDK's Beta Cell Biology Consortium (BCBC) could help overcome that barrier. The scientists discovered a method to produce, or differentiate, beta cells in the laboratory. Previous attempts resulted in cells that produce insulin, but that do not respond to changing glucose levels. Recently, scientists developed a multistep differentiation process in which they coaxed large numbers of human stem cells into a state that closely resembles beta cells. Importantly, this process can use induced pluripotent stem cells that can be made from adult skin cells obtained from patients with type 1 diabetes. Importantly, these new cells respond to fluctuating glucose levels by increasing or decreasing secretion of insulin, as appropriate. This dramatically improved process for making large amounts of beta cells is a promising step toward developing donor-derived stem cell therapies to replace beta cells lost in type 1 diabetes.[9]

Another barrier to islet transplantation is the need for transplant recipients to take lifelong immunosuppressive medicines, which often have serious side effects, to prevent their body from rejecting the transplanted islets. One approach to protect the transplanted islets is to encapsulate them in a material that would protect them from an immune attack but still allow them to

[9] http://www.ncbi.nlm.nih.gov/pubmed/25303535

function. Thus, the ability to make large amounts of beta cells for transplantation which I just described makes developing new approaches to immunomodulation and encapsulation even more urgent.

Another group of BCBC researchers discovered that delta cells in the pancreas, which produce a hormone called somatostatin, could be reprogrammed into beta cells, representing another potential way to restore lost beta cells in type 1 diabetes.[10] Building on these and other ground-breaking successes of the BCBC, the NIDDK recently transitioned to a new effort, the Human Islet Research Network (HIRN). HIRN is supporting collaborative, translational beta cell research that can further our understanding of the human disease process and lead to innovative treatment strategies.

PREVENTING, TREATING, AND REVERSING DIABETIC COMPLICATIONS

Chronic elevation of blood glucose levels slowly damages organs and can result in life-threatening diabetes complications. Until prevention or cure of type 1 diabetes is possible, it is critical to pursue research toward preventing, treating, and reversing diabetes complications.

Diabetic eye disease is a debilitating complication of type 1 diabetes and is a cause of vision loss in working age adults. This vision loss is often due to diabetic macular edema (DME), a condition in which fluid leaks from blood vessels and causes swelling and damage to the central retina.

The development of intravitreal anti-vascular endothelial growth factor (VEGF), drug and biologic products has more recently led to improved treatment. Previously, patients might have had to resort to laser treatment procedures in an attempt to preserve some measure of vision. The National Eye Institute-led Diabetic Retinopathy Clinical Research Network

[10] http://www.ncbi.nlm.nih.gov/pubmed/25141178

(DRCR.net) showed that the anti-VEGF drug, ranibizumab, often in conjunction with laser treatment, is a more effective treatment for DME than laser treatment alone.[11] Ranibizumab blocks the function of VEGF, a protein that promotes blood vessel growth. Clinical practice has now changed dramatically—anti-VEGF therapy, where the drug is injected directly into the eye's vitreous, is one of the standard treatments for people with vision loss from diabetic macular edema.

Building on this result, another recent DRCR.net comparative effectiveness trial compared safety and efficacy of three anti-VEGF drugs commonly used to treat DME: Eylea® (aflibercept), Avastin® (bevacizumab), and Lucentis® (ranibizumab). The trial showed that, in people with DME and mild visual impairment, any of the three drugs, on average, improved visual acuity and that the drugs were equally effective. Researchers found no major differences in the safety of the three drugs.[12] The costs of these drugs differ widely: based on Medicare allowable charges, the per-injection costs of each drug at the doses used in this study were about $1,960 for Eylea®, about $1,200 for Lucentis®, and about $70 for Avastin®. Many patients required 10-12 injections. Thus, these results offer important data for informing clinical decisions for DME, while having significant cost implications. The study reinforced the previously reported finding that anti-VEGF therapy actually improves vision, as compared to laser treatment that is effective in preventing blindness but does not improve and often somewhat worsens vision in the short term. Improving vision with anti-VEGF therapy can make the difference between people being able to drive or not, which greatly affects quality of life.

Because the study compared drugs from different companies and the results of the recent DRCR.net trial had large cost implications, the Government was in a unique position to support

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[11] http://www.ncbi.nlm.nih.gov/pubmed/20427088
[12] http://www.ncbi.nlm.nih.gov/pubmed/25692915

it, as it would not have been conducted by the private sector. Another new clinical trial that would also not be supported by the private sector is the NIDDK's Preventing Early Renal Loss in Diabetes (PERL). PERL is testing whether the inexpensive, generic medication allopurinol, currently used for the treatment of gout, could preserve kidney function in people with type 1 diabetes who are at high risk of kidney disease. If this inexpensive drug proves effective, it has the potential to be the first new therapy to reduce risk for diabetic kidney disease in over two decades. Diabetic kidney disease is a major risk factor for cardiovascular disease (CVD) in people with type 1 diabetes, underscoring the importance of studying new strategies to prevent kidney disease.

Although blindness, amputation, and kidney disease are what people with the disease fear most, CVD is the leading cause of death. It is important to determine when to start prevention efforts in people with type 1 diabetes to reduce their risk of CVD and lengthen their life. The SEARCH for Diabetes in Youth Study is shedding light on this by studying the natural history of CVD and examining CVD risk factors in youth with type 1 diabetes. SEARCH researchers found that youth with the disease, particularly those with suboptimal blood glucose control, had reduced overall heart rate variability compared to youth without type 1 diabetes.[13] Reduced heart rate variability is a sign of cardiac autonomic neuropathy, a complication of diabetes that increases the risk of mortality. SEARCH also found that youth with type 1 diabetes had increased carotid intima-media thickness (indicative of the presence of atherosclerosis) compared to youth without type 1 diabetes, and that this association may be attributable to poor blood glucose control.[14] These data indicate that this population shows signs of CVD risk early in the course of the disease. To inform future research directions related to CVD in type 1 diabetes, the

[13] http://www.ncbi.nlm.nih.gov/pubmed/22961570
[14] http://www.ncbi.nlm.nih.gov/pubmed/23564920

NIDDK and the National Heart, Lung, and Blood Institute co-sponsored a workshop in October 2014, at which experts discussed research questions that are important to pursue.

EMERGING OPPORTUNITIES IN TYPE 1 DIABETES RESEARCH

Building on the recent research advances I have described, the NIH is supporting new and emerging research in type 1 diabetes and its complications. For example, the NIDDK supports behavioral research to identify ways to improve adherence to the difficult treatment regimens required to manage type 1 diabetes. Data from children participating in the SEARCH study indicate that most teenagers do not meet the goals for intensive glucose control recommended by the ADA. Average glucose control is closer to that of the conventional, rather than the intensive treatment group of the DCCT. This information is worrisome because we know that the intensive control group had a dramatic reduction in long-term complications compared to the conventional control group. Thus, it is imperative that research identify ways to help people manage their disease to improve long-term outcomes. Toward this end, the NIDDK is supporting behavioral research studying different age groups—from young children, to adolescents, to adults—because each age group faces unique challenges when it comes to managing the disease.

Since currently clinical research is often costly and time-consuming, the NIDDK is focusing on approaches to streamline and accelerate type 1 diabetes research and make it possible to get answers more quickly. Thus, lack of biomarkers that predict disease progression and response to therapy is a major obstacle to the development and testing of new therapeutic approaches. To overcome this obstacle, NIDDK is fostering creative new research to develop biomarkers for complications and for progressive loss of beta cells.

The NIDDK also remains committed to providing access to research resources that will increase our understanding of type 1 diabetes and its complications. For example, we support distribution of human islets from organ donors and ancillary studies of type 1 diabetes clinical studies and make samples and data from completed studies available to the research community through the NIDDK Central Repositories. These types of approaches reduce duplication, make resources broadly available, and maximize the return on our past scientific research investments. The NIDDK is also supporting training and career development programs to recruit and retain scientists with different areas of expertise whose talents will enhance the type 1 diabetes research field.

Looking forward, the NIDDK support of type 1 diabetes research will continue to be guided by the 2011 Diabetes Research Strategic Plan, which the Institute spearheaded with broad external input. The statutory Diabetes Mellitus Interagency Coordinating Committee (DMICC), chaired by NIDDK, also serves a key function by coordinating activities and reducing duplication across several HHS and non-HHS government entities. Earlier this year, under the auspices of the DMICC, we solicited input from scientific and lay experts about future directions that could be supported with the recent extension of the Special Diabetes Program through FY 2017. Guided by that input, strategic plans, and input that the NIH receives at venues such as scientific conferences and workshops, the NIH is now identifying the most compelling areas of current research opportunity to pursue with the new funds and will ensure that the Program continues its exceptional track record of supporting cutting-edge type 1 diabetes research.

CONCLUDING REMARKS

I appreciate this opportunity to share with you these few recent advances, ongoing efforts, and emerging opportunities in type 1 diabetes research. We are grateful for the continued support of the Congress and the Administration that has allowed the NIH to vigorously support research to combat type 1 diabetes and its complications. We look forward to continuing our strong partnerships with patient advocacy groups, research institutions, and our sister Federal Agencies. We also thank all of the clinical study volunteers, without whom the clinical research I described today would not be possible. Working with all of these partners, the NIH remains steadfast in our goals of preventing, treating, and ultimately curing type 1 diabetes.

Thank you, Chairman Collins, Senator McCaskill, and Members of the Committee for your attention. I will be pleased to answer any questions you may have.

Griffin P. Rodgers, M.D., M.A.C.P.

National Institute of Diabetes and Digestive and Kidney Diseases

Dr. Griffin P. Rodgers was named Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)--one of the National Institutes of Health (NIH)--on April 1, 2007. He had served as NIDDK's Acting Director since March 2006 and had been the Institute's Deputy Director since January 2001. As the Director of NIDDK, Dr. Rodgers provides scientific leadership and manages a staff of over 600 employees and a budget of $1.9 billion.

Dr. Rodgers received his undergraduate, graduate, and medical degrees from Brown University in Providence, R.I. He performed his residency and chief residency in internal medicine at Barnes Hospital and the Washington University School of Medicine in St. Louis. His fellowship training in hematology was in a joint program of the NIH with George Washington University and the Washington Veterans Administration Medical Center. In addition to his medical and research training, he earned an MBA, with a focus on the business of medicine/science, from Johns Hopkins University in 2005.

As a research investigator, Dr. Rodgers is widely recognized for his contributions to the development of the first effective — and now FDA approved — therapy for sickle cell anemia. He was a principal investigator in clinical trials to develop therapy for patients with sickle cell disease and also performed basic research that focused on understanding the molecular basis of how certain drugs induce gamma-globin gene expression. Recently, he and his collaborators have reported on a modified blood stem-cell transplant regimen that is highly effective in reversing sickle cell disease in adults and is associated with relatively low toxicity. He has been honored for his research with numerous awards including the 1998 Richard and Hinda Rosenthal

Foundation Award, the 2000 Arthur S. Flemming Award, the Legacy of Leadership Award in 2002, and a Mastership from the American College of Physicians in 2005.

Dr. Rodgers has been an invited professor at medical schools and hospitals both nationally and internationally. He has been honored with many named lectureships at American medical centers and has published over 200 original research articles, reviews, and book chapters, has edited four books and monographs, and holds three patents.

Dr. Rodgers is a member of the American Society of Hematology, the American Society of Clinical Investigation, the Association of American Physicians, the American Academy of Arts and Sciences, and the Institute of Medicine of the National Academy of Science, among others. He served as Governor to the American College of Physicians and as Chair of the Hematology Subspecialty Board and a member of the American Board of Internal Medicine Board of Directors.

Statement of Habib Zaghouani

J. Lavenia Edwards Endowed Chair in Pediatrics

Professor, Department of Molecular Microbiology and Immunology, Department of Child Health, and Department of Neurology.

The University of Missouri School of Medicine, Columbia, MO

Before the

Special Committee on Aging

United States Senate

Washington, DC

July 15, 2015

Chairman Collins, Ranking Member McCaskill, and members of the Special Committee, I am delighted to be here and thank you for the invitation to appear before you today. My name is Habib Zaghouani. I am a professor and the J. Lavenia Edwards Endowed Chair in Pediatrics at the University of Missouri School of Medicine. Let me state that the views expressed here today are my own and are not given on behalf of the University of Missouri or its Curators.

My research focuses on determining why and how the immune system reacts against our own tissues and organs to cause autoimmune diseases such as type 1 diabetes (T1D) and multiple sclerosis (MS). Also, my laboratory is devoted to developing approaches to halt such adverse reactions and cure these diseases. Other research in my laboratory is focused on studying immunity in newborns and how the function of neonatal immunity impacts the development of pediatric vaccines. My testimony today focuses mostly on a new approach we recently developed that cures T1D in mice and on the perspectives for translation of this approach to humans.

The first part of the testimony describes our clinical trial, which successfully cured T1D in mice. The second part highlights the challenges the field of T1D faces. The third part defines the opportunities for translational research, and the last part highlights the importance of NIH funding.

Introduction

T1D is a chronic condition that usually occurs in children and young adults when cells of the immune system attack the insulin producing beta (β)-cells of the pancreatic islets. Researchers have always thought that halting the immune attack of β-cells would help overcome the disease. This proved feasible for prevention of T1D in animal models, however curing the disease in humans has proven difficult to achieve.

Combination therapy successfully cured T1D in mice

In recent years my laboratory developed a protein based drug referred to as Ig-GAD2, which prevented progression of disease in pre-diabetic mice (1). We learned from this initial trial that Ig-GAD2 was able to rid the pancreatic islets of pathogenic immune cells. Additionally, we discovered that new insulin-producing β-cells were formed. This is crucial information indicating that the pancreas can generate new insulin-producing β-cells.

In humans, T1D is diagnosed when the disease is already established. Thus, in order to cure T1D, the drug has to be effective after diagnosis of the disease. The logic then was to carry out a trial with Ig-GAD2 when the mice have established or overt T1D in the hope that formation of new insulin-producing β-cells will occur and support recovery from the disease. The trial with Ig-GAD2 in overtly diabetic mice was performed but recovery from T1D was not achieved (2). This was intriguing, as pathogenic immune cells were no longer found in the pancreas (2).

The conclusion that was drawn from this failed trial was that new insulin-producing β-cells could not form perhaps because there was not a sufficient number of residual β-cells or stem cell precursors to reproduce β-cells from.

The logic, then, was to infuse the sick mice with bone marrow cells from healthy donors during treatment with Ig-GAD2 in the hope of enriching the recipients with stem cell precursors for β-cells. A clinical trial was then performed in which the sick mice were given Ig-GAD2 and bone marrow stem cells from healthy donors. The results were successful, as the sick mice were cured from T1D (2). After this trial, it was discovered that the bone marrow cells were giving rise to endothelial cells, the cells that form the walls of blood vessels. This conclusion was confirmed by the observation that infusion of the sick mice with endothelial stem cell precursors from adult healthy donor mice during treatment with Ig-GAD2 can substitute for infusion with bone marrow cells and repair islets' vascular networks. This facilitates the formation of new insulin-producing β-cells and thus recovery from overt T1D.

The knowledge gained from these trials suggests that the immune attack in the pancreatic islets destroys the insulin-producing β-cells and causes collateral damage to the blood vessels forming the islets' vascular network. The lack of insulin causes loss of function in endothelial cells and their precursors so that the mice cannot repair their islets' vascular network.

In conclusion, to cure T1D, the therapeutic strategy has to be able to modulate the immune attack and repair the islets' vascular network in order for insulin-producing β-cells to reproduce and thrive.

Exhibits A, B and C below represent schematic illustrations of the Ig-GAD2 and stem cells combination therapy.

Exhibit A. Shows a sick mouse that received adult endothelial stem cells from a healthy donor and the drug Ig-GAD2. The mouse recovered from disease and regained a normal lifestyle. The reason for the recovery is that the mouse, which had very little insulin (brown spot) before treatment, regained production of normal amounts of insulin.

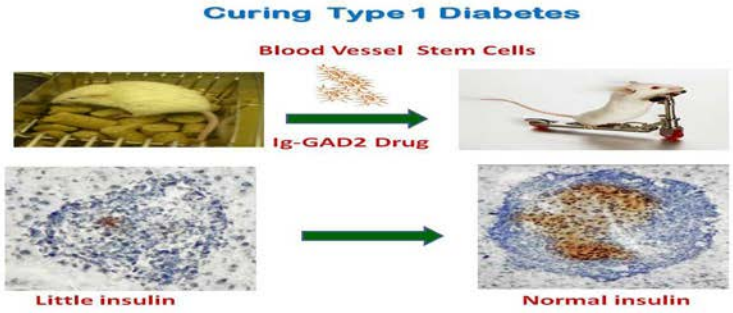


Exhibit B. Activated pathogenic immune system cells (bugs) destroy insulin-producing β-cells (black flowers) and cause collateral damage to tiny blood vessels in pancreatic islets (water pipe).

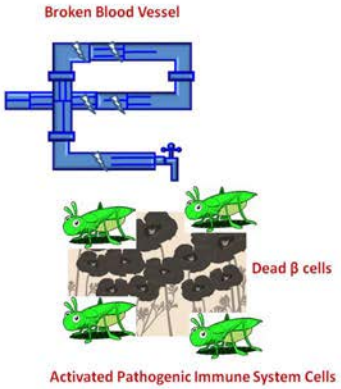
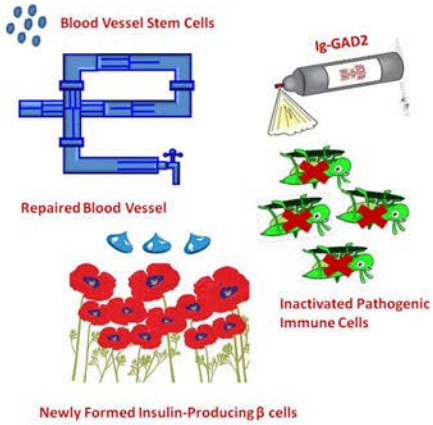


Exhibit C. Ig-GAD2 (spray can) inactivates pathogenic immune system cells (dead bugs), and the blood vessel stem cells repair the tiny blood vessels in pancreatic islets (repaired water pipe), leading to formation of new insulin-producing β-cells.



References

1. Jain et al., 2008. Journal of Experimental Medicine. 205:207-218.

2. Wan et al., 2013. Diabetes. 62:2879-2889.

Challenges the field of T1D research faces

In my opinion, meeting the challenges listed below is likely to foster progress toward a cure for T1D.

- The disease involves the endocrine system, the immune system, and now the vascular system. Collaborative efforts among researchers in the fields of endocrinology, immunology, and vascular biology will provide the multidisciplinary knowledge this disease demand and ensure better progress toward finding a cure for T1D.

- Development of humanized T1D animal (preferably mouse) models will certainly facilitate research that cannot be performed in humans and foster progress toward finding a cure for T1D.

- Focusing research on stimulation of beta cell proliferation and differentiation of their stem cell precursors is likely to foster progress toward developing a cure for T1D.

- Fostering the concept that more than one drug is needed to cure T1D will likely focus the research in a bidirectional path and ensure better progress toward finding a cure for T1D.

- Encouraging young and fresh minds to pursue careers in research in T1D research will ensure continued progress toward finding a cure for T1D and toward improving and adapting futures cures.

Challenges to translational T1D research

Research findings so far suggest that islet transplantation, which is associated with great limitations, may not be the major avenue for the cure of T1D. In order to achieve progress toward the cure with the alternative approach that I put forward, however, we must meet certain challenges.

- Fostering trials for combinatorial drugs.

- Fostering trials involving drugs and stem cells.

- Founding of specialized centers for large-scale production of drugs and for toxicology studies.

- Engaging the pharmaceutical industry in progressive clinical trial design and consideration of combinatorial therapeutics.

NIH funding and investment in T1D research and drug development

In my opinion, the challenges facing T1D fundamental and translational research will only be met by boosting availability of funds, optimizing access to these resources, and devising strategic programs for fund allocation.

- Enhancing the budget for T1D research and clinical translation is the principal requirement for progress toward a cure for T1D.

- Developing cross institute funding programs to meet the multidisciplinary requirement for progress in T1D research and translation. Joint programs by the NIAID, NIDDK and NHLBI will meet the need for expertise in immunology, endocrinology and vascular biology.

- Developing collaboration and developing a targeted funding program with foundations and charitable organizations is key for progress toward a cure for T1D.

- Developing programs that support collaboration with the pharmaceutical industry is likely to foster progress in translation and in the development of a cure for T1D.

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