

Preventing, Delaying and Reversing the Progression of Type I Diabetes

The Division of Pediatric Endocrinology and Diabetes is committed to providing patients the best medical care possible.

This commitment goes hand in hand with their dedication to discovering and pioneering the latest treatment methods through ongoing clinical research.

Their research areas include a vast range of topics associated with endocrinology, including diabetes, growth and growth hormone.

At Children's Mercy Kansas City, approximately 200 children, adolescents and young adults are diagnosed with type I diabetes each year.

Patient volume, combined with a diverse patient population, the broad geographic area covered, and a full-service program, means Children's Mercy is well positioned to conduct research on diabetes prevention, and serve as an Affiliate of the National Institutes of Health's TrialNet.

The work TrialNet and Children's Mercy do today may help prevent type I diabetes tomorrow or at least make it easier to control by preserving beta cell mass.

Mark Clements, MD is here to discuss how the goal is to identify individuals who have the genetic predisposition, but who haven't develop the autoimmunity and have not experienced destruction of beta cells in order to preserve their beta cell mass and prevent the development of type I diabetes in these individuals.



Featured Speaker:

Mark Clements, MD, PhD

Dr. Clements specializes in glucose variability, diabetes care technology and chronic complications in diabetes. Dr. Clements is an AAP fellow and received his medical degree and PhD in Developmental Neuroscience from the Washington University Medical School in St. Louis, Mo. He completed his Pediatric Endocrinology fellowship at Children's Mercy Kansas City. Dr. Clements brings a passion for data analytics and insights to his pediatric endocrinology practice at Children's Mercy and is known as a passionate innovator for the children he treats.

[Learn more about Dr. Clements](#)

[https://www.childrensmercy.org/Clinics and Services/Clinics and Departments doc=4500](https://www.childrensmercy.org/Clinics_and_Services/Clinics_and_Departments/doc=4500)

Transcription:

Dr. Michael Smith (Host): Welcome to *Transformational Pediatrics*. I'm Dr. Michael Smith and our topic

is "Preventing, Delaying and Reversing the Progression of Type 1 Diabetes." My guest is Dr. Mark Clements. Dr. Clements is an Endocrinologist and Associate Professor of Pediatrics at the University Of Missouri Kansas City School of Medicine. Dr. Clements specializes in glucose variability, diabetes care technology and chronic complications in diabetes. Dr. Clements, welcome to the show.

Dr. Mark Clements (Guest): Thank you. Thank you very much. Glad to be here.

Dr. Smith: Thank you for coming on. At Children's Mercy, approximately how many kids, adolescents and young adults are diagnosed with Type 1 diabetes each year?

Dr. Clements: We diagnose approximately 220-260 children in adolescents per year with Type 1 diabetes in the Kansas City area and across the states of Kansas and Missouri and our Children's Mercy Wichita site, which is also part of our diabetes center, diagnoses approximately an additional 50 per year at this time. So, we are diagnosing about 300-330 cases a year.

Dr. Smith: Wow. Okay. So, since you are seeing so many cases, Children's Mercy sounds like a great place to conduct diabetes research. What are some of the other things that Children's Mercy offers that makes it such a great place for research?

Dr. Clements: Sure. There are several characteristics of Children's Mercy as an institution and of our diabetes center that make this a fantastic place in which to conduct diabetes research. Number one is that we have an incredibly engaged and large population of kids and families who have Type 1 diabetes. We see approximately 2,000 children with Type 1 diabetes in our center right now, an additional 300 children and adolescents with Type 2 diabetes. We have a very large department with 19 physicians, a number of nurse practitioners, about 16 diabetes educators now and it really allows us to think about how we deliver care and to think about how to innovate in the way we deliver care. So, that's number one. Number two is that we're very interested in studying health outcomes in Type 1 diabetes. Children's Mercy actually has approximately 27 years of experience with electronic health records in one form or another. That has really been beneficial to our research to understand how risks for the complications for diabetes have changed over time. We can actually follow a patient from diagnosis forward until they graduate our clinic into adult care or until they develop any one of a number of complications of the disease. So, that's number two. Number three is really that Children's Mercy has an incredibly strong clinical pharmacology program. It has an incredibly strong clinical investigator program. I've been through FDA investigator training. I've been through training as a clinical trialist through the Association of Clinical Research Professionals and a number of my colleagues in the Diabetes Center have as well. So, I think that positions us well to do what I consider to be research of a meeting a really high standard.

Dr. Smith: Tell us about TrialNet and I think the full URL is diabetestrialnet.org and what you've accomplished with them.

Dr. Clements: Absolutely. So, under the leadership of Dr. Wayne Moore at our site, Children's Mercy has been a participant in TrialNet for a number of years. We have been what's been called an affiliate site of the network so there are dozens and dozens of sites across the country. I don't recall whether it has surpassed 200 but there are quite a few sites around the country and there are small contingents of sites who are funded by the National Institutes of Health to lead the network nationally. Currently, I

believe there are approximately 18 sites and I'm pleased to report that in June of this year Children's Mercy became one of the leading sites in the nation. So, we are now at the leadership table for TrialNet whose mission is really to identify family members of patients with Type 1 diabetes who are themselves at risk for getting the disease. Then, once we identify those family members who have a positive risk for getting Type 1 diabetes, to invite them to participate in clinical trials designed to prevent, delay or alter the course of the disease.

Dr. Smith: So, I actually went on diabetestrialnet.org. I just pulled it up and there's a nice spot for study participants where you can join a trial but then there's a spot for healthcare professionals where you can refer a patient, learn about different trials that are going on. Let's move the conversation over to something that, as a general physician, Dr. Clements, when I read this or I see this, it makes me ask the question, "How?" and that is the prevention. When I think of Type 1 diabetes, I am thinking insulin dependent diabetes. I'm thinking genetic factors. I know there are some viral theories out there but how do we actually prevent Type 1?

Dr. Clements: Sure. So, as you alluded to, Type 1 diabetes is a problem of the immune system. The immune system goes on the attack against the cells in the pancreas that make insulin which, of course, is needed to control blood glucose levels. Insulin helps move glucose from the blood into the cells to use as energy. Without insulin, blood glucose levels rise very high and that becomes a problem because it can affect the health of your heart and blood vessels and a number of your organs. The prevention strategy for Type 1 diabetes in TrialNet is simple. Let's take the best information we have available from a number of autoimmune diseases. Again, those are the diseases in which the immune system goes on the attack against some organ or tissue in the body; and let's find the immune modulating medication. So, medications that modify the way the immune system is functioning and let's give them to people who don't have diabetes yet who are healthy but who we know, based on biomarkers that we can measure in the blood, are at high risk for developing the disease in the next five years. So, a number of those immune modulating drugs have been used in diseases like rheumatoid arthritis, psoriasis, inflammatory bowel disease and have shown success. So, it makes sense to think that you might be able to transfer that to other autoimmune diseases like Type 1 diabetes.

Dr. Smith: So, it's interesting when you talk about immune modulators and you think about, for instance, we have some of the biologics out there and many of these are inhibiting TNF alpha, for instance. How is an immune modulator different than that though? Obviously, it's not just pure inhibition of TNF alpha. There must be some other balancing act going on with some of these drugs.

Dr. Clements: Right.

Dr. Smith: How does that actually work?

Dr. Clements: There are multiple arms to the immune system so it can accomplish its function and the arm or activity of the immune system that's really essential to the prevention of Type 1 diabetes is the interaction between the antigen presenting cell or the dendritic cell and the T cell. So, when antigen presenting cells present what we call "antigens," which are usually bits of protein or molecules, from the pancreas to a T cell, then that T cell, if it is of the right flavor, can then react. Once it reacts, it can activate and sort of build a small army of T cells that can then cause tissue damage and inflammation in the area of the pancreas that's producing insulin. What is central to the prevention of Type 1 diabetes is

disrupting the signaling or the interaction between these antigen presenting cells and these T cells.

Dr. Smith: Moving the conversation over now to reversing the progressing of, so let's take it a step further. So, now you have an established diagnosis of Type 1 diabetes. What's the latest research in slowing or even, as you mentioned in the title, reversing the progression of Type 1 diabetes?

Dr. Clements: Right. I would say where we are today, we have identified some therapies that are really good at slowing the progression of Type 1 diabetes and even delaying the onset of Type 1 diabetes. We're not so good yet at reversing the progression of Type 1 diabetes. It's something that's of great interest to us. We do know that when patients are diagnosed with Type 1 diabetes and are placed on insulin therapy, that some of the cells in the pancreas have the ability to recover function. So, we call that period of time after diagnosis when they're still able to make some of their own insulin, the honeymoon phase. I'm not really sure why we've chosen the term the "honeymoon phase" but we do know that the autoimmunity continues even during that period of time and the inflammation causes the patient to continue to lose cells that make insulin. Anything that we can do to basically preserve those cells which we call "residual beta cells", is both protective to the patient because it's been shown to delay the onset of complications of the disease many years down the road and also to decrease the burden on the patient. It decreases that chances that they'll be exposed to extreme high blood sugars or extreme low blood sugars if they have some functioning beta cells in the pancreas.

Dr. Smith: If we've destroyed the beta cells in the pancreas, where does something like stem cell therapy play a role?

Dr. Clements: I think that there are a number of companies funded by the JDRF and the National Institutes of Health who are looking at various sources of adult stem cells to treat Type 1 diabetes and potentially to replace the function of the pancreas. There is also some really exciting work happening at Harvard and elsewhere in trying to identify stem cells in the pancreas that can be transformed into insulin producing and glucose responsive cells. So, that research is all happening at a very basic level right now. Some of the work that's being done using adult stem cells as a source of insulin in early clinical trials is ongoing. So, we're really waiting for answers from those at this time.

Dr. Smith: Dr. Clements, we obviously could talk for a long time on everything that's going on in the work that you're doing. I want to thank you everything you're doing and working with Children's Mercy and thanks for coming on the show. You're listening to *Transformational Pediatrics* with Children's Mercy Kansas City. For more information you can go to childrensmercy.org. That's childrensmercy.org. I'm Dr. Michael Smith. Have a great day.

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