| TPWKY |  | This is Exactly Right. |
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| Carla Williamson |  | Hi, I'm Carla Williamson, I'm a type 1 diabetic, 43 years this August. I was diagnosed in 1977. I was drinking all the time, could not get enough water, my mom said I would go from a water fountain, drink a coke, then drink milk, couldn't get enough, I was losing weight. My dad was a type 1 diabetic also and my mom had recognized the symptoms pretty early. And back then they did not have home blood glucose monitoring so I was out doing yard work and my dad came home for lunch and they called me in the house and said, 'Go in the bathroom, I want you to use the restroom on this litmus paper'. And I went to the restroom, urinated on the litmus paper and it turned bright blue which I knew and my parents knew then that I was a diabetic. |
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|  |  | So I got diagnosed in the summer before 6th grade, so I started a new middle school, I had one other classmate that was also a diabetic but I was really embarrassed to tell anybody, I didn't want anybody to know. So if I had a low blood sugar I wouldn't want to tell anybody so I would wait until I was in a dead sweat and almost out of it, my teacher would say something cause she would keep orange juice in her desk. But I did not want to be called out or tell anybody, I didn't wanna be different than anybody. It was not until I was a nurse working in a hospital that I had a friend that was also on a pump and we started talking. |
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|  |  | And I loved talking about it and I loved educating and I found even now that I'm a school nurse, talking to kids with diabetes and letting them see that you can live a normal life, you're not any different than anybody else, you can do anything you want and live with this disease but you have to acknowledge it and take care of it is huge and I love playing that role now. So growing up my friends were very understanding, you would go over and parents would be very scared to have you over cause they were like, 'Oh gosh, she's a diabetic. How do we take care of someone with diabetes?' And my mom would say, 'She can take care of it, she knows what to do.' My parents handed me the disease at 10 years old and said, 'This is yours, you're gonna live with it the rest of your life, you've got to learn to make good decisions.' |
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|  |  | So I got out of the hospital on a Monday and I was at a sleepover on a Friday. So I was always given freedoms - good or bad I don't know - to handle this disease. Back in 1977 was so different than it is now. Everything was no sugar. You could eat anything you wanted, you just couldn't have sugar. It was one shot a day, it was all long-acting insulin, it was beef and pork-based insulin back then so control was not good. Being 10 number one but also just no way to monitor what you're doing. You peed on a keto strip that showed glucose and ketones and then you went to the doctor and had blood work done and he always said, 'You're not in control, you're awful. You're gonna be dead before you're 30. You've got to take care of yourself.' So it was not a good thing to hear when you're 11 years old, 10/11 years old. So I was never well controlled. |
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|  |  | At 16 I went into a diabetic coma for 4 days. During that they found that I was immune to the beef and pork insulin. And thankfully at that time they had developed the humulin insulin, so they put me on humulin N or NPH which is a buffered long-acting insulin and humulin R which is a regular short-acting insulin. But even then it was just two shots a day, everything was still based on sugars not carbs, really the concept was not there yet for that. So when I was in college I was in DKA like every semester, strain too much, you think you're taking your two shots a day you're gonna be fine. When I was 19 years old in 1987 I told my mom I think I'm dying, I don't feel good, I felt horrible. She said, 'You're a lazy teenager.' And I found a doctor and I said I don't feel good and I'm taking the insulin, I don't feel good. He put me in the hospital right away and I was immune to all buffered insulin. |
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|  |  | So in 1987 my life changed forever cause I got placed on an insulin pump. I have been under tight control ever since. I just think it's come a long way, I think pump therapy, now I'm on a sensor, they got sensor therapy so it reads your blood sugar all the time. You have so much more freedom now. Just coming from someone from 43 years of having diabetes, I will never complain that I have it. It's part of me, it's who I am. But diabetes is huge, it changes every aspect of your life, you have to think about everything before you do it. You just have to be prepared for high blood sugars, low blood sugars, you have to be able to have a positive attitude and not ignore it, you can't ignore it. And you have to take care of yourself. |
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| TPWKY |  | (This Podcast Will Kill You intro theme) |
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| Erin Welsh |  | Thank you so much Carla for coming on and chatting with us, we really appreciate it. |
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| Erin Allmann Updyke |  | We do. |
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| Erin Welsh |  | Hi, I'm Erin Welsh. |
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| Erin Allmann Updyke |  | And I'm Erin Allmann Updyke. |
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| Erin Welsh |  | And this is This Podcast Will Kill You. |
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| Erin Allmann Updyke |  | Yeah. This is gonna be a good episode, Erin. |
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| Erin Welsh |  | I think so. I mean we say this every time, this is this podcast and we are excited about this episode and it's gonna be a good one and we can't wait to get into it. |
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| Erin Allmann Updyke |  | Yeah. We're gonna try and keep it short and sweet, right? |
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| Erin Welsh |  | Yeah but we will fail in our attempt. (laughs) |
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| Erin Allmann Updyke |  | Should we start off with a quarantini? |
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| Erin Welsh |  | Let's do it. |
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| Erin Allmann Updyke |  | What are we drinking this week, Erin? |
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| Erin Welsh |  | This week I can barely hold in the laughter. This week we are drinking the aptly named Sweet Pee. |
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| Erin Allmann Updyke |  | Sweet Pee! It's spelled P-E-E. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | You get it? |
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| Erin Welsh |  | Erin do you wanna explain why we're calling it Sweet Pee? |
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| Erin Allmann Updyke |  | Well I'll explain a lot in the biology section but that is one of the hallmark symptoms of diabetes mellitus which is the topic of today and that's having excess glucose or sugar in your pee. |
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| Erin Welsh |  | Yeah. It's true. But unlike that pee, Sweet Pee the quarantini and placeborita does not have any sugar in it. |
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| Erin Allmann Updyke |  | No, it's diabetes-friendly! |
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| Erin Welsh |  | Yeah. The thing is we were researching what are good cocktails for people with diabetes and again and again it kind of came up as no sugar, pretty simple stuff. And so what we wanted to do was kind of keep it simple and approachable and it's actually one of my favorite go-to drinks. It's a vodka soda. |
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| Erin Allmann Updyke |  | It's a vodka soda. And if you want the placeborita version it's a soda water with lime. |
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| Erin Welsh |  | Yeah and the thing is you can really spice it up or flavor it up however you want to do it, right. You can use infused vodka, you can use lemon or a different kind of fruit instead of lime, you can do anything you want. You can do stevia syrup or whatever. But as a baseline, start with a vodka soda. |
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| Erin Allmann Updyke |  | Yeah, do that. If you need a full recipe we will post one on our website thispodcastwillkillyou.com and all of our social media channels. |
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| Erin Welsh |  | So more business. On our website you can also find things like transcripts, you can find things like a link to our Goodreads list, to our bookshop.org affiliate account. You can find all of the references to past episodes, promo codes for all of the things we talk about in the ads. What else, Erin? |
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| Erin Allmann Updyke |  | Oh everything. Everything you need, thispodcastwillkillyou.com. |
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| Erin Welsh |  | Oh yeah. Merch and music, two more things. I feel like at this point in the season and in our podcasting career we should have that part down but somehow we don't. |
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| Erin Allmann Updyke |  | We never do. |
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| Erin Welsh |  | It's okay. We never do. Before we dive into the episode I have one more piece of exciting business and that is that if you think back to our organ transplant episode many months ago, we had on two incredible guests Carol and Betsy who shared their firsthand accounts with us. And their book titled 'The Insider's Guide to Living Kidney DOnation' is now available. So go check it out. |
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| Erin Allmann Updyke |  | Yay! |
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| Erin Welsh |  | We'll put a link in that episode's show notes and on our website and stuff. |
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| Erin Allmann Updyke |  | Awesome. Should we dive into this probably long episode? |
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| Erin Welsh |  | Let's do it. |
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| Erin Allmann Updyke |  | Okay. Right after this break. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | So here's the thing about diabetes, Erin. We always say that we're not experts on any of the topics that we cover. |
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| Erin Welsh |  | True. |
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| Erin Allmann Updyke |  | And it's still true here today. So certainly there are probably going to be endocrinologists or PhDs in biochemistry who are like, 'You're missing crucial pieces'. We're focusing here on the broad strokes, folks. So what I'm hoping that listeners come away with by the end of this episode is an understanding from the biology side of what insulin is and what it normally does, what the essential underlying problems are in diabetes, whatever type we talk about about, and why you see the complications that you see. So those are the three main pictures, okay? |
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| Erin Welsh |  | Excellent. |
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| Erin Allmann Updyke |  | All right, so let's start with some basic physiology. When a person eats a meal, okay, when you just take a meal, you chew up your food, you swallow it, you digest it, it goes through your small intestine, blah, blah, blah, breaks down into simple sugars, proteins break down into amino acids, we absorb them through our gut. Right? We've covered that a lot on this podcast because we've talked about a lot of gut bugs. But usually that's where we end the conversation is after things get absorbed or don't get absorbed into our bloodstream. So now we're gonna talk about everything that happens after that. |
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|  |  | So in our bloodstream these nutrients, sugars, amino acids, fatty acids, these are what our cells use for energy so that we can live and grow and exist. And one of those sources of energy that our cells use is glucose which is a single sugar, like a one sugar molecule. A lot of tissues use other sources of energy more than glucose but some of our tissues including our brain can pretty much only use glucose. And the way that this gets to our tissues is through our bloodstream. And so that's what we call plasma glucose, that's like the primary source of fuel for our brain and some other tissues. And it turns out for reasons that we'll talk about later on, it's very important for our bodies to keep really tight control on our plasma glucose levels, so the amount of sugar in your blood has to be really tightly controlled so that it doesn't go too high or too low. |
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|  |  | But the problem then is that the majority of our intake of energy like when we eat happens in discrete time periods, it's not like we're eating continuously throughout the day, we have periods like overnight where we don't eat at all and periods like Thanksgiving where we eat way too much all at once. So our body has to have mechanisms to store excess glucose right after we eat a meal and then also to liberate glucose from storage so that it's available in our bloodstream when we haven't eaten or when we're fasting. And it has to be able to do this is a very narrow window of healthy plasma glucose levels. We can't let the blood sugars get too high and they also can't get too low. So the question is how do we do this in our bodies? The answer is insulin. (trumpeting sound) Can we have a trumpet play whenever I say 'insulin' in this episode? |
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| Erin Welsh |  | That would be a lot of trumpeting I would think. |
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| Erin Allmann Updyke |  | Way too many trumpets. So insulin is a peptide that is synthesized in the pancreas. Your pancreas is just a really incredible organ, it excretes a lot of digestive enzymes that allow the breakdown of nutrients and then a whole range of different hormones that enter the bloodstream and have a variety of effects. But one of these major hormones is insulin and it's secreted specifically by these cells called beta cells in response to elevated blood glucose levels. And insulin has three or kind of four major effects. Number one, what it does is suppress the release of glucose form the liver which is one of the main storage sites for extra sugar. It also turns on glucose transporters on our muscle tissue and our adipose tissue so that that glucose can actually get into our cells and then be stored or used. And it also stimulates glycogen synthesis which is the way that our body stores glucose. And it does so much, it also inhibits the release of free fatty acids which are another one of the major forms of energy that our body uses and it stimulates those to be stored instead, so we store fat when we have insulin secretion. |
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| Erin Welsh |  | Okay, gotcha. |
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| Erin Allmann Updyke |  | All right. That was a lot, I know. But the TLDR of all of that is that insulin is a hormone that is secreted when glucose levels are high and insulin's role is to decrease plasma or blood levels of glucose in our bodies. |
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| Erin Welsh |  | This is like flashback from teaching IB 150 or 151 or whatever it is. |
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| Erin Allmann Updyke |  | Right, yeah. It's like way back into bio, bio chem. |
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| Erin Welsh |  | Oh yeah. |
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| Erin Allmann Updyke |  | But I haven't even gotten to diabetes. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So the question is what is diabetes? And at its core diabetes is a problem of insulin. I think that a lot of people think of diabetes in terms of glucose, they're like diabetes, sugar, blah, blah, blah. But diabetes is a problem of insulin, so if insulin's normal function is to decrease blood levels of glucose and diabetes is a problem where insulin isn't working correctly, then the problem in diabetes is you have too much glucose in your bloodstream. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | Right. So now the episode's over and you understand everything about diabetes. Okay. Obviously that's not true. We're gonna choose your own adventure a little bit here, okay Erin? |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Are you ready for this? Cause there's two things that we still need to understand. We need to understand why it's a problem that glucose levels get too high, like what is it that's happening, why is that problematic. And then we also need to know how does diabetes actually happen, like what is the essential problem in this pathway with insulin and glucose. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So which do you wanna go over first? |
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| Erin Welsh |  | Well I think the problems. |
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| Erin Allmann Updyke |  | Okay, like what happens with the problem with insulin. |
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| Erin Welsh |  | Yeah, exactly. |
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| Erin Allmann Updyke |  | Okay, great. Great answer, Erin. Everyone is probably well aware that there are multiple different types of diabetes which have a number of different names that I'm guessing you're probably gonna go into in a little bit, right Erin? |
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| Erin Welsh |  | I mean only actually very briefly. |
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| Erin Allmann Updyke |  | Okay, that's fine. |
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| Erin Welsh |  | For most of the history I just say diabetes. |
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| Erin Allmann Updyke |  | Oh that's fair. Well the different types of diabetes, it is really important to understand the distinctions between them so we'll go over it here. But essentially the way that we classify it today is type 1 diabetes, type 2 diabetes, and then there's like gestational diabetes and there's a few other more rare forms. So we're gonna focus on type 1 and type 2. So type 1 diabetes in general results form a destruction of the beta cells of the pancreas, usually from autoantibodies. So type 1 diabetes is an autoimmune condition where our bodies start to make antibodies against our own pancreas' beta cells which are so important because they produce and secrete insulin and these antibodies destroy those beta cells. |
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| Erin Welsh |  | What do we know of the triggers for this autoimmune reaction? |
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| Erin Allmann Updyke |  | Really good question, Erin. We don't. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So there is a genetic component to type 1 diabetes, however what is interesting is that the genetic links with type 1 diabetes, it's not like a hereditary disease. So the genetic links are not nearly as strong actually as in type 2 diabetes for example. |
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| Erin Welsh |  | Oh, interesting. |
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| Erin Allmann Updyke |  | Yeah. So while there are these genetic factors that certainly play a role, it's also environmental factors and we don't know exactly what those environmental factors are that then lead to this autoimmune disease. There's a lot of thought that maybe it's viral involvement like in people with certain susceptible genotypes, exposure to certain viruses or certain other environmental conditions trigger this autoimmune response that then leads to type 1 diabetes. |
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| Erin Welsh |  | Which viruses? |
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| Erin Allmann Updyke |  | Great question, we don't know. People have proposed, like name a virus, it's probably been proposed as a potential cause. Especially viruses that are really common. |
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| Erin Welsh |  | Epstein-Barr. |
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| Erin Allmann Updyke |  | Epstein-Barr, definitely. CMV, absolutely. All of them. |
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| Erin Welsh |  | Yeah, I was gonna say CMV was my next one. Influenza. |
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| Erin Allmann Updyke |  | Yeah, influenza I think has been on that list too. But nothing that's a strong association to be able to pin down one specific virus. Yeah. But in short because of this type 1 diabetes results from a complete inability to make insulin. So no insulin in your body means nothing to bring down those blood glucose levels, nothing to signal your body to store that glucose or allow that glucose into our cells so that we can actually use it. And for the most part this disease tends to happen on a pretty quick timescale, especially when it happens in kids or adolescents, like the process of starting to generate these antibodies and then the slow destruction of these beta cells and then the onset of diabetes symptoms happens pretty rapidly. It can happen in adults as well and then it tends to be a bit slower of a course and we don't know why. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So that's type 1 diabetes and kind of the underlying causes. You look like you have a question. |
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| Erin Welsh |  | Well I don't know if it's something that you're gonna go over in the other path of my choose my own adventure. |
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| Erin Allmann Updyke |  | Well okay then let's wait and if you still have it at the end, then ask it. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Just like in class. |
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| Erin Welsh |  | Hold all questions til the end of the presentation, please. |
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| Erin Allmann Updyke |  | And then it'll be more of a comment. |
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| Erin Welsh |  | Yep. |
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| Erin Allmann Updyke |  | All right so type 2 diabetes is a bit more complicated than that. Type 2 diabetes results from a combination of different things including beta cell dysfunction but not necessarily destruction. |
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| Erin Welsh |  | What's the difference between dysfunction and disruption? Just like producing less insulin? |
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| Erin Allmann Updyke |  | Right, yeah. So either producing not great insulin or just not being able to produce enough insulin or making insulin but not being able to secrete it whereas in type 1 diabetes your beta cells are obliterated, they're gone. |
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| Erin Welsh |  | Right. Okay, yeah. |
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| Erin Allmann Updyke |  | So it's a combination of beta cell dysfunction and insulin resistance. So you have insulin, you're making insulin, but your tissues are not responding to it the way that they're supposed to. So what does that really mean? |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | It means that in general people with type 2 diabetes have either one or both of two different problems going on. Problem one, like I said their beta cells are not making enough insulin for whatever reason, they just stop being able to produce enough insulin or secrete that insulin into the bloodstream. Or problem number two, their tissues become resistant to these effects. So then the pancreas secretes more and more insulin so what we actually see is a hyperinsulinemia, that means you have a lot of insulin in your bloodstream but it's not being used properly and so it's not effective and therefore you still have too much glucose in your bloodstream. |
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| Erin Welsh |  | So you just have a bunch of insulin and glucose just circulating around. |
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| Erin Allmann Updyke |  | Exactly. |
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| Erin Welsh |  | So what does it mean that your tissues are no longer responding to insulin in the right way? What's going on there? |
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| Erin Allmann Updyke |  | Yeah, good question. A whole bunch of different things. In part it's that you actually can see downregulation of the number of glucose receptors on tissues. So glucose has to be actively transported into your skeletal muscle and your adipose tissue, it can't just wiggle it's way in there. And so in type 2 diabetes you can have less receptors on those cells, like they progressively get lower. Or a whole host of other things can happen but that's kind of the main ones. |
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| Erin Welsh |  | But why? |
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| Erin Allmann Updyke |  | We'll get to the why. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Hopefully, maybe. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Maybe. |
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| Erin Welsh |  | We'll approach the why. |
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| Erin Allmann Updyke |  | We'll slowly get to the why. But one question, because in many cases we actually see both of these things happening simultaneously, so then there comes this question of which comes first. So the way that I like to think of it and again this is very simplified but I think it's kind of just a nice framework to have is that as you start to have this increase in insulin resistance, so your tissues are downregulating the amount of receptors that they have so that the glucose can't get into the tissues. You have an increase in insulin resistance and your pancreas recognizes this and it's like, 'Gosh, we have just so much glucose running around.' |
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|  |  | So your pancreas is working really hard, like working overtime to make more and more insulin and that then causes your tissues to become even more desensitized to that insulin because they're just overloaded, it's like insulin overload, there's so much of it. So then your pancreas makes even more and then eventually your pancreas is just exhausted because it's been working overtime for so long that it starts to just give up and then either making cruddy insulin or just not making insulin or not secreting it, like what's the point, you're not gonna even respond to it, I'm gonna quit. So now you have both problem one and problem two. Problem two exacerbating problem one and causing this vicious cycle. |
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| Erin Welsh |  | What's the timeline for that to happen? |
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| Erin Allmann Updyke |  | That's a good question and it's hard to put an actual timeline on it especially because when you look at a population level there are a whole lot of people who have what is sometimes called pre-diabetes or just... I forget the other proper term for it but it's like increased fasting glucose levels where they have this higher than what is considered typical baseline glucose. And so some of those people will then progress to type 2 diabetes, some people won't and some people have both problems going on, some people maybe have only a little of one. So type 2 diabetes is very complicated. |
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| Erin Welsh |  | Interesting. And so when it comes to type 2, part of the problem is the resistance seems like the biggest part to target for treatment, right. Like how do you reduce resistance? Because it seems like that's sort of what's contributing to the pancreas just being overloaded and poof, I can't do this anymore. |
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| Erin Allmann Updyke |  | Yeah, that's a good thought. And we actually have a lot of medicines that do exactly that to try and make your tissues more sensitive to the effects of insulin and that is for some people really good treatment for diabetes. But we'll just have to keep talking (singing) cause there's more to the story. |
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| Erin Welsh |  | Excellent. Love that song, my favorite track. |
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| Erin Allmann Updyke |  | Thanks, I just made it up. Just right off the top of my head. All right so now let's talk now that we understand the underlying problem with these two different types of diabetes, let's talk about what the symptoms of these diseases are and then we'll finally get to that second part of the choose your own adventure which is understanding why this high glucose is a problem cause that really is what drives the symptoms. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So classically especially with type 1 diabetes, however all of these symptoms that I'm going to talk about can happen with type 1 or type 2 diabetes but because type 1 tends to happen faster and type 2 tends to be a much longer course, the more acute symptoms tend to happen more in type 1 diabetes and the chronic complications can happen in both but certainly in type 2 diabetes. So classically somebody with diabetes presents with what is often called the three Ps, that is polyuria, polydipsia, and polyphagia, and also weight loss. So what do thos mean and how does it happen? So as your blood glucose levels rise, eventually your kidney which is responsible for filtering everything in your blood just can't filter all of that glucose and get it back into your bloodstream because there's just so much of it. So your kidney starts excreting glucose after your blood levels reach about 180, you start peeing out sugar. Hence the name of our quarantini. |
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| Erin Welsh |  | Sweet Pee. |
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| Erin Allmann Updyke |  | And glucose just like lactose does in our guts, see our lactose intolerance episode, glucose is an osmotic diuretic so it holds onto the water along with it. So now your peeing out a ton of water because your kidneys aren't holding onto the glucose or the water. So that's the first P, polyuria, which leads unsurprisingly to massive dehydration causing the second P, polydipsia which means major increase in thirst, like unquenchable thirst. And at the same time the lack of insulin in your body which is driving all of this essentially means that your body is unable to use any of the glucose that you have in your bloodstream. So while you technically have plenty of fuel, your body thinks that it's in starvation mode and so it switches to what's called catabolic metabolism and that is breaking down your tissues to use for fuel which leads to major hunger that is polyphagia, the third P. But despite this you see weight loss because you're literally eating your own body tissues to use as fuel. |
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| Erin Welsh |  | Really, really bad things. |
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| Erin Allmann Updyke |  | Very bad things. And then you have other symptoms like fatigue, unsurprising because this is taking a major toll on your body, blurry vision, muscle cramps because your electrolytes are way out of whack, etc. And when this gets very severe which happens in about 20-40% of cases in people presenting for the first time with something like type 1 diabetes, it's called diabetic ketoacidosis. A lot of people have probably heard of this. It is exactly what the name implies. |
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| Erin Welsh |  | So I just looked this up to clarify something that had popped into my head and I remember, did you ever see the movie Steel Magnolias with Julia Roberts? |
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| Erin Allmann Updyke |  | I have never seen Steel Magnolias. |
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| Erin Welsh |  | Okay well I hope this isn't too much of a spoiler but there's definitely, Julia Roberts plays someone who had type 1 diabetes and I thought it was a ketoacidosis attack, no it was actually hypoglycemia. But I need to rewatch that movie now after doing this episode. |
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| Erin Allmann Updyke |  | Well you saying that just made me think of Honey I Shrunk The... Is it Honey We Shrunk Ourselves? |
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| Erin Welsh |  | I think it's number three, yeah. Or no number three is the baby. |
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| Erin Allmann Updyke |  | But I don't remember what happened in that. |
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| Erin Welsh |  | It's the banana scene. |
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| Erin Allmann Updyke |  | He needs bananas because of the potassium but is that because he's diabetic? Cause you do need potassium. |
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| Erin Welsh |  | I think so. |
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| Erin Allmann Updyke |  | I don't know. Anyways. |
|  |  |  |
| Erin Welsh |  | Pop culture references. There are many of them I believe. |
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| Erin Allmann Updyke |  | So classically especially with type 1 diabetes, however all of these symptoms that I'm going to talk about can happen with type 1 or type 2 diabetes but because type 1 tends to happen faster and type 2 tends to be a much longer course, the more acute symptoms tend to happen more in type 1 diabetes and the chronic complications can happen in both but certainly in type 2 diabetes. So classically somebody with diabetes presents with what is often called the three Ps, that is polyuria, polydipsia, and polyphagia, and also weight loss. So what do those mean and how does it happen? So as your blood glucose levels rise, eventually your kidney which is responsible for filtering everything in your blood just can't filter all of that glucose and get it back into your bloodstream because there's just so much of it. So your kidney starts excreting glucose after your blood levels reach about 180, you start peeing out sugar. Hence the name of our quarantini. |
|  |  |  |
| Erin Welsh |  | Okay. So when people refer to diabetic coma it's ketoacidosis. |
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| Erin Allmann Updyke |  | Very often yes, it can be. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. So that's kind of the acute complications of diabetes type 1 or type 2 but those tend to happen more in type 1. But certainly somebody with undiagnosed type 2 diabetes might have symptoms like a little bit of polydipsia, maybe some polyuria, etc. So now let's think of it in terms of long term. Why is having too much sugar in your blood bad long term? And a lot of people might know of some of the common side effects of diabetes. Erin, do you know some of them just off the top of your head? |
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| Erin Welsh |  | I mean I know that kidney disease is a big problem, I know ulcers are a big problem, amputations are really common, blindness or retinopathy is really common. I think just loss of sensation in your extremities. |
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| Erin Allmann Updyke |  | Yeah, peripheral neuropathy. |
|  |  |  |
| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | And all of those things that you just talked about plus the cardiovascular risk, so risk of clots especially in your heart or your brain. |
|  |  |  |
| Erin Welsh |  | Right, heart attacks are really common too, yeah. |
|  |  |  |
| Erin Allmann Updyke |  | All of those can be split into two different but very similar processes. Those are microvascular complications, so small blood vessel problems, and macrovascular problems, so large blood vessels, heart, brain. |
|  |  |  |
| Erin Welsh |  | Okay. |
|  |  |  |
| Erin Allmann Updyke |  | But either way we're dealing with vascular complications and in some cases direct damage to nerves as well as blood vessels. So the question is how exactly do these complications occur and that is probably the subject of many different PhDs worth of research. But in general chronically having way too much glucose in your bloodstream leads to a state of chronic inflammation. This then leads to the production of reactive oxygen species which we've talked about a number of times on the podcast which are basically things that then cause a bunch of tissue damage especially in blood vessels causing vascular injury and that can lead to all of those complications that you mentioned, Erin. |
|  |  |  |
|  |  | So it had major effects on the kidneys especially if you think about it, this is where all of that glucose is going and the kidneys are filtering everything in your bloodstream. So kidney damage is a major one, blindness is caused from retinopathy where you have damage to the nerves of the eye and also increased blood vessel formation that leads to increased pressures behind the eye. The peripheral neuropathies which can lead to a loss of sensation that can then lead to injuries that are complicated by poor perfusion because those blood vessels are damaged so then those ulcers don't heal because they don't have any blood flow so then they become gangrenous and yes, you have to do amputations. |
|  |  |  |
| Erin Welsh |  | It seems like there are parts of the body that are more sensitive to this. Kidneys make sense because they're having a difficult time with the filtration, heart makes sense because blood, blah, blah, blah. What about your stomach or other organs? What's going on with those? |
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| Erin Allmann Updyke |  | Yeah, great question. I think a lot of people think that diabetes, oh your kidneys, your eyes, diabetes is a disease that affects every single organ in your body, so your stomach, diabetes can affect your autonomic nervous system as well as your peripheral nerves and that damage along with a host of other things can lead to delayed gastric emptying, so it can cause your stomach to not be able to contract the way that it's supposed to so that you can actually get your food to empty from your stomach which can lead to a whole host of problems. So yeah, diabetes affects every part of your body. It has the greatest effects and the earliest effects on small blood vessels, that's why we see things like neuropathy or retinopathy cause those are really small vessels. But then it also has the potential to have complications on larger vessels like your heart, your brain, it affects the entirety of your body. |
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| Erin Welsh |  | Yeah. Okay, that makes sense. |
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| Erin Allmann Updyke |  | And that's the biology of diabetes, Erin. |
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| Erin Welsh |  | Did we get to the why? I've been waiting. |
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| Erin Allmann Updyke |  | (laughs) I know, you have been waiting. We don't have a great answer to the why but I have a guess as to the answer in our current events section so we'll just have to wait. |
|  |  |  |
| Erin Welsh |  | Oh, okay. Okay. |
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| Erin Allmann Updyke |  | So Erin tell me what do we know about this? I assume it's been with us since forever. |
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| Erin Welsh |  | Yeah. Let's start back at forever right after this break. |
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| TPWKY |  | (transition theme) |
|  |  |  |
| Erin Welsh |  | All right. So this is a long episode so far. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And I'm gonna add to that. I'm gonna do something a little bit different for this episode and that is to divide the history section into two parts. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | Not like sequential chapters like this happened and then this happened but more like parallel histories in a way. |
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| Erin Allmann Updyke |  | Awesome. |
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| Erin Welsh |  | And for this first part I'm going to focus on the history that I usually cover for a disease, you know things like early writings, increasing recognition of the condition, and medical advancements especially when it comes to diabetes, the discovery of insulin. All the things that completely changed the landscape of diabetes especially in the 20th century. And then for part two I really wanna go through the other transformation that diabetes went through around that same time and that is the social perception or portrayal of the disease especially focusing on the US. |
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| Erin Allmann Updyke |  | Excellent. I can't wait. |
|  |  |  |
| Erin Welsh |  | All right, so let's begin at the beginning. It probably doesn't surprise you to know that diabetes has long been recognized by many different ancient cultures. You went through the symptoms of diabetes and especially for the acute symptoms and they're pretty recognizable and unique. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So it makes sense that they were written about at length for thousands of years. It was mentioned in the Ebers Papyrus, our favorite. |
|  |  |  |
| Erin Allmann Updyke |  | Yay! |
|  |  |  |
| Erin Welsh |  | In the form of a treatment for a symptom of the disease. So quote, "a medicine to drive away the passing of too much urine". And in the 6th century BCE the Hindu physician Sushruta described a disease of honey urine which could be detected either through tasting it directly or by observing ants gathering around a pool of urine. |
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| Erin Allmann Updyke |  | Ooh. |
|  |  |  |
| Erin Welsh |  | Yeah. And the word 'diabetes' itself comes from the 2nd century CE when the ancient Greek physician Aretaeus coined it from the Greek word for to run through or pipe-like. He also described the disease as quote, "melting down of the flesh and limbs into urine". And the word 'mellitus' from the Latin word for honey or sweet was added later on to again indicate the sweetness of the urine. Galen around the same time as Aretaeus described it as quote, "diarrhea of urine". And Avicenna in the 10th century CE wrote a thorough description of the disease and its complications. So the sweetness of the urine had long been recognized, the sweet pee, people were very familiar with it but it wasn't until the 1600s that a physician in Liverpool named Matthew Dobson realized that it was actually sugar causing the sweetness. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | He made the observation when treating a patient who was urinating 15 liters of fluid a day. |
|  |  |  |
| Erin Allmann Updyke |  | Oh my. |
|  |  |  |
| Erin Welsh |  | Cause I think when we say 'oh you pee a lot', what does that actually mean? |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And so this person was peeing 15 liters of fluid a day. |
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| Erin Allmann Updyke |  | That is way too much. |
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| Erin Welsh |  | Oh yeah. We just had a little... |
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| Erin Allmann Updyke |  | We had a little sidebar to do a little calculation. |
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| Erin Welsh |  | It was really boring so we had to cut it. |
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| Erin Allmann Updyke |  | For reference a typical amount of urine output is between 800 and about 2000 milliliters or 2 liters a day. |
|  |  |  |
| Erin Welsh |  | A day. |
|  |  |  |
| Erin Allmann Updyke |  | This person had 15. |
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| Erin Welsh |  | So compare that to 15, yeah. |
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| Erin Allmann Updyke |  | Oof. |
|  |  |  |
| Erin Welsh |  | So we've been talking about sweet pee and yeah, people did have to taste it. That was how a lot of the diagnoses were made, mostly were made. But at least one doctor successfully fermented the urine to produce what he described as a weak beer. |
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| Erin Allmann Updyke |  | Urine beer? That should have been our quarantini. |
|  |  |  |
| Erin Welsh |  | That should have been our quarantini. And this taste test remained the main way of diagnosing someone with diabetes until the 1800s when chemical tests were developed to detect and measure glucose in the urine much to many physicians' relief, I'm sure. Around the time that these tests were developed the medical world was undergoing a pretty big transformation in terms of our understanding of disease. Yes, I'm bringing up germ theory in the history of diabetes. |
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| Erin Allmann Updyke |  | Oh, okay. |
|  |  |  |
| Erin Welsh |  | But as researchers and clinicians learned about infectious diseases and applied that knowledge to prevention, a lot of chronic diseases grew more visible as morbidity and mortality from infectious diseases dropped, right. And when they did they grabbed some research attention to themselves. So from the middle of the 1800s it was increasingly recognized that the pancreas played some role in the disease thanks to the rise in autopsies that had been happening that showed that damaged pancreas' were often found in people with diabetes. And in 1889 at the University of Strasbourg, two researchers named Oskar Minkowski and Josef von Mering showed this experimentally that the pancreas was involved when they induced diabetes in a dog after removing its pancreas. And it was peeing everywhere in the lab and Minkowski was like, 'What's going on? I'm so annoyed, this dog is house trained, why is it peeing everywhere? Oh my gosh, it has diabetes.' |
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| Erin Allmann Updyke |  | That'll do it. |
|  |  |  |
| Erin Welsh |  | But how exactly was the pancreas involved? What was happening? Additional experiments removing part of the pancreas or grafting bits of a pancreas showed eventually that the pancreas seemed to have two secretions. One external that seemed to help with digestion and one internal that went right into the bloodstream to help with carbohydrate regulation. But where did the internal secretion come from? In 1901 Eugene Opie at Johns Hopkins showed that damage to the islets of Langerhans which were named for their discoverer, that that damage prevented the production of this internal secretion which then led researchers to speculate that if this internal secretion which by the way was totally hypothetical at the time, if it could be isolated, it could potentially be used to treat diabetes. |
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| Erin Allmann Updyke |  | Wow. This is so cool, Erin. |
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| Erin Welsh |  | It is amazing that people, I just can't believe... Like the pancreas, the functions of the pancreas at a time when bioassays were nonexistent. |
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| Erin Allmann Updyke |  | Right. It's just people being so kind of intuitive or maybe it's deductive, I don't know. But it's smarter than me is what it is. And so I'm so impressed by it. |
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| Erin Welsh |  | Well I think also to give a little bit more historical context, at the time this wasn't necessarily as huge a leap in thinking as we are looking at it to be, right. This was actually in line with a lot of other medical advancements that were happening, showing how certain organs produced hormones, like the field of endocrinology was kind of burgeoning at this time, and that it was recognized that these hormones regulated bodily functions and disruptions in the production of these hormones could then lead to certain diseases. Especially once germ theory was like, 'All right, let's do the low-hanging fruit, we've got all these diseases, okay what are all these now?' |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | What's happening? And then in the 1890s it was found that giving someone thyroid extract could actually help treat some conditions. So in this line of reasoning it made sense that pancreas extract could possibly do the same. But early experiments with these pancreas extracts that were performed around the very early 1900s on humans had mixed results, if I'm feeling generous. |
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| Erin Allmann Updyke |  | Unsurprising. |
|  |  |  |
| Erin Welsh |  | Yep. |
|  |  |  |
| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | And if I'm not feeling generous I would say mostly harmful and sometimes outright dangerous. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | But in any case they didn't really suggest that this was a good path forward, like this was not the clear way to go. So what was? Well despite the growing visibility of diabetes and all these advancements in understanding its pathology and being able to diagnose it, one area that was sorely lacking was in treatment. Throughout the 1700s and much of the 1800s the leading treatments for diabetes were basically the same things that you would use to treat anything, right. Bleed them and shoot them up with opium. Boom. If you know how to do those things, you're a doctor in the 1700s. And there are very few diseases that would actually benefit from bleeding but they did exist, hemochromatosis, but diabetes was not one of these. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And opium of course, that isn't gonna make diabetes or many things better. |
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| Erin Allmann Updyke |  | No, no, no. |
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| Erin Welsh |  | No. Diabetes was generally viewed as a disease of downhill progress and for someone diagnosed with what was then known as acute or juvenile onset diabetes now type 1, the life expectancy following diagnosis was like 1-3 years. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Often it was months. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | It wasn't that much longer for those with what was viewed as the chronic form either. It was essentially a death sentence across the board. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Medications and tinctures and fusions seemed to be of no help for the disease but there was one thing that seemed to slow the progression of the disease maybe even though it did nothing to cure it. Starvation diets. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Yeah. So during the 1870 siege of Paris when food was rationed and many people were near starvation, one doctor noticed that the urine of some of his patients with diabetes had dropped in their glucose levels and that their symptoms had begun to improve a little bit. So the logical step was well if we severely limit the caloric intake of people with diabetes, we can reduce the symptoms of the disease. And this was the opposite of previous thinking which was like, 'Oh this person is losing weight, we need to feed them more.' |
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| Erin Allmann Updyke |  | Right, right. |
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| Erin Welsh |  | So after this observation, starvation diets really kind of got their start. And it wasn't always strictly starvation, some diets were just no carb diets, some were just certain carbs like oats only. But in general they were calorie cutting with most diets restricting you to fewer than 500 calories a day. |
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| Erin Allmann Updyke |  | Oh my. |
|  |  |  |
| Erin Welsh |  | Yeah, that is not a lot. |
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| Erin Allmann Updyke |  | No, you can't live on that long term. |
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| Erin Welsh |  | Exactly, yeah. And these starvation diets did seem to work to a degree. I mean they did nothing at all to cure or even effectively treat the disease but they did in some cases just slow the progression and help manage these glucose levels. But the stories are horrifying, right. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | For instance one woman, 43 years old, was admitted to the hospital in 1916 weighing 79 pounds or 36 kilograms and was told to fast. And the last record of this patient showed her weighing 60 pounds, less than 30 kilograms before she broke her fasting diet and died shortly after. |
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| Erin Allmann Updyke |  | Oh my goodness. |
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| Erin Welsh |  | And another really sad story is of a 12 year old boy with diabetes, already blind from the disease, he was brought to the hospital so that his food could be closely monitored and his calories even more restricted. His weight dropped to 40 pounds but the blood glucose didn't seem to be dropping and so they cut even more and he died of starvation. |
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| Erin Allmann Updyke |  | Oh my god. |
|  |  |  |
| Erin Welsh |  | So these starvation diets in addition to slowly killing you were also largely unachievable for most people with diabetes because they required the time and the money to monitor and weigh each individual food item and rest and it was just not a reality. |
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| Erin Allmann Updyke |  | Yeah. |
|  |  |  |
| Erin Welsh |  | So going into the 20th century the available treatments for diabetes were really more of a choice among evils, right. Die of diabetes or of starvation or opium addiction, just take your pick. So the need for effective treatment was very obvious and incredibly pressing, even more so since cases seemed to be on the rise. And so far the only thing that had showed any real promise were the experiments with pancreas extracts that I had mentioned earlier despite their limited success. In particular the work of two researchers, Georg Sulzer from Germany and Nicolae Paulescu from Romania, showed that there might be something in it. In 1906 in Berlin Sulzer had treated some humans with pancreatic extract but the side effects produced were really severe and so he had to stop the project. And 10 years later in 1916 Paulescu had succeeded in treating a diabetic dog with a solution of pancreatic extract, like it lowered it's blood sugar levels. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | Super cool, promising. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | But his work was disrupted by WWI when he was called to service and by the time he got back he picked up his work again but funds were super limited and he was working almost by himself so it was just kind of hard to get things moving. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And neither Sulzer or Paulescu would end up getting the recognition they felt they deserved for their role in one of the most monumental and one of the most contentious medical advancements in the 20th century: the discovery of insulin. |
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| Erin Allmann Updyke |  | Insulin! Do that horn again. (trumpeting sound) |
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| Erin Welsh |  | (laughs) In fact, the history of this discovery continues to be a fairly debated topic in medical history, like who should get credit for it. And so I'm just gonna do the best I can to navigate those tensions. |
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| Erin Allmann Updyke |  | Contentious waters? |
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| Erin Welsh |  | Yeah. So let's meet one of the central characters of this story, Frederick Banting, born in Ontario in 1891. Banting began med school just a couple of years before WWI broke out, he joined up, he helped treat combat soldiers, and after the war was over he tried unsuccessfully to get a permanent position at the Toronto hospital where he did his residency in orthopedic medicine. So he decided that he was gonna move to London, Ontario and set up a private practice but it was really pretty unsuccessful, like he couldn't quite get it off the ground and in fact it seemed like a lot of areas in his life were just filled with struggle and strife and uncertainty. He was always on and off again with his fiance, he was always sending out job applications, and he seemed desperate for a change of scenery or a change of pace in his career. Late one October night in 1920 while trying to fall asleep and what seems as he described it stress spiraling- |
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| Erin Allmann Updyke |  | Been there. |
|  |  |  |
| Erin Welsh |  | Yeah, absolutely. His mind drifted to a paper that he had recently read to prep for a lecture that he was giving on carbohydrate regulation. And this paper which was written by Moses Barron discussed the role of the islets of Langerhans in the internal secretion of the pancreas and its possible role in diabetes. And he turned the idea over and over in his mind and kept thinking about it and came up with what he thought was the solution to the problem, like a way to isolate that internal pancreatic secretion. And it would involve surgical removal of degenerated pancreas' in dogs and extraction of the secretion from those pancreas'. |
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|  |  | And the next time he was on campus he brought up the idea to a professor at the university where he was affiliated and the professor was like, 'No, sorry but we just don't have the resources for that and also there's no one at the university here that knows enough about it to be able to help you. But hang on a second, there happens to be somebody visiting who might.' And that somebody turned out to be J. J. R. MacLeod, visiting from the University of Toronto who was an expert in diabetes and carbohydrate metabolism. So Banting met with MacLeod. MacLeod wasn't super impressed by Banting who had a lot of enthusiasm and confidence but that confidence wasn't really backed by a lot of background reading on the subject, he was just like, 'I'm gonna do this and it's gonna be great.' |
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| Erin Allmann Updyke |  | Oh. We've met those. |
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| Erin Welsh |  | Yeah. And MacLeod was like, 'People have spent their entire careers working on this problem, do you know about these people? Do you know the work that they've done?' But over the conversation MacLeod became more and more convinced and became eventually interested enough to say, 'Okay, you know what? Sure. Come to the University of Toronto whenever and we can try to set something up. But think carefully about this decision because it would mean giving up your practice and your affiliation here and also there's kind of a low chance that you would be successful because this is not a new problem. People have tried this before.' So Banting gave it some time and thought and decided to give it a go but after the other job applications that he had sent out had fallen through and after his fiance had dumped him yet again. So he was like, 'You know what? I'm getting out of here.' |
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| Erin Allmann Updyke |  | Nothing to lose. |
|  |  |  |
| Erin Welsh |  | So yeah. So he packed up his apartment, he headed to Toronto and got there in April 1921. And apparently he had done no more reading on the subject in the meantime. |
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| Erin Allmann Updyke |  | Oh my goodness. |
|  |  |  |
| Erin Welsh |  | Or not very much because when he met with MacLeod, MacLeod was like, 'Okay so I think this is how the experiments should go. Start with this and then we'll do this and then we'll do this, let's see how we begin.' He showed him how to do the procedures, etc. And then he was like, 'Also maybe you should read these papers, read these books, get a little more background in it.' And then MacLeod headed back to Scotland where he was from for the summer break. But before he did that he gave Banting an undergraduate research assistant named Charles Best to help on the project and he kind of spent a little bit of time, like a month and a half or so kind of walking them through these surgical procedures that they would use on the dogs. The experimental plan went a little something like this. First Banting and Best would get practice. Banting on performing the pancreatectomies and Best using the blood and urine tests and both of them observing what diabetes in dogs looks like, like the course of disease. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | And then Banting would ligate the pancreatic ducts in other dogs, allow them to recover while their pancreas' atrophied, and then reoperate on these dogs, removing their degenerated pancreas' and extracting the internal secretion from them which he would then inject into the dogs that had been made diabetic from the complete removal of their pancreas. So it was late realized that the atrophy didn't need to happen but that was what they thought needed to happen first. |
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| Erin Allmann Updyke |  | Yeah. It's interesting that that part of it worked. |
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| Erin Welsh |  | I know. Well it didn't really work at first. Things got off to a really rocky start and it's really sad because a lot of dogs died in the course of this experiment and many other experiments especially after the surgeries which keep in mind, these were the days pre-Antibiotic. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | So they would just die of sepsis. |
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| Erin Allmann Updyke |  | Yeah, these are not good surgeries. |
|  |  |  |
| Erin Welsh |  | No, no. And in fact so many dogs died that they began to buy dogs off of the street because they had almost depleted the stored university dogs. |
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| Erin Allmann Updyke |  | Oh dear. |
|  |  |  |
| Erin Welsh |  | This would not fly nowadays, just FYI everyone. |
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| Erin Allmann Updyke |  | No, no. |
|  |  |  |
| Erin Welsh |  | IACUC would be like, 'Nope. You are getting your research whatever-' |
|  |  |  |
| Erin Allmann Updyke |  | Pulled. |
|  |  |  |
| Erin Welsh |  | Yeah. You're not allowed to do research at this university anymore. |
|  |  |  |
| Erin Allmann Updyke |  | Or any ever again. |
|  |  |  |
| Erin Welsh |  | Or any, yeah. But finally after many failures things began looking up. They were able to successfully extract the secretion from the pancreas, inject it into depancreatized diabetic dogs, and bring them back from the brink of death and out of a diabetic coma by rapidly dropping their blood sugar. This was thrilling. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And Banting was quick to see and believe in the potential of this extract for the treatment of diabetes in humans. But McLeod who was now back from his trip, he was urging a bit more caution. He was like, 'Alright, why don't we just try repeating these experiments first, making sure we have good sample size and we'll publish the results, see if we can refine the process and make sure that we know exactly what we're doing and that other people can replicate it.' |
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| Erin Allmann Updyke |  | Uh oh. I don't like where this is going by your tone. |
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| Erin Welsh |  | (laughs) There's so much drama it's absurd. And I won't even go into it all. So Banting was like I don't wanna have to wait for this but also he didn't really have a lot of bargaining power. Banting had been working these past few months on no salary, on no official position with the university, he was just sort of there and so he said to MacLeod, 'You know what? You're gonna pay me, you're gonna give me another assistant to take care of the dogs, and you're gonna have repairs done to the operating room.' |
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| Erin Allmann Updyke |  | Wow. |
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| Erin Welsh |  | And MacLeod was like, 'Okay you're asking for quite a lot and other research at the university would suffer if I were to give all of this to you.' And Banting's like, 'I am gonna walk away from this, blah, blah, blah.' And so MacLeod was like, 'You know what? Okay fine. You're right, your work does show promise, let's keep it going.' So this meeting might be where we first see the tension rise between Banting and MacLeod. And at this point Best was already aware of Banting's tendency to be scornful, disparaging, impatient, and quick to anger. He had been yelled at at least once for dirty glassware. But this might have been the first time that MacLeod saw it in action. And this meeting might also have been when the seed of hate was planted in Banting for MacLeod. Yeah, it's really a whole toxic story and toxic place. |
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| Erin Allmann Updyke |  | Yeah, oh my gosh. |
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| Erin Welsh |  | Yeah. But that seed of hate, it bloomed like wild that December of 1921 at the annual Physiological Society meeting. Banting and Best were due to present their research on the internal secretion of the pancreas which had progressed since the summer with the use of pancreas' from cow fetuses and then alcohol for extraction from whole fresh pancreas and things were ticking along and all of their results were pointing towards successful treatment of diabetes in the animals that they were working with. But at this meeting during his presentation Banting totally flubbed it. He was a terrible speaker, he stumbled over the results, and it got so bad that MacLeod had to keep stepping in to clarify something or to include a crucial detail that banting had left out and he answered questions. And then to add insult to injury or at least perceived by Banting, MacLeod kept saying 'we'. 'We extracted this' and 'we injected that'. Banting was fuming. There he was, I can only imagine just standing up there in front of the who's who of diabetes researchers in North America and basically not being able to string a coherent sentence together while your supervisor taking what is perceived to be taking all of the credit from you. |
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| Erin Allmann Updyke |  | I can 100% imagine that and it is so cringe. |
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| Erin Welsh |  | It is really, yeah. And so Banting, he wasn't the type to just silently fume, he was like ranting and raving to all of his friends. Like, 'MacLeod is a horrible person, he's stealing all of my results, blah, blah, blah.' It really became very bad and I will say in defense of MacLeod, anyone else who worked with him doesn't describe him that way. It seems like Banting was the only one to sort of accuse him of being incredibly territorial or taking credit or stealing credit. So anyway, I don't wanna get too much into the whole... |
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| Erin Allmann Updyke |  | Inter-lab drama. |
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| Erin Welsh |  | Right. And at this point it was the entire lab. MacLeod had shifted gears, like these results were super promising and so MacLeod was like, 'You know what? Almost everyone in this lab is gonna start working on this pancreas problem.' And he also brought on eventually a visiting biochemist by the name of James Collip who was added to speed up the extraction and purification process. And so things were happening quickly now with the first human clinical trial in January of 1922. |
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| Erin Allmann Updyke |  | Wow. |
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| Erin Welsh |  | From April 1921 when Banting arrived to Toronto to the first clinical trial, January 1922. That's very fast. Too fast. So the first person to ever receive this pancreatic extract was Leonard Thompson, a 14 year old boy who on admission weighed only 65 pounds, whose hair was falling out, abdomen distended, breath smelling of acetone, and who was on a diet of 450 calories a day. |
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| Erin Allmann Updyke |  | Oh my gracious. |
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| Erin Welsh |  | On January 11th, Leonard received the first injection which led to a 25% reduction in blood sugar and a slight reduction in urine glucose but overall the results weren't super promising, especially since the impurities in the extract led to an abscess forming at the injection site. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So the trial was deemed premature and there was a rush to make a more pure sample, something that Banting took upon himself to make a competition with Collip who was like, 'This doesn't need to be a competition. Can't we just work on this?' |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Tensions mounted. Collip won, he found a better purification process and the new more purified extract was injected into Leonard with much better results on January 23. |
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| Erin Allmann Updyke |  | Oh wow. |
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| Erin Welsh |  | But a few days before then, before this injection happened, Banting and Collip had gotten into a fight that was at least verbal and possibly physical. |
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| Erin Allmann Updyke |  | Oh my. |
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| Erin Welsh |  | Because accounts differ when Collip walked into the room and announced that he A) fine tuned the purification protocol, B) was going to keep it a secret from Banting and Best and not reveal any part of it, and C) that he was going to file a patent on it under his name alone. |
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| Erin Allmann Updyke |  | Oh my gracious. |
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| Erin Welsh |  | And apparently MacLeod had okayed all of this. |
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| Erin Allmann Updyke |  | What? |
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| Erin Welsh |  | So then this led to I would imagine a huge yelling match among most if not all parties, Banting and Best and MacLeod and Collip, I mean the battle lines were very clearly drawn with those two groups, Banting and Best on one side, Collip and MacLeod on the other. And then a ceasefire of sorts came in the form of a signed agreement that none of them would patent the process and that they would have to be transparent with each other about research developments. They didn't become friends or anything but at least for now it seemed to have deescalated. But in any case the animosity and drama was there to stay. It wasn't going anywhere. |
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| Erin Allmann Updyke |  | Wow. |
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| Erin Welsh |  | Again I can't even get into it all. There's a great book I'll recommend where you're just like, 'What?! He said that?' Yeah. (laughs) And so beginning in the spring of 1922 the lab group began publishing their results but the important thing is that the popular press picked it up and that generated a lot of hype among the many people who lived with diabetes. It was in one of these first publications that was a big comprehensive one from April 1922 that the term 'insulin' was first used. And there's no record as to why or how they chose that word but it's based on the Latin root for 'island' referring to the islets of Langerhans. |
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| Erin Allmann Updyke |  | Okay, okay. |
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| Erin Welsh |  | It was clear to everyone in the field that this research marked a new era for diabetes research and treatment. It would certainly be a bad time for things to fall apart, wouldn't it? |
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| Erin Allmann Updyke |  | Oh Erin. |
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| Erin Welsh |  | So Banting had begun to drink heavily and several times decided, 'You know what? I'm quitting this whole thing, I don't wanna be a part of this anymore.' Until Best talked him out of it. And Collip on the other hand was having more lab-centric problems. He had lost the knack for insulin production, he couldn't figure out, he was like, 'Whatever I was doing before is no longer working for me and I don't know why.' |
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| Erin Allmann Updyke |  | What? That's weird. |
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| Erin Welsh |  | It's weird and it's bad because it led to this insulin famine among the people who had already received injections and were needing those to help regulate their blood sugar. And then MacLeod was simultaneously worried about the lives of the people who needed that insulin and he was also worried that someone else was gonna figure out the production process and patent it. And so even though MacLeod, Banting, and Best were reluctant to patent it on principle they wanted to stop other people from creating a monopoly and so they filed this type of patent that would prevent that from happening. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | MacLeod also realized that if they wanted to turn this insulin into an actually medical product that people could reliably get their hands on, they needed to get a pharmaceutical company involved which is how Eli Lilly came to be so closely associated with insulin. There was someone from Eli Lilly at that very first meeting and they were working very closely with the Toronto team to get the sole ability or license to try to manufacture this new insulin. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | But the drama of discovery, the incredible tension among the researchers, the difficulties in streamlining or fine-tuning the production process, all of these problems were overshadowed by the absolutely enormous impact that insulin was having on the lives of people with diabetes. A lot of accounts at the time describe the drug, describe insulin as miraculous and it's kind of hard to disagree with that. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Like a 16 year old boy brought out of a diabetic coma from an insulin injection, the first time that had ever happened. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | A bedridden child jumping around the room hours after being given insulin. Perhaps the most famous patient from the time was Elizabeth Hughes who was daughter of the US Secretary of State who kept journals of her life pre and post insulin. At the time of her first insulin shot, the 15 year old Elizabeth weighed less than 50 pounds, that's 22 kilograms, and she was close to death. A few weeks after receiving her first insulin shot she gained 10 pounds and a lot of health problems resolved for her and she went on to live a healthy and relatively long life. And there were a million more stories just like these. Insulin saved and continues to save so very many people from what was absolutely a death sentence. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | It kind of reminds me a lot of the stories of when antibiotics were first developed and first introduced. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And it was miraculous, it was coming back from the brink of death. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | It must have been unbelievable to witness. So who was responsible for insulin's development and who gets the credit? And are the answers to those questions the same? Well it depends on who you ask, right. If you ask Banting it was Banting with a little help from Best. If you ask MacLeod it was MacLeod, Banting, and Collip. If you ask Paulescu it was Paulescu. And if you ask the Nobel Prize Committee it was Banting and MacLeod. So in 1923 the two were awarded the Nobel Prize, Banting was only 32 at the time. |
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| Erin Allmann Updyke |  | Oh gosh. |
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| Erin Welsh |  | Yeah. At the time I think he was the youngest for physiology and medicine or whatever the grouping was at the time. |
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| Erin Allmann Updyke |  | Wow. |
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| Erin Welsh |  | But Banting was furious. He could not believe that his and MacLeod's name were both on the prize. |
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| Erin Allmann Updyke |  | Oh my goodness, this guy. |
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| Erin Welsh |  | He believed it should have been him and Best and so at first he was like, 'You know what? I'm gonna refuse this prize, I don't want anything to do with it.' And then eventually he was like, 'Actually what I'm gonna do is I'm gonna split it with Best.' And that's what he did. And MacLeod in turn decided that he was going to split it with Collip. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | I don't know who deserves it honestly. I mean does Paulescu deserve some credit? Absolutely. Sole credit? Probably not. Would Banting have gotten there without MacLeod or without Collip? Probably not. All these tensions and credit debates aside though, the important thing is that insulin was now available and just in the way that blood transfusions for hemophilia turned that disease from an acute to disease to a chronic one, insulin prolonged the lives of those with diabetes but it was also not a cure and the long term consequences of diabetes, particularly type 1, were emerging. Such as kidney disease and retinopathy and all the ones that you already discussed in the biology. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So I'm not gonna go through these next things in detail but following the discovery and production of insulin, a lot of other important developments occurred. Frederick Sanger discovered that insulin was a protein and described its structure for which he was awarded a Nobel Prize in 1958, his first of two. |
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| Erin Allmann Updyke |  | Ooh. |
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| Erin Welsh |  | Yep. And Dorothy Hodgkin whose name you might remember from our antibiotics episode and our radiation episodes. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So she used X-ray crystallography to work out the 3D structure of insulin. A lot of research focused on treatments of the long term consequences of diabetes such as kidney disease and ulcers and kidney transplants. And some really important work was done by Priscilla White on reducing perinatal mortality in people with diabetes by introducing sex hormones treatment which hugely increased survival of the babies. And there was yet another Nobel Prize for diabetes research co-awarded to Rosalyn Yalow in 1977 for developing the radioimmunoassay to measure the concentration of hormones like insulin, vitamins, viruses, enzymes, and lots more stuff in humans. Genetic engineering allowed for the mass production of biosynthetic insulin and I think we might've touched on that briefly in our E. coli episode, it was basically like engineering E. coli to just make a ton of insulin. |
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| Erin Allmann Updyke |  | Pump out insulin, okay. That sounds vaguely familiar. |
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| Erin Welsh |  | And then the threat of bovine spongiform encephalopathy in bovine-derived insulin then kind of pushed for this switch towards human insulin. And then insulin pumps were developed and since the 1970s they've shrunk in size considerably and increased their capabilities considerably. In 1979 diabetes was officially divided into two types: insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus, or type 1 and type 2 as they were called beginning in 1995. And in the late 1970s is also when gestational diabetes and what was called maturity onset diabetes of the young were also recognized. There have been too many developments to eve mention. This year, 2021, marks the 100 year anniversary of insulin and over that time diabetes has undergone a huge transformation in terms of our understanding of the disease and our ability to treat it. But the story isn't over because alongside these medical developments, diabetes was going through another kind of transformation in the 20th century, a social transformation if you will. Okay. Diabetes part two. I promise this is a lot shorter, I know I've been talking for ages. |
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| Erin Allmann Updyke |  | I have been enjoying it. |
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| Erin Welsh |  | Okay good. I hope that remains true. So I can only speak for the US or my experience in the US but in many things that I've read or seen on TV or have heard in the classroom, there's this sense that diabetes type 2 in particular is a personal choice with this tinge of morality surrounding it, similar in some ways to how STIs are talked about. Like, 'Oh you did these things so what do you expect? You deserve this, these are the consequences for your actions.' And this I think reflects a huge problem not just in showing a complete absence of empathy but also in revealing a general lack of understanding about the multifaceted nature of this disease and refusing to acknowledge the institutional drivers that increase the risk of diabetes. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So when I was prepping for this episode I read a book called 'Diabetes: A History of Race and Disease' by Arleen Marcia Tuchman where I learned that it's kind of always been this way, like there's always been sort of this, 'Oh well these are the consequences of your actions' or ' Oh this is a personal disease, this is something that you did.' Right? It's always been very much like a blame the individual or the identity of the individual kind of a disease with a particular trait or group at fault being the main thing that has changed over the decades. I had no idea before researching this episode but it turns out that diabetes started out as a quote "Jewish disease". |
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|  |  | In the late 1800s when the visibility of diabetes and other chronic diseases was increasing as infectious diseases declined, diabetes was literally given the name quote "the Jewish disease" in Europe because of the supposed high prevalence of the disease among Jewish people. And the reason for this high prevalence varied based on individual views of the person you asked or the person who is writing this article. It could be because of the long years of cruel persecution faced by Jewish people that led to high levels of stress or it was because they overindulged and ate rich foods or maybe it's cause they had a quote "nervous disposition". Or it was just a way of saying that this disease had foreign roots since the immigration of Jewish people from Eastern Europe was really high during this period. But whatever the perceived reason or stated reason at the time, this association grew global and it became entrenched in medical literature in the minds of practicing doctors for decades, so like from the late 1800s to a few decades into the 20th century. |
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|  |  | Yeah. Was there actually an association? I mean without any quality statistics from the time we can't say for sure but it seems unlikely. It seems that it was more bad statistics turned into common knowledge and then helped along by confirmation bias. Definitely citation needed moment. And that was a big problem, it just kept being repeated in the literature without any citation or citing someone who just said, 'It's really highly prevalent in Jewish people'. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And even if there were numbers in these articles, was the characterization of Jewish and non-Jewish even helpful? Was it meaningful? Both groups were very heterogeneous. So drawing those lines was really a way of kind of pushing a certain narrative, the way that you draw the lines is definitely like you have a bit of forethought about what statements you want to make when the numbers all kind of fall out, right. What's important to you about those divisions? |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And often as it is now but as it was back then, those divisions were a way of saying that something about your race or your background or your culture made you more likely to have this disease. And we see this theme, race presented as an explanation for disease, again and again in the history of diabetes with black Americans and Native Americans and Mexican Americans and so on. And certainly the use of racial categories in epidemiological studies can be very helpful but they're helpful for confronting and trying to understand institutional racism and inequalities in healthcare or access, not to further the myth of race as a biological construct. |
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| Erin Allmann Updyke |  | And yet, Erin. |
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| Erin Welsh |  | And yet, Erin. (laughs) Okay so from its reputation as a quote "Jewish disease" in the late 1800s, diabetes slowly began to be viewed as a disease of moral failing, especially in the years following WWI which were a period of economic growth, an increase in consumables, and big cultural shifts leading to culturally conservative people shouting that the increasing rates of diabetes were a sign of moral decay, of this gluttonous overindulgent society that has no self control. The shifting from a Jewish disease to a more general sign of moral decay or whatever also happened as more studies were done to show that there wasn't actually much of a difference in terms of stats. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And this moral failing or overindulgence or just the rate of diabetes had a class structure to it. Diabetes had shifted its reputation to one of middle and upper class and generally white people. In fact it was thought and published in medical journals that black people were immune to diabetes. |
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| Erin Allmann Updyke |  | What? |
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| Erin Welsh |  | It was literally in medical journals, 'Well they are known to be immune.' Same was said about Native Americans also. So why did people think they were immune to diabetes? |
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| Erin Allmann Updyke |  | I don't know Erin, why? |
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| Erin Welsh |  | We don't know for sure but we can speculate. It's likely that it had a large part to do with lack of access to primary care physicians or hospitals. So doctors just simply weren't seeing diabetes in black people because they weren't treating black people. And it's also possible that doctors simply were like, 'Well I'm not gonna test the urine of a black person because they're immune and I read that in the literature so there's no point in even testing you for diabetes.' But the reasons for this lower prevalence were given or written about in racist terms, right. Black people didn't have the quote "nervous strain" or quote "mental strength" for diabetes. |
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| Erin Allmann Updyke |  | What? |
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| Erin Welsh |  | I know! |
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| Erin Allmann Updyke |  | What does that even mean? |
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| Erin Welsh |  | Basically what I gather from this is that people wanted diabetes to mean whatever they wanted it to mean. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | They couldn't find a cause, they couldn't explain why it happened, and so then they looked around and thought, 'Okay, what is the narrative I want to push?' |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | I all had to do with just individual biases, societal biases, and racist ideals. Yeah. |
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| Erin Allmann Updyke |  | That's so weird, Erin. |
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| Erin Welsh |  | It is, yeah. It's all about the narrative. But then here comes another shift, right, another transformation of diabetes. So when actual statistics introduced in the 1920s showed that rates of diabetes didn't differ much between black and white Americans, but do you know what did? Mortality rates from diabetes. And another factor that contributed to the overall growing visibility of diabetes among black Americans was the increase in black medical doctors who wanted to help improve the health of the communities that they served. And what many of these doctors saw was also reflected in the stats from the time and also from today that as poverty increased, the rates of diabetes rose and that diabetes in general seemed to be on the rise. In the 1930s an estimated 0.5 million to 2 million people in the US were living with the disease and it rose to be the 9th leading cause of death in the US in 1936 which is up from the 27th in 1890. The development of insulin in the early 1920s helped out a bit with the management of diabetes but a lifetime of injections was still costly and long term effects were still present. And also since this is an episode of TWPKY I have to mention eugenics. So here we go. |
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| Erin Allmann Updyke |  | We're obligated. |
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| Erin Welsh |  | Eugenicists as you might guess were not a fan of insulin, saying that it would increase the numbers of unfit people in society. |
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| Erin Allmann Updyke |  | Saw it coming, Erin. |
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| Erin Welsh |  | I know. |
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| Erin Allmann Updyke |  | And it still hurts every time. |
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| Erin Welsh |  | Every time. But a huge problem with the eugenicists' arguments besides the fact that they're terrible and they were making judgements on who should or should not reproduce was that no one could predict who would get diabetes. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | That still is true today. The how of diabetes was beginning to be worked out but the why had not yet been answered and still isn't really fully answerable. |
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| Erin Allmann Updyke |  | Yeah. We'll get back to it, Erin. |
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| Erin Welsh |  | Well why did some people get it and others not? Why were we seeing an increase in the US? In 1962 James Neel thought he might have the answer. Have you heard of the thrifty genotype? |
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| Erin Allmann Updyke |  | Yeah! |
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| Erin Welsh |  | Okay. It's basically this idea proposed by Neel that this thrifty genotype would've helped early humans live through periods of unpredictable food availability. So we would store more fat in times of plenty to prepare for times of famine. But in the US and other develop countries where diabetes was on the rise, there weren't really these times of famine and so the thrifty genotype went from good to bad, it began to backfire. And at first this thrifty genotype hypothesis was just used to explain a global growth in diabetes prevalence but with recent reports showing a disproportionately high rate of diabetes among some Native American groups, it became used in this colonial narrative of quote "primitive" and quote "advanced" societies. |
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| Erin Allmann Updyke |  | Ew. |
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| Erin Welsh |  | And in this narrative some Native American groups were said to be more prone to develop diabetes because they were quote "primitive people" who were rushed into quote "modern living conditions" and they were unequipped to deal with the diet and lifestyle. |
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| Erin Allmann Updyke |  | That is such a mischaracterization of... Yeah, I can't. |
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| Erin Welsh |  | Yeah, yeah. It's quite the turn from diabetes as a mark of civilized society that was popular earlier in the century. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And the thrifty genotype hypothesis is not well supported at all I should note despite it continuing to be pushed by some people - ahem, Jared Diamond. But by couching the high prevalence of diabetes in certain Native American groups in biological or genetic terms or concepts it made and continues to make it possible for the government to ignore their own role in the cycle of poverty and the impact of displacement, genocide, and federal policies that lead to higher rates of disease, not just diabetes. |
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|  |  | Speaking of federal government, in the 1980s a nationwide study called the Heckler Report investigated racial and ethnic health disparities in the US. And what they found was that diabetes, specifically type 2 and mortality from diabetes occurred at disproportionately high rates among non white people. The report framed diabetes as a quote "disease of minority groups". It barely acknowledged the role that poverty played but rather it emphasized the racial and ethnicity differences and to some degree sex differences. This continued the long tradition of attributing diabetes to a moral failing or personal quality or to a certain racial or ethnic background. All the while ignoring the role that poverty and other factors like food deserts, like the ability to be active, all of these things can play. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Diabetes is such a nuanced disease but it seems as though somehow we struggle still to make sense of that nuance and present it in a way that is like oh okay, there are multiple parts to this story. So I've rambled on and on and Erin, why don't you bring me up to speed on what's happening with diabetes today? |
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| Erin Allmann Updyke |  | Oh I'll do my best, Erin. Let's take a quick break first. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | Why don't we just start straight in with the numbers and get right to it and then we'll go through advances in treatment and then hopefully answer a little bit more of your question of the why and how. Okay? |
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| Erin Welsh |  | Oh good. |
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| Erin Allmann Updyke |  | So according to the International Diabetes Federation in 2019 diabetes - and this is all types of diabetes of which generally 90% or so are type 2 and 5-10% type 1 and then gestational and the other types of diabetes account for the other percentages. So in 2019 diabetes caused 4.2 million deaths worldwide and 463 million adults, this is just adults between age 20 and 79 were estimated to be living with diabetes. And that number is likely to rise to up to 700 million by 2045 because both type 1 and type 2 diabetes have been increasing. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | And it gets a little worse. The true disease burden especially for type 2 diabetes is likely a gross underestimation because 1 in 3 people who have diabetes are underdiagnosed, that's over 200 million people. |
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| Erin Welsh |  | Whoa. |
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| Erin Allmann Updyke |  | Yeah. And then if you also account for all of the people who have impaired fasting glucose or what sometimes is called prediabetes, the vast majority of those people have no idea that that's what's happening inside of their bodies. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And a good proportion of those people may go on to develop type 2 diabetes. A little worse than that, while there's a lot of variation in both incidence and prevalence of both types of diabetes across the globe, like different prevalences in different areas, overall more than 80% of people currently living with type 2 diabetes are currently living in low or middle income countries which especially as we talk about the new developments in treatment poses additional challenges because most of these are unsurprisingly very expensive. |
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|  |  | And there are of course major economic and social hurdles for people living with diabetes in low and middle income countries but also across the globe including her in the US. For example, insulin prices in the US are truly an abomination. In 2018 a unit of insulin was $98.70 in the US compared to $8.81 in 32 other countries. And while diabetes is certainly not exclusively a disease of low income, when you consider not only the price of insulin but the price like I already said of so many of the newer and in some cases better drugs for type 2 diabetes that are also incredibly expensive, diabetes certainly contributes to the cycle of poverty across the globe. |
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|  |  | So that's all the bad news and I know there's a lot of it but there's at least some good news on the horizon. I usually talk about whatever's going on in terms of research and a lot of times I feel like I'm like oh well there's not much going on and it's depressing. But today I don't have a lot of very specific things to go over but that's because there's so much research going on in terms of diabetes that there's simply too much ground to cover which is amazing, that means that there's so many people working on so many different aspects of this. In terms of new treatments, when we look at type 1 diabetes in general, and I apologize if there's even newer things that I have missed but in general the treatment is still just insulin. And while that sounds simple, it's very complex to get regimens and know how much you have to give, etc. |
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|  |  | But some incredible advancements for type 1 diabetes or insulin-dependent type 2 diabetes is the development of continuous glucose monitors and like you mentioned, increasingly small and easy to use insulin pumps that can keep much tighter control of that glucose which can then prevent the development of complications. So that's incredible. When it comes to type 2 diabetes, oh my gracious. The number of new drugs, I think there's a new one every day and a lot of them like we kind of touched on before are touching on different mechanisms of diabetes control. So previously things were just working on increasing the amount of insulin that people secrete but now because we know that insulin resistance is a big component, there's other types of treatments that are targeting tissues to make them more susceptible to the effects. There's a lot of really cool stuff going on with type 2 diabetes treatment. |
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| Erin Welsh |  | Ooh, that's interesting. |
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| Erin Allmann Updyke |  | Yeah. It's very, very cool. There's also so much work being done to better understand the genetic components of both types of diabetes. So I want to kind of stick with that for just a moment and then we'll wrap up. So both type 1 and type 2 diabetes have genetic links but it's not like any of the genetic disorders that we've covered in the past where it's like a single gene, it's many different genes and it's not a strong genetic component for either type 2 or type 1 diabetes. But one of the biggest questions Erin that you kept asking me was the why, the how, especially when it comes to type 2 diabetes. And so like I mentioned, both type 1 and type 2 diabetes have a genetic component. Type 2 diabetes has a much stronger genetic component meaning if you have a first degree relative with type 2 diabetes, you are much more likely to develop type 2 diabetes yourself than you are if you had someone with type 1 diabetes to develop type 1. That make sense? |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So there's a much stronger genetic component to type 2 diabetes but it's not a single gene, it's very multivariate. And just like with type 1 diabetes there's also a huge amount of environmental components that go into the development of type 2 diabetes. And some of these are what are often called modifiable risk factors and these are factors in the environment that can change and that can lead to risk of diabetes. The things that we know that are the most strongly associated are sedentary lifestyle which essentially just means not getting a lot of physical activity throughout the day. Another is diet, so having a diet that's really high in sugars that are the kind you find in soda is really strongly associated with type 2 diabetes. |
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|  |  | And then the one that's cited the most frequently is obesity. So BMI is the indicator that we use to classify obesity and obesity in the US at least is considered a disease which is then also considered a risk factor for diabetes among other things, type 2 diabetes specifically. And BMI is not just in my opinion but also in my opinion not a good indicator of health, not only does BMI not take into account things like muscle mass or the distribution of adipose tissue whether it's central and around your organs vs on your legs and arms, etc. BMI also ignores so many of the social determinants of health that play into the overall risks of diabetes and so many other diseases. So BMI and obesity in general, it's not a good indicator. But in the literature it is considered a risk factor for type 2 diabetes. |
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| Erin Welsh |  | Mechanistically what is it about those things that causes insulin resistance and a faulty production of insulin? |
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| Erin Allmann Updyke |  | Yeah. And that is the question that we still absolutely do not know the answer to. But here's something exciting and it still doesn't address the question of why those risk factors then lead to this but I found a couple of articles that are really promising on the underlying mechanism before you even get to insulin resistance. And that is dysfunction in the brain itself. So dysfunction in the hypothalamus that was treated with a single dose of something called fiberglass growth factor resulted in mice in sustained diabetes remission, a single dose. So these papers were basically suggesting that what happens for whatever reason from this genetic susceptibility and these environmental factors is that the effect on the hypothalamus in your brain is to increase your body's set point for what is an okay level of glucose. |
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| Erin Welsh |  | That is super interesting. |
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| Erin Allmann Updyke |  | Isn't it fascinating? And so then by giving this dose of this FGF1, what they were doing was lowering back that set point to something more like 120 instead of 200 or whatever. So then your pancreas doesn't have to compensate to try and increase insulin because your brain is telling your body, 'It's okay to let my blood glucose get this high.' And your pancreas is like, 'No it's not, it's really not.' Again that still doesn't address this underlying question but it does give us a much better target for the mechanistic cause. |
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| Erin Welsh |  | Right. Did you come across anything about epigenetics? |
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| Erin Allmann Updyke |  | I mean epigenetics is a huge part of this. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | But no, I didn't read any papers about it and so I don't know what those mechanisms are. |
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| Erin Welsh |  | Oh okay. |
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| Erin Allmann Updyke |  | But with any of these like polygenic and gene and environment things, I think epigenetics plays a huge role. But I think too Erin, getting back to what you were saying in the last part of your history section is it's so important especially in a disease like diabetes when we're talking about things like these modifiable risk factors to not lose sight of the environment that we are in and the structures of government of our society that force us into this environment where we can't do physical activity because we're sitting at a desk at our jobs for 10 hours a day and then we're driving in our car an hour each way to work and then we can't afford to buy fresh leafy greens cause they go bad in 20 minutes in your fridge and also they don't taste that good. Like there are so many things that play into this, it's not an individual choice, it's so much bigger than that. |
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| Erin Welsh |  | Yeah it's a really multifaceted issue and discussion. |
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| Erin Allmann Updyke |  | Yeah. And again, BMI is a bad indicator. Yeah, don't get me started on that one. |
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| Erin Welsh |  | Yeah, it is. (laughs) |
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| Erin Allmann Updyke |  | So that is diabetes in brief. |
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| Erin Welsh |  | In brief. Short and sweet, we kept it nice, long and sweet. |
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| Erin Allmann Updyke |  | Yeah. Sources? |
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| Erin Welsh |  | So I will mention I basically relied on three books. The first one is 'The Discovery of Insulin' by Michael Bliss. I feel like it's a really well researched and even handed look at credit for the discovery of insulin and apparently there's also a miniseries about this story called Glory Enough For All, I think it's on YouTube. |
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| Erin Allmann Updyke |  | Okay. |
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| Erin Welsh |  | And then I also read as I mentioned earlier 'Diabetes: A History of Race and Disease' by Arleen Marcia Tuchman. And finally 'Diabetes: The Biography' by Robert Tattersall. |
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| Erin Allmann Updyke |  | Awesome. The vast majority of my biology for the first time in forever came from a single textbook so big shout out to 'The Principles of Diabetes Mellitus' by Poretsky, editor. And then a few other papers here and there for a little bit of specifics. And if you're interested in that brain glucose research I have two papers, one from Nature Communications 2020 and another from Diabetes that was from 2019. They were both really interesting but very detailed papers. And we'll post all of these sources from this episode and every episode on our website thispodcastwillkillyou.com. |
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| Erin Welsh |  | Thank you again so much Carla for coming on and chatting with us, we really appreciate it. |
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| Erin Allmann Updyke |  | Yeah, thank you so much. |
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| Erin Welsh |  | And thank you to Bloodmobile for providing the music for this episode and all of our episodes. |
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| Erin Allmann Updyke |  | Thank you to the Exactly Right network of whom we are very proud to be a part. |
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| Erin Welsh |  | And thank you to you, listeners for listening to this very long episode. |
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| Erin Allmann Updyke |  | Yay! It's a real doozy. |
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| Erin Welsh |  | It is. And thanks also especially to all of our supporters on Patreon, we love you and appreciate you. I mean the depth of our appreciation knows no bounds. |
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| Erin Allmann Updyke |  | Yeah. No bounds whatsoever. |
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| Erin Welsh |  | Okay well until next time, wash your hands. |
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| Erin Allmann Updyke |  | You filthy animals. |