

# Targeting the Toughest Diseases

## Episode 4 – Targeting Type 1 Diabetes

**Madison:** *I'm so goal oriented. I'm always just charging ahead. Like we're going to get it done by any means possible.*

**Focused and fearless: That's the best way to describe Madison Carter.**

Those qualities have helped Madison break a lot of important stories as an award-winning investigative reporter in Atlanta, Georgia.

She's investigated white nationalists, political corruption, and the parole system. Those are stories that take a lot of guts to cover.

And Madison has done it all without hesitation.

**Madison:** *People will tell you, I go for everything. I say everything that needs to be said, like I have no fear. Like I don't have a lot to lose.*

That fearlessness comes from a dark place.

**Madison:** *It's because of my diabetes. I'm like I could die at any second.*

Hi. I'm Jordan Gass-Pooré, a member of the University of Southern California's Center for Health Journalism.

This is *Targeting the Toughest Diseases*, produced by Bloomberg Media Studios and Vertex Pharmaceuticals.

In this series, we look at some of humanity's most challenging diseases, and how Vertex – a Boston-based biotech company – is using innovative tools, methods, and a unique philosophy to search for treatments and cures.

Today, we're targeting type 1 diabetes: A chronic disease that affects more than 8 million people around the world, a number that's expected to increase rapidly. In the U.S. alone, approximately 1.4 million people, including nearly 170,000 under the age of 20, have type 1 diabetes.

**Madison:** *I don't think I ever had the opportunity to be a kid.*

Since she was three years old, Madison's life has included a highly controlled diet, constantly measuring her blood sugar levels and insulin shots.

**Madison:** *And it's something that I have spent the past couple of years in therapy really working through because it's not fair. It's not just that I feel like it's not fair. It is not.*

**When she was just a toddler, Madison started showing signs that something was off.**

**Madison:** *I was getting really, really skinny, which is weird because the people in my family are not very skinny.*

**She was thin, feeling thirsty all the time, and constantly tired.**

**Madison:** *I would be falling asleep in random places. My mom found me asleep next to my oatmeal one morning. Found me asleep on the toilet one day. You know I'm a toddler, I'm three years old, so that was really strange, especially when I'm supposed to be running around. And one night my mom was putting me to bed, and she said that she could count every single one of my ribs. And in that moment, she picked me up, put me in the back of the car, gave me a Sprite, which later on we would find out was a very bad idea, and took me to Children's Hospital.*

**When they got there – the medical team found Madison's blood sugar level was dangerously elevated. Nearly 200 percent higher than it should have been.**

**Madison:** *They told my mom I should be dead. Had she had put me to bed that night I would have been dead. And that's how I was diagnosed.*

**Madison:** *I think my parents had about a year of giving me injections until I told them to never touch me with the needle again.*

**By the time she was five – Madison was doing all her injections herself.**

**Madison:** *It was harder for me to see my mom inflict pain upon me than it was for me to just do it myself. Like seeing her face, that upset me. It wasn't even that it hurt because it hurt sometimes when I would do it myself, but I just didn't want her to have that responsibility of feeling like she was hurting me.*

**Our pancreas produces insulin: A special hormone that the body needs to process glucose – a key source of energy.**

**For people who have type 1 diabetes – those insulin-producing cells in the pancreas are destroyed. That means the glucose stays in the blood, resulting in high blood sugar levels, also known as hyperglycemia.**

**The symptoms include increased thirst, hunger, frequent urination, and weight loss. If left untreated, this can lead to excessively high glucose levels and eventually could even be fatal.**

People with type 1 diabetes rely on giving themselves insulin every single day to survive and have to be super vigilant:

- ‘Not enough’ insulin can lead to *high* blood glucose levels – and over time, complications like kidney disease, vision loss, nerve damage, heart attacks, and strokes.
- ‘Too much’ insulin can result in *low* blood sugar. If left unaddressed, blood glucose levels can fall dangerously low and can lead to severe hypoglycemia, resulting in seizures, loss of consciousness – or even death.

**Madison:** *I remember it was President's Day weekend. She was playing volleyball. So, she had this tournament.*

**Madison's younger sister Cameron also had type 1 diabetes. She was 14.**

**Madison:** *And I got pulled out of class. They said, “Hey, um, you know, we're going to take you to the hospital. Your sister had a seizure.”*

**Madison rushed to the hospital.**

**Madison:** *My parents met us at the door, and they said, you know, she didn't make it. She was dead when they took her in the ambulance.*

**Her sister’s sudden death from diabetes devastated Madison.**

**Madison:** *I would call her “the good diabetic.” Like she really did everything she needed to do. And I was kind of in that phase of doing just enough to stay alive. And she died and that upset me. And I was like, well, what is the point of doing everything you're supposed to do like my sister Cameron did, if it's still not enough?*

**Madison lost all motivation to manage her own health.**

**Madison:** *For a year after she died, I told people that I took a year off of being diabetic. The responsibilities, the checking your blood sugar, the making sure you're taking your injections or changing your pump. I refused to do, and my mom stepped in and did it for me.*

**After a year, Madison resumed doing her own care. It’s a daily grind but it keeps her alive.**

**Aaron Kowalski:** *It's a very, very difficult disease to manage.*

**The constant managing of type 1 diabetes is something Dr. Aaron Kowalski knows intimately.**

**Aaron Kowalski:** *When my brother was diagnosed in the late seventies, you were pretty much told that you had about 20 years before complications would form. Your life would be shortened*

*pretty significantly. You had a very high likelihood of going blind. You had these dosing of insulin issues that could cause severe hypoglycemia and potentially death on a daily basis.*

**A few years after his brother was diagnosed, Kowalski discovered he had type 1 diabetes as well.**

**Today he's the CEO of JDRF – the world's largest nonprofit funder of type 1 diabetes research.**

***Aaron Kowalski:** We are just celebrating the hundred-year anniversary of the discovery of insulin, which won multiple Nobel prizes and saved millions of lives. Before the discovery of insulin in 1921, every single type 1 person died.*

**That's every single person, for centuries.**

***Aaron Kowalski:** The disease actually was described in ancient Egyptian and Greek writings. And this observation that people made was the fact that people with this syndrome wasted away.*

**The term 'diabetes mellitus' was coined because it roughly translates to 'sweet siphon.'**

***Aaron Kowalski:** The sugar would just pass through people. The food would just pass through them. And the sweetness was observed when ants would be attracted to the urine of these people.*

**Modern times have brought us modern discoveries. Apart from the breakthrough of insulin, there was a landmark study in 1983 called the DCCT trial, which stands for the Diabetes Control and Complications Trial. It showed the connection between high blood sugar and complications.**

**It also showed that with more intensive therapy, people with type 1 diabetes could prevent long-term eye, kidney, and nerve complications.**

**And more recently there's been huge improvements in glucose monitoring. This includes smartphone apps with sensors which can monitor blood sugar levels continually.**

***Aaron Kowalski:** Not surprisingly, if you have more information, you do better. I certainly think that's been one of the biggest changes in my life and my brother's life.*

**Despite all those improvements in managing type 1 diabetes, there's still no cure – and people with the disease are still at risk of developing really severe, potentially fatal, complications.**

***Felicia Pagliuca:** Type 1 diabetes has such a significant burden on individuals, on families, on communities, and it is a 24-7 relentless job.*

**That's Dr. Felicia Pagliuca. She's the Vice President and Disease Area Executive for type 1 diabetes at Vertex.**

**They are researching type 1 diabetes at the *cellular level* – something she first got interested in when she was a student.**

*Felicia Pagliuca: It was really a lecture that I saw when I was a Ph.D. student by Professor Doug Melton that turned that paradigm on its head that not only could we think about cells as being a cause of disease, but think about cells as being a solution to diseases.*

**That's what Vertex is investigating – cell therapy as a potential treatment for type 1 diabetes.**

*Felicia Pagliuca: Vertex has a really unique research and development strategy that focuses first and foremost on diseases where we understand the causal biology really well, so that we can rationally design therapies that could have a major transformative impact on patients if we're successful in developing them.*

**Type 1 diabetes definitely fits that description.**

*Felicia Pagliuca: Clearly, it's a disease with enormous, unmet medical need. It's a disease where we understand that these missing insulin-producing islet cells are at the heart of the disease.*

**And this knowledge is what drives Vertex forward.**

*Felicia Pagliuca: Science has advanced to a place where even a decade ago it was unthinkable. It was science fiction to think that you could make replacement islet cells in the laboratory. And so, to be at the moment now, it really feels like a inflection point, and we hope it really will be in the history of the treatment of type 1 diabetes.*

**The professor who first inspired Dr. Pagliuca to think of cells as living problem-solvers was Dr. Doug Melton – one of the world's leading stem cell researchers. A former Harvard professor, he's been in this area of research for more than 20 years. And this year, he joined Vertex as a distinguished fellow.**

**But working on an investigational treatment for type 1 diabetes wasn't always on his radar.**

*Dr. Doug Melton: Well, I didn't think much about diabetes until my six-month-old son contracted the disease. From a parental point of view, you have to manage that little baby's blood sugars by pricking their fingers or their toes and squeezing blood out and measuring how much sugar there is, and then inject them with insulin. You can imagine how hard it is in a six-month-old that doesn't talk.*

**His son Sam was the youngest person at Children's Hospital in Boston to be diagnosed with type 1 diabetes.**

*Dr. Doug Melton: My wife had to deal with the fact that she was also breastfeeding Sam at the time. When you're eating food, like a candy bar or an apple or something, you know how much sugar you're taking in, but you can't tell how much sugar you take in or energy from breast milk, because you don't know what the volume is. So, she's up all night testing his blood sugars and injecting insulin. And she looked at me, more or less and said, look, you're a scientist. Go do something about this.*

**And so, he set out to do just that.**

**It was understood that people with type 1 were missing insulin-producing cells – also known as beta cells. Dr. Melton figured – if the beta cells were missing – they needed to make new ones.**

*Dr. Doug Melton: There was this nice commercial about a man and he would say time to make the donuts. And so, I used to go to the lab and say time to make beta cells. That was our job.*

*Jordan Gass-Pooré: I love that. What are the differences between type 1 and type 2 diabetes?*

*Dr. Doug Melton: Well type 1 diabetes is caused by the problem that one's immune system makes a mistake. Instead of just attacking foreign entities like a virus, it decides for reasons we don't understand to attack the patient's own beta cells and destroys those cells.*

*That is not the cause of type 2 diabetes. In type 2 diabetes, the patient still makes insulin, but their body has a greater and greater demand for insulin. So, it's called insulin resistance, meaning that the patient's muscle and fat cells require more and more insulin all the time. Type 2 diabetes can be treated in many cases by changes in diet and exercise. That is not true for type 1. So, no behavioral change will prevent or treat type 1 diabetes.*

*Jordan Gass-Pooré: What was that Aha moment?*

*Dr. Doug Melton: The real turning point was in 2013, 2014, where we figured out the right factors or molecules to give to the cells that made them respond to glucose. Because the beta cells' job is to read or measure the amount of sugar in the blood and then squirt out just the right amount of insulin. So, the moment where we had a test, and when we added glucose, the cells squirted out insulin, and then we knew we were on the right track.*

**As part of his work at Vertex, Dr. Melton is helping develop a potential treatment that addresses the root cause of type 1 diabetes: the absence of those insulin-producing cells in the pancreas.**

**The company is investigating how to replace those destroyed cells with insulin-producing cells and making sure they can get into patients in a way where they can survive and function for a long time.**

**And progress so far gives Dr. Melton confidence in their path forward.**

***Dr. Doug Melton:** Let's put it this way: 30 years ago, if you had told someone you would take a human stem cell and turn it into functional insulin-producing cells, people would have said, 'yeah, good luck with that.'*

**One last thing that Dr Melton told me – something that made me smile the rest of the day. He says that everywhere he goes, he always carries a little vial in his pocket.**

***Dr. Doug Melton:** It has in it cells that have been turned into insulin-producing cells. Sometimes I take it out like a snow globe and just turn it up and down and look at it because it reminds me that this is possible. We now know the problem, and we just have to do it.*

**Madison Carter is hoping for a better treatment for type 1 diabetes because she doesn't want another generation of young people to feel how she did.**

***Madison Carter:** I was like, I don't want to take the shot. I don't want to do this again tomorrow. I don't, I don't want to, not that I wanted to die, but I just did not want to work this hard to be alive.*

**To ease that burden, she is now looking to technology.**

***Madison Carter:** Things have improved so much. Having a continuous glucose monitor is probably one of the best inventions, so now I can glance at my blood sugars and I can then pick up my insulin pump, which is right next to that device and just input the numbers.*

**And maybe more important than tech, Madison still has her fearless determination.**

***Madison Carter:** I had a friend point out to me she goes, oh, that's why you are the way you are. You know? And I didn't even realize that, I didn't even associate it back to my diabetes.*

**This is *Targeting the Toughest Diseases* a podcast from Bloomberg Media Studios and Vertex Pharmaceuticals.**

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**I'm Jordan Gass-Pooré, thanks for listening.**

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