Toni Pollin:

Seeing a genetic counselor can be useful if you have an extensive family history of diabetes, particularly if the people with diabetes in the family don't seem to have a lot of risk factors for more common types of diabetes.

Intro:

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Kenny Wong:

Hi everyone. Welcome to our next episode of the Genetic Counselors and You podcast. As some of you may already know, November is American Diabetes Month. The CDC Center for Disease Control and prevention estimated last year, that around one in 10 Americans has diabetes. And since November is a time when we often get together with relatives, some of you may be wondering how worried should I be about diabetes based on my family history. This episode will help to answer some of these questions.

Kenny Wong:

We invited Dr. Toni Pollin to share her thoughts. Dr. Pollin is an associate professor in the Department of Medicine Division of Endocrinology, Diabetes and Nutrition, and in the Department of Epidemiology and Public Health at the University of Maryland School of Medicine, where she also leads a PhD MS track in human genetics. She is a board certified genetic counselor and has a PhD in human genetics. Welcome Toni. And thank you for joining me today.

Toni Pollin:

Thank you for having me.

Kenny Wong:

So thanks Toni. And so maybe as a start, it would be helpful to share with the audience what diabetes is.

Toni Pollin:

So the simple answer to that, Kenny, is that diabetes refers to high blood sugar. The word diabetes originally referred to excess urine production. Usually when we say diabetes, we're talking about the group of disorders called diabetes mellitus, which literally means sweet urine, because the excess urine production is due to high levels of sugar in the blood and considered a disease because it can be lead to complications in both what are a microvascular complication. So it can lead to problems with the eyes and kidneys and nerves, and also macrovascular complications. It's associated with heart disease. And so that's essentially what it is. And it's a common disease and it happens, and it's in a crucial part of kind of what keeps us going because it's a problem in how we're regulating our main source of energy.

Kenny Wong:

Thanks, Toni. And you mentioned how common is it actually, and I've heard sort of type one and type two diabetes. I'm sure many of the listeners have heard these terminologies as well. Can you share how common it is and really what the differences are between these different quote unquote types?

Toni Pollin:

Sure. So diabetes is quite common in the United States. It's now at a point where it appears to be affecting more than one in 10 people among children, a bit lower, more like one in 400. And so, yeah, so there are different types of diabetes. And I think many people are aware of the classifications type one and type two. There are actually more than that. And even type two itself is multiple diseases. So just to give you a quick overview type one, diabetes is an autoimmune disease generally where the body's immune system turns against the cells and the pancreas that produce insulin, which are called the beta cells. And it usually affects children, but it can also affect adults, but because it primarily affects children, it was once also called juvenile diabetes.

Toni Pollin:

Type two diabetes, I'm going to kind of come back around on to, because type two diabetes is kind of diabetes that is not type one diabetes, but it's also not one of the other types that I'm going to talk about, but type two diabetes is kind of an umbrella term for diabetes that mostly occurs in adults, but can occur in children.

Toni Pollin:

So once it was called adult onset diabetes. Now it's called type two diabetes. And it's some combination of difficulty using insulin, which is called insulin resistance and some relative difficulty, but usually not complete difficulty producing insulin. And so those are sort of, kind of the main categories where we place that diabetes, but the way that the American Diabetes Association divides it, not into four types, but four categories.

Toni Pollin:

So the third category is called diabetes due to other specific causes. So this includes diabetes, where there is a very strong genetic component. We also have a category of diabetes called gestational diabetes mellitus, and that's where some people, strictly speaking, some women will only have hyperglycemia during pregnancy because pregnancy places people more vulnerable to high blood sugar.

Kenny Wong:

Well, thanks, Toni so it sounds like it's diabetes is common. You mentioned one in 10 in Americans. And also there are many subtypes or many types beyond the type one and type two that most listeners may be familiar with as well. So I think one of the other questions that obviously this podcast is focused more on genetics aspects is how do genes or founding history play a role in these different types of spot diabetes? I think you briefly mentioned certain types obviously will have a higher play on this. Can you elaborate a little bit more in terms of how it plays a role in all these different types of diabetes you mentioned?

Toni Pollin:

Absolutely. The overall answer is in a major way, but it's very different in each of the categories. So if we take type one diabetes, I mentioned that type one is generally an autoimmune disease. And there are actually been discovered to be about 50 genes where variants have been found to influence the risk of type one diabetes, but they don't necessarily cause it. They increase the risk. The most important is what's called the human leukocyte antigen of the major histocompatibility complex region, the HLA genes in type one diabetes. So there are certain genetic variants in the part of the genome that regulate immune response that make people more vulnerable to type one. There are also some of these that can protect people from type one, but it's some of these risk variants in HLA are considered necessary, but not sufficient.

Toni Pollin:

And so there's a great variability in whether people have these and whether they'll go on to develop type one diabetes. And we actually used to think that if a sibling had it, that identical twins even were not completely concordant. Your identical twin might have a 40% chance of having it, which is much higher than the general population. We actually now know, because we know the age of onset varies so much in type one diabetes, so it's very likely at some point in their life that an identical twin would get it, but it's very variable. Type two diabetes, like I said, it's a lot of different diseases but it has a lot to do with.... And so there are many different pathways that play into it. Type two diabetes, it turns out aggregates in families very much. And I think there's probably a couple reasons for that.

Toni Pollin:

One is that there are a lot of different genetic factors involved that influence how the body makes and uses insulin. And the other thing is that there are risk factors for type two diabetes that can congregate in families. So people who are overweight are not guaranteed to, but are more likely to get type two diabetes. So sometimes that can kind of increase how family history will play a role, but it can also potentially increase opportunities for intervention. And so that's kind of the genetics of type one and type two, even though type two is generally a later onset disease is actually overall. If you kind of look at somebody's family history, people with type two diabetes are more likely to have a family history than people with type one diabetes.

Kenny Wong:

Thanks, Toni. So going back to type one and type two diabetes, sounds like What you're saying is that for both type one type two, there are many genes that could be involved and other environmental factors as well. But in general, though, if your family has multiple relatives with type one or type two diabetes, that there will be a higher risk in developing that type of diabetes. Is that correct?

Toni Pollin:

That is correct. So having diabetes in your family influences your risk. Having a family history of type two diabetes influences your risk probably more than it does in type one. And I should mention, whereas there's kind of 50 genes with no involved in influencing type one, there's over 200 genetic variants that have been bound to influence type two diabetes. And then of course, if you have, monogenic types of diabetes then not only are you risk for diabetes, but you can start getting into really more specific numbers and prognosis information based on if you know what gene is affected in that family.

Kenny Wong:

Thanks, Toni. And just want to confirm too, if basically let's say I hypothetically have many relatives, a few uncles and cousins with type two diabetes increases my risk for type two diabetes, but not type one necessarily. Is that correct? So it's more around that type of diabetes...

Toni Pollin:

Not necessarily. Yeah, I mean, they really are different diseases on the one hand. On the other hand, diabetes is really... First of all, you could theoretically have multiple causes of diabetes. Within type two diabetes is a lot of different diseases. So there's a lot that we don't know about.

Kenny Wong:

That's helpful. Thanks, Toni. I think this leads into my next question well. What are the common questions that you hear from patients related to diabetes and specifically related to genetics or genetic testing around diabetes?

Toni Pollin:

Yeah. So I think some of them that you've said and really have started this, that people want to know if their family history is important. Obviously it is. Diabetes does run in families. It does have a lot of genetics to it. I think sometimes I've heard people say, well, how could that person have diabetes if they aren't overweight? And also sort of what does being overweight or obese or sedentary have to do with diabetes? The answer is that those things can be risk factors for developing type two diabetes because they're risk factors for something called insulin resistant, where for some people, the more weight they gain and the more sedentary they are, the less well that they process insulin to use it, to get the glucose into their tissues. And some people ask that. And so along with that, people ask is diabetes preventable, is it curable?

Toni Pollin:

And so that again depends on the type. Sometimes people like to simplify things and say that type two diabetes is a lifestyle disease. It is not. On the other hand, if there are these factors that can be minimized through lifestyle change. So some people have a very high genetic loading, if you will, for diabetes. They may have a lot of variants inherited from one or both parents that are increasing their predisposition to diabetes. And so they may get type two diabetes at a younger age or in the setting of a more active lifestyle. And then, there might be people who on the other end of spectrum might not have that much genetic loading, but if they have very strong other risk factors, then they may be vulnerable. And some people may have very strong risk factors.

Toni Pollin:

And so on the one hand, you can have a very simple message that excess consuming more energy than you need and not having enough activity are certainly big contributors, but they can prevent diabetes or delay diabetes in some people, but not in everybody. I guess the other question about people ask about is, is it curable? And I think we know now much more about how to treat diabetes and prevent its complications than we used to. And we know that trying to control blood sugar and keep it within those two normal ranges as possible.

Kenny Wong:

I see. Thanks, Toni. And I think this earlier, too, in terms of genetic testing. What are your thoughts around genetic testing? Is it useful? I understand that for certain types of diabetes, the monogenic ones where clearly, it may be useful, but what about for type one or type two diabetes? Is it useful for a consumer to consider this if they have a family history, quite a few relatives of type two diabetes, for example?

Toni Pollin:

Yeah, just to go in numerical order. I mean, I'll start with type one diabetes. So type one diabetes, there's really not currently clinically useful genetic testing. There are studies looking at something called a type one diabetes risk score, and there's also type two diabetes risk score that looks at a bunch of different variants to kind of stratify people into different risk groups. Again, not really being used clinically, but there are some studies that are kind of taking people who come from high risk families who might already have a relative with diabetes, looking at their genetics, looking at those antibodies. I mentioned, and, trying to see using that as kind of a predictor and also kind of to follow people to see if you can figure out like what are the triggers to increase the risk so really more useful on a research basis.

Toni Pollin:

There's some suggestion that this risk score, this kind of seeing, if you're more likely to have this autoimmune type one diabetes can be a first step to kind of help to figure out what type of diabetes you have along with other information, especially because testing for the other forms I talked about monogenic diabetes can be expensive. So it be sort of helpful as kind of a first step to see how likely you are to test for that. In type two diabetes, there also are risk scores available. In fact possible, there's a direct to consumer test available.

Kenny Wong:

Thanks, Toni. So I think just going back to type one and type two diabetes to what you mentioned earlier. So what I'm hearing is that there may be some tests available in the market right now that look at the risk of you developing these diabetes. But at this time you don't believe that this is helpful for the average consumer. It's more for research applicable for research at this time.

Toni Pollin:

Yeah, that's correct. With one caveat that I not have emphasized this enough, but most of the time, because many people don't know about these monogenic forms of diabetes, they can go underdiagnosed. So they can often be diagnosed as type one or type two. So this thing that's critical in thinking about family history is looking at what the family history looks like. And some combination of the person's individual diabetes history and what it looks like in their family could be a clue that actually this may be a type of diabetes that fits more into the monogenic. And so that can be, as I said, that babies who are diagnosed with type one diabetes, but actually probably have a monogenic form. If there's a family where maybe not everybody has this profile, but several people are getting what looks like type two diabetes, diabetes where there is insulin produced, but a lot of them are young, maybe in their twenties or early thirties and may not have other risk factors.

Toni Pollin:

Then you start to wonder, well, it's really looking like it's running in the family the way a dominant genetic disease would. Then you start to wonder, well, maybe all these people don't have type two diabetes. Maybe the family history is telling me something else is going on. Again, most of the diabetes is type two diabetes, but there are these kind of a atypical situations that are challenging to tease out, but are important to be aware of because they could have strong implications.

Kenny Wong:

Thanks, Toni. So you mentioned challenging situations. So when would it be appropriate for someone to speak to a genetic counselor so that there's more help in determining where their family history is more complicated than it seems to see whether additional testing is needed, for example?

Toni Pollin:

Seeing a genetic counselor can be useful if you have an extensive family history of diabetes, particularly if the people with diabetes in the family don't seem to have a lot of risk factors for more common types of diabetes. So a lot of type two diabetes, where people are not necessarily getting at older ages or particularly overweight. So type two diabetes in people who are young and lean, that can be a sign. As I said, anytime, there's a baby in the family who gets diabetes before the age of six months and people who have an unusual presentation of diabetes. And so there are examples and there are websites that we'll send you to with more specific lists. But mostly we think about it in a child who has diabetes, but it's not consistent with being type one diabetes. They don't require insulin, or maybe they went off of their insulin for extended period of time.

Toni Pollin:

That can be a clue, especially if they don't have the antibodies that are associated with autoimmune diabetes, people with type two diabetes, who again, don't fit the profile of type two diabetes that we often expect, but really it's useful to speak to a genetic counselor. And what I'd really like to emphasize is if you have diabetes and you want to investigate the possibility of genetic testing because you think it may be one of these unusual, well, but highly genetic forms of diabetes, then it would be good to not only speak to a genetic counselor, but to try to engage a genetic counselor with your diabetes provider and kind of a collaborative approach to trying to diagnose and figure out if there might be something going on in you or your family that's different from the more common types of diabetes.

Kenny Wong:

Well, thanks Toni, for joining us today and sharing your experience with the listeners. Do you mind sharing a few takeaways that you would love the audience in general to be aware of related to diabetes?

Toni Pollin:

Sure. The main things I think to be aware of is that diabetes is very common, and it's now affecting more than one in 10 Americans and probably about one in 400 children. And also diabetes is not just one disease. It's many different diseases that are defined by high blood sugar, with different causes. So we talked about one diabetes, which is an autoimmune disease, often occurring in children, but also adults. Type two diabetes is kind of a diagnosis of exclusion with a variety of causes. You have diabetes that's due to other specific causes that includes these highly genetic monogenic forms of diabetes and some other types that we talked about. And then there's also this category of gestational diabetes. And then finally, what I hope people take home from this is not in everybody, but in some percent, probably one or 2% of individuals with diabetes, genetic testing can really profoundly influence how the diabetes is treated and the outcome.

Toni Pollin:

And then easy to remember saying, but it's hard to remember because it's a rare situation is that diabetes is diagnosed before the age of six months, then genetic testing should be done. That individuals with atypical features, and so they could consider going to a genetic counseling or a diabetes genetic specialty. When you see kind of non insulin requiring non autoimmune diabetes in young people. When you see what looks like type two diabetes occurring in young, non overweight, non obese individuals with a very clear, dominant inheritance patterns. And then also others who that should think about it are people with other congenital conditions that might along with the diabetes, make up a syndrome where it's important to know that in order to think about what other conditions they might be a risk for.

Kenny Wong:

And thanks, Toni. Just so that the listeners are familiar with congenital conditions, can you share one or two examples of something?

Toni Pollin:

Yes, yes. So this can again be tricky too because some of these conditions can be complications of diabetes. But for example, there's some type of monogenic diabetes where people have both from birth, they might have cysts in their kidneys or other abnormal to their kidneys or other parts of their urogenital system. There are certain syndromes where diabetes is accompanied by hearing loss or vision loss that's all kind of present very early, like from birth or close to birth. So rather than being a complication of the diabetes, it's kind of occurring in parallel. That's really what I was talking about there.

Kenny Wong:

That's helpful. Thanks, Toni. Well, thanks again for your time today. And hopefully our listeners have lot of information absorbed, and we'll also share resources online as well that Tony was nice enough to share with us.

Toni Pollin:

Thank you very much for Kenny and the NSGC for having me on the podcast. I'm delighted to share this information.

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