Islets in the Stream: Diabetes and How to Treat it with Dr. Krishana Sankar

Nerdin' About Podcast Transcript, Season 1 Episode 6

Michael
Hey everyone! Welcome to Nerdin' About I'm Space Michael, and with me as always is Kaylee, who we learned from last episode that she was delving into some short stories on sci-fi, and her love of robotic animals like Tamagotchis and Giga Pets. Hey, Kaylee, have you got your Tamagotchi ready?

Kaylee
No, you know, actually, reading those stories was both really exciting for me, but a little triggering because my Tamagotchi died all the time. So I don't know if I'm ready to commit to another digital pet. Did you have those when you were growing up?

Michael
You know, I worked at Toys R Us in the late 90s, and I remember the year that it came out. It was the hottest thing, and I worked in the electronics department. It was one of those things where people were banging down the door trying to get the Tamagotchis. I felt like I had so much power. I was like 17 years old, opening the box of Tamogotchis, like "No, I'm not gonna sell to you, weird 40 year old man buying 10 of them."

Kaylee
It would probably be a little weird for you to go and buy 10 of them now at this age, someone would have questions. Speaking of lots of questions, we have lots of questions today for our guest. Our guest today is Dr. Krishana Sankar, and Krishana is a research scientist in the Faculty of Medicine at the University of Toronto. Her doctoral research was focused on studying diabetes to better understand potential treatments. Krishana is also the founder of the group GradWriteSlack that supports graduate students in their academic writing. Hi Krishana, welcome to Nerdin' About!

Krishana
Hi, Kaylee. Hi, Michael, well, Space Michael.

Kaylee
It's really lovely that you were able to join us. So today we're going to be talking about some of your doctoral work and in anticipation of this episode, I was doing a little bit of reading about diabetes, and I was actually really surprised to find that in 2017 over 7% of Canadians over the age of 12 had been diagnosed with diabetes. Is Canada higher up on the scale for having diabetes in comparison to other countries?

Krishana
So that's actually a pretty high rate. I would say it's comparable to other countries that are not low income countries, but typically speaking we do know in Canada we have about 11 million people with the different types of diabetes. So 7.3% is not super bad, but it's not great either.

Michael
So Dr. Sankar, if you could, maybe bring it back to help explain to dummies like me, what is diabetes? What causes it? And probably the more important question, is it pronounced di-a-bee-tees or di-a-bet-is?

Krishana
Okay, I think I want to start with your third. As far as I know, it's pronounced di-a-bee-tees, and not di-a-bet-is, although I have heard some people pronounce it that way. It's pronounced di-a-bee-tees, and diabetes is a metabolic syndrome, but occurs when our body is unable to either make or use a hormone called insulin. That means that we're unable to use sugar from our foods when we eat it, and not only that, when the sugar gets into our blood, typically the insulin or the hormone insulin usually removes it from our blood, and is able to store it in the different organs where we use it for energy. If the sugar stays in our blood, and it's not removed, and put into different organs, what tends to happen is it causes damage to the different organs in our body as well as in our blood vessels, and that typically leads to other issues down the road.

Kaylee
What kind of issues does it lead to? What parts of the body does it affect the most?

Krishana
Interestingly enough, and I think this is actually an important point that a lot of people are not aware of. Some of the secondary complications of diabetes tend to be things like heart disease, and stroke, as well as neuropathy, having your nerves die, so people tend to feel tingling or numbness in their extremities and that can eventually lead to amputation. Also blindness and kidney damage. So those are some of the main secondary complications that people with diabetes can develop.

Kaylee
Do those complications take a long time to develop, are we talking 20 years to develop or 10 years? I'm sure it varies, of course with severity, but is that sort of a long term complication issue?

Krishana
Exactly. So yes, those are long term complications. So they tend to come around after having the disease for quite a number of years, especially depending on when you've been diagnosed. So some people if they're diagnosed younger, they're able to then better maintain and manage their diabetes and hopefully able to prevent some of the longer term complications. Then there are other people who tend to get diagnosed later in life, and may have had the disease for a little while, and so their complications would seem to come on a lot sooner than if they were diagnosed earlier.

Michael
So it sounds like if you have diabetes it's a pretty severe condition. But how long have we known about it? Is this a relatively new disease for humanity? Or did we just not know about it and lots of people suffered not knowing why?

Krishana
No, this condition has been around for a really long time. Even one of the particular symptoms of frequent urination was given a name by one of the Greek philosophers back in the day. So it's been around for a long time, but it's only very recently been treatable, and when I say that I am talking about in the 1920s. Typically, people who had diabetes prior to 1920 would die just a few months or sometimes just a few weeks after being diagnosed with the disease. So it wasn't until 1920 of course, when it was Dr. Frederick Banting, and Charles Best who both discovered insulin, and particularly for people with type 1 diabetes, so they were now able to use insulin in order to prolong their life.

Kaylee
So, Krishana, how do we treat diabetes?

Krishana
So there are different ways to treat diabetes, and one of the most popular or important ways of treating it, specifically for type 1 diabetes, is the use of insulin. So whether that be insulin injections, or insulin pumps, and that's because of course in diabetes it is because of the lack of insulin, or the inability of the body to use insulin that people develop the disease. So having insulin as either an injection, or a pump is a main treatment for diabetes. There's also another treatment for diabetes called islet transplantation, and that's where my work comes in. So islet transplantation started many years ago in the 1960s, I believe, by Paul Lacy, and it was then picked up in Edmonton in the 1980s by a lab there, and so the first protocol that was done there was actually called the Edmonton Protocol. That is another treatment for diabetes, the islet transplantation.

Kaylee
I'm from Edmonton, and this whole time I thought our only claim to fame was Wayne Gretzky, but it's very exciting to hear that we have this other amazing protocol. So what are islets? How are they involved? Why do we need to transplant them? What does that do for us?

Krishana
That's a great question. I'm really happy you asked it, because many people don't know what islets are. So islets of Langerhans are tiny mini organs that are found within our pancreas, and our pancreas usually holds about 1 to 3 million of these tiny balls of cells. So they're super small. They're on average like 200 microns in size, which means you need a microscope to see detail, but you can actually see them with your naked eye, it kind of looks like a speck of dust. So these mini organs inside a pancreas are the ones that are actually responsible for making, producing, and secreting insulin. So when certain cells in that islet dies, that's what causes the lack of insulin and then eventually development of diabetes.

Kaylee
Is there anything you can do to keep them from dying?

Krishana
One of the important parts of islet transplantation is to ensure that there's survival of these islets for the transplantation process. That has been one of the limiting factors of the procedure for

many years, that as well as the amount of islets that are needed for the transplantation itself. So my research actually looks at trying to get these islets of Langerhans to stay alive longer for transplantation. So typically, what happens in the procedure for transplantation is the islets are removed from a cadaver's pancreas. So they're cut off from their blood supply, then we clean them up in a procedure, and then we take these islets and then transplant them into someone else. So someone who has type 1 diabetes, for example. Now during that whole process with the removing of the blood vessels, and making sure the islets are nice and clean and ready to be transplanted, some of the cells within the islets start to die. Then they undergo something called hypoxia, or basically they experience something called low oxygen that also perpetuates death within the islets. So my research comes in because I'm trying to actually keep these islets alive longer and help them be more viable for this transplantation procedure. I use different methods and techniques for that where I combined biology and engineering to sort of mimic a flow within these islets. So typically, when the islets are in our bodies, they receive blood flow, and the blood flow itself is a signal for survival, but they also get nutrients and they're also able to remove waste. So that's what I mimic on the benchtop, or *in vitro*, that's what we call it once it's outside of the body.

Kaylee
So you're essentially trying to mimic as if it was still in a live person?

Krishana
Exactly.

Kaylee
Let's say you have indicated that you're an organ donor. This might be something that would happen with those organs?

Krishana
Exactly. So if someone's an organ donor, what would happen is, if someone requires an islet transplantation, then the organ donors pancreas gets removed. Then they undergo a procedure where we remove those islets from the pancreas, and then they're actually shipped out to the person that requires the islets for transplantation. Then usually that's done as quickly as possible, of course, but then also at the same time, we want to make sure that the cells that the other person or the recipient is receiving are ready and compatible for their body, and they don't react adversely to these new cells.

Kaylee
You mentioned that you want to, of course, do this as quickly as possible. What's the kind of the timeframe that you would have from removal from one person getting it, to the person who needs them?

Krishana
So typically, the whole process might take just a couple of days, perhaps one to three days. That's because it depends on how soon and how severe the whole procedure is, with the person requiring the islets, but then also to ensure, once again, that the islets are safe to be used for transplantation, and to use that we typically need to keep it, and evaluate the islets, make sure

that they're alive, and they're properly functioning before we actually transplant it into someone else.

Kaylee
So that's actually a question that I had that you just lead really nicely into. How do you determine if these are still living versus not living? Do you have to actually watch them go through these biological processes or is there a way to tag them so that you can observe them more easily?

Krishana
So for these islets there are a few different tests that you can do to figure out if they're still viable. So one of the main tests is to ensure that they're still secreting insulin, because that's the main function of the islet that we want when we transplant them. So it's essentially to stimulate them with sugar or glucose, and at different levels, and to then measure the amount of insulin they're secreting, and to determine are they secreting enough insulin, and are they secreting the insulin at the right times, because all of that is important. So that is one measure of the function of the islet, but then also you want to make sure that the islets are still viable. So there are also tests to make sure that the cells are still living versus if the cells are dead. So some of those, for example, are either called Caspace-3, so that's a protein you would tag the islets for, or something else called TUNEL staining, which is cool as well because it pretty much tags DNA that are cut off. So if it fluoresces for that colour, then you know that the islets are dead.

Kaylee
So you were talking about this process of having the cells, it's really important that we understand if we can keep them alive longer so that they're more viable for transplantation, and you go through these steps of giving them these nutrients. How long can they survive? What have you found? How helpful is this? Have you been able to keep them in the lab alive longer?

Krishana
Yeah, so actually, my results were quite, exciting. So typically, when you remove the islets from the blood supply, especially the blood vessels, they start to die quite quickly. After 24 hours, you see about 50% less blood vessels than when you first took them out of the body. Then they of course continue to die over time. By day four, you have no blood vessels in the islet. So with my treatments when I've combined it with a bioengineering method called a microfluidic device, which is essentially a tiny device that's the size of a toonie. Imagine putting like tiny, tiny cells within a device that's the size of a toonie, and then stimulating them with some flow and some media. I've managed to keep those blood vessels around for a longer period of time than if they were typically just sitting in a dish. So that's classically how they're treated. They're classically just put in a dish with this media without any flow, but when I put it under the conditions of my experiment with flow, and the media, we actually see them sticking around for a longer period of time.

Kaylee
That's very cool. So we could imagine a future in which someone is extracting these cells from one person and then putting them in a Dr. Sankar medium with flow and sending them off to the next person for implantation.

Krishana
That would be amazing.

Kaylee
We'll need to start thinking of some marketing, a really good catchy name.

Michael
So you founded something called the #150MinuteCampaign. Could you tell us a little bit about that?

Krishana
Sure. So the 150 minute campaign came about because of my love for exercise, and then combining my passions in general. So exercise and science, and my science happens to be in diabetes research. So when trying to figure out how to do that I actually came across the American Heart Association, which is also now adopted by the diabetes Canada organization, and there was research to show that 150 minutes of moderate to vigorous exercise per week helps to keep us healthy. So I thought this would be a great way to get people active, and get them involved as well as to teach people a bit about diabetes, and help to dispel some of the myths around it. So in 2017, in the month of November, which happens to be Diabetes Awareness Month globally, I decided to launch this campaign, and so I did so on Instagram, and I told people to snap a picture video of them being active, and then hashtag 150 minutes. So it took off, and it was quite fun, and during that time what I would do is I would set up different quizzes on Instagram or on social media about diabetes and ask people questions about dispelling myths around diabetes, and then I would go on to explain what the answers are. So yeah, it all came about because of my love for exercise and combining that with my research.

Michael
So if you did take us through some of those most common myths, what would some of them be?

Krishana
So some of them would be people thinking that only eating too much sugar causes diabetes. So that one is a big myth, and that's because diabetes is so complex, and complicated that it's not just about the amount of sugar that we intake, and for example, type 2 diabetes actually has a huge link to genetics. So if you have a father, who tend to be males over the age of 40, and have a certain BMI (body mass index), they tend to have a higher risk for diabetes. If you have people in your family with diabetes, then you also have a higher risk of getting diabetes. So there's a large genetic component to this, as well as of course, environment, and nurture versus nature. You know, your exercising, and your lifestyle, and the food that you eat, and just not sugar, but also bad fats as well. So those all contribute to getting diabetes.

Michael
All right, let's get to some Nerd Herd questions!

Kaylee
We have a question from Janica who asks whether or not type 1 diabetics can be vegetarian?

Krishana
Oh, that's an interesting question. So I actually do know a few people who have type 1 diabetes and they are vegetarian, and they live quite healthy lives. Of course, regardless of whatever type of diet someone wants to have, especially if they have a chronic disease, it's always important to get input and feedback from your physician. So that would be one thing I would just want people to take away, but yes, I do know people with type 1 diabetes who are vegetarian.

Michael
Also just to follow up on another dumb question: "What is the difference between the different types of diabetes? So a type 1 diabetic, a type 2, and a type 3?"

Krishana
Yeah, so that's not a dumb question at all. It's a really good question. So there are actually more than three types of diabetes. Typically, we tend to speak about the three main types of diabetes because the others are more newly formed, but the three main types are type 1, type 2 and type 3. Type 1 is an autoimmune disease, which means that it's a disease where your body is actually attacking its own cells. So your body creates and mounts an immune response to those islets of Langerhans. So the cells in there actually attack and kills those cells that make the insulin. So they're no longer around, and then you get type 1 diabetes, so it means your body can't make insulin. With type 2 diabetes, however, your body can make insulin, but the problem is your body's resistant to the insulin it makes. So therefore it has no effect on the sugar that gets into your body. So that's the main difference between those two. The third type is typically gestational diabetes, which some women get when they're pregnant, and it's usually temporary, but of course if it's not properly managed and maintained, then it can become permanent after birth.

Kaylee
So we have another question that's sort of around nutrition and diabetes. Kim was wondering how diabetes affects digestion and absorption of nutrients?

Krishana
That's a really good question. So diabetes, like I mentioned before, can affect many different parts of the body. It also particularly affects our nervous system, and so typically, we normally hear about it affecting the nerves in our limbs, and eventually causing amputation if it's not properly managed, but when it comes to digestion, there's the main nerve called the vagus nerve. That usually controls how our stomach will empty food into our small intestines, and so people who have diabetes. in those people their vagus nerve may actually be damaged. For that reason they usually have issues of their food emptying from their stomach into their small intestines, and then that tends to create other problems within their body and their digestion.

Michael
Our final question comes from Richard, who asks: "Is there any new discoveries or data about the success of the Edmonton protocol?"

Krishana
That's another good question, and a very specific one. For the Edmonton protocol, it's been around for a long time since 1989, but if we think about it, it's not that long when we're talking about health and science and discovery. So more recently, what has happened over the many years is that there have been over 500 islet transplantations around the world, but from 1989 to now that's not as many as you would probably think would happen. So far one of the main improvements to the process is actually the safety in the islet transplantation procedure itself. It's actually become safer over time. The amount of people that are able to get islets, and then become independent of insulin is about the same that has been maintained. Then when we look at the number of islet transplantations that have been occurring over time, it's actually decreased over the years, and I'm not entirely sure why there are several reasons why islet transplantation can be limiting, and one reason is the fact that there's a shortage of organs. So that may be one, and also two it may be a procedure that is very difficult to replicate in other parts of the world. So some of the biggest successes have been in Edmonton, Alberta. So beyond that we've seen a decline in the amount of the procedures that have been done around the world.

Michael
It's really interesting that the Edmonton protocol happened in 1989, which was just after Wayne Gretzky got traded. All right, I think it's time for our segment Whatcha Nerdin' About! So Krishana, what have you been nerding out about recently?

Krishana
So I've been nerding out about something called GradWriteSlack, and GradWriteSlack is actually a community that I founded two years ago, and it's a slack group where a bunch of academic trainees from all over the world have joined. They come in for accountability and community when they're doing their academic writing, and so from the time I started it to now we've grown to over 600 people, which to me is amazing. We've had amazing successes with over 50 people in this time managing to come in and finish writing up their theses, and defending, or passing their comprehensive exams. So some of the best feedback that I've gotten is that people would put us in their thesis acknowledgments, and they come back and say how amazing the community has been in getting them to the finish line. So you know, helping to remove that isolation, giving that camaraderie as well as giving the accountability has been amazing.

Kaylee
I love that there's this combination where you're not just going to you know, get your work done, but you also have a support system that you might not otherwise have access to. Michael are there any amazing global groups that you founded lately that you've been nerding out about?

Michael
So for everyone listening that may know Kaylee and I, we've decided to do this sort of obsession swap. So Kaylee has been going through all of Star Trek: The Next Generation, which is my favourite show of all time, and I've also been watching for the first time her favourite show Buffy: The Vampire Slayer. So I'm watching season one: episode eight, the episode is called "I Robot, You Jane", and something really weird happened as I'm watching it. So in this episode

Willow falls for a demon that is disguising as sort of like this weird cyber guy that's living in the computer. Now I'm watching this and I'm like, this show came out in 1997 which means they probably wrote it in '96, and I must have lived like a super sheltered life because I got email for the first time in 1999. So I started asking a lot of my friends, when did the internet start to come into their consciousness let alone cyber stalking, or online dating or things like that, and I got a range of answers. It was really interesting. I think it largely it was because I graduated in 95, which was right before I think a lot of internet stuff happened. So once I left high school, I just went into a different world, and because I wasn't connected to the internet, I didn't learn anything about the internet. I was literally like, in a weird bubble of non-internet for about a good five years. So I've been asking a lot of questions of my friends, you know, trying to figure out where everyone's entry point to the internet was.

Kaylee
I love that this has been such an awakening to you about your own history and relationship with the internet.

Michael
Well, when was the first time you started thinking about the internet?

Kaylee
I honestly can't remember.

Michael
Krishana how about you? Do you remember the first time the internet became a thing for you?

Krishana
I was actually just trying to think about that. I think 1998 I can't quite put my finger on it. I think maybe then.

Michael
Buffy the Vampire Slayer was ahead of its time.

Kaylee
It was way ahead of its time in so many things. Apparently also in access to the internet.

Michael
What about you, Kaylee, what have you been nerding out about?

Kaylee
Well, if you'll indulge me for a moment, I've actually been nerding out about One Health, and One Health Systems. So One Health is this idea that your health is not just about you. It's also about the health of animals in the environment and also the environment itself, and COVID is actually a really great example of this because the virus that causes COVID-19 has been linked to originating in wild animals. I've been thinking a lot about this recently because I've been writing a piece about, you know, what can One Health tell us about the spaces in which we live. And as I was working on this, I started reading about Nipah virus and Nipah virus is a really

interesting case of how you can have similar One Health systems but your approaches to them have to be different because they're so complex. So Nipah virus is a virus that is zoonotic. So zoonotic means it's transmissible between animals and people, and it's carried by fruit bats. It was actually first discovered in Malaysia in 1998, and in Malaysia the cases in people were actually linked to agriculture. So there was planting of fruit trees next to pig farms and bats were feeding on the fruit and the virus is shed in the saliva of the bats. Then pigs were eating bat-bitten fruits and potentially got the virus that way. Then from pigs, it spread to people, but there have also been cases of Nipah in Bangladesh and in Bangladesh it's a totally different story, it doesn't involve pigs at all. In Bangladesh, you're more likely to get Nipah virus if you have been consuming raw date palm sap. In that instance, they think maybe what's happening is that the bats are also feeding on that sap, they're contaminating the sap with their saliva, and then people get it that way. So, same virus, but in Malaysia, you would deal with it by increasing the distance between fruit trees and pigsties, and that has happened, and it seemed to have had a positive impact. Whereas in Bangladesh, you might try to reduce the amount of date palm consumed by people, or you might try to put up barriers to keep fruit bats from landing and contaminating that date palm sap. So in anticipation of this episode, I've been thinking a lot about how health systems are so complex and how you have to understand all the pieces around them in order to make informed decisions. I think that's similar to diabetes, it's not just can I just not drink sugary drinks and not get diabetes, there's actually so many factors that you have to consider. And so that's actually what I've been nerding out about.

Michael
Well, that brings us to the end of another episode, Dr. Krishana Sankar. Thank you so much for joining us. If people want to learn more about you and your work, where can they go?

Krishana
Yeah, thank you so much for having me. This was such fun. You can find me on Twitter, I'm @krishanasankar. That's my handle. I'm also on Instagram at @beyond.the.ivory.tower. On my Twitter I also have my website there so once you find me on Twitter, you can find my website as well.

Kaylee
And you can hear more from Nerdin' About, or more about us @NerdNiteYVR on Twitter, Instagram and Facebook. And until next time, in the immortal words of Hal Johnson and Joanne MacLeod: "Keep fit and have fun!"

Transcribed by https://otter.ai