

Episode 40: Diabetes in Children

Dr. Rita Kalyani, MD: Welcome to Diabetes Deconstructed, a podcast for people interested in learning more about diabetes. I'm your host, Dr. Rita Kalyani at Johns Hopkins. We developed this podcast as a companion to our patient guide to diabetes website. If you want a trusted and easy to understand resource for diabetes or to listen to previous podcasts, please visit hopkinsdiabetesinfo.org.

Today, we are thrilled to welcome two colleagues in Pediatric Endocrinology, Doctors Sheela Magge and Risa Wolf, who will be speaking with us about diabetes in children. Dr. Magge is a professor of pediatrics and Lawson Wilkins Endowed Chair of Pediatric Endocrinology at the Johns Hopkins University School of Medicine. She is the director of the Division of Pediatric Endocrinology and Diabetes at Johns Hopkins and a clinician investigator dedicated to improving the lives of youth with type 2 diabetes, obesity, and the cardiovascular complications of these conditions. Dr. Magge has been continually funded by the NIH for the last 16 years. She is currently PI of an NIDDK R01 examining how differential body composition can impact cardiometabolic risk and is also the Johns Hopkins Principal Investigator of the U01 Discovery Study, a longitudinal cohort aimed at understanding and targeting the pathophysiology of youth onset type 2 diabetes.

Dr. Risa Wolf is an associate professor of pediatrics and the director of the Pediatric Diabetes Program at the Johns Hopkins University School of Medicine. She's an NIH funded investigator with research focused on using innovative technologies to improve outcomes in pediatric diabetes. Dr. Wolf is the principal investigator of the ACCESS trials, implementing autonomous, artificial intelligence, diabetic retinopathy screening in the pediatric population. She's the founder and medical director of Camp Charm City Diabetes Camp, a collaboration with the American Diabetes Association to improve access to diabetes camping for underserved youth. Thank you both for being here, Dr. Magge and Dr. Wolf. We're so excited to have you.

Dr. Risa Wolf, MD: Excited to be here.

Dr. Sheela Magge, MD: Thanks for having us.

RK: Diabetes in children has been getting increasing attention, over the past few years and we're really looking forward to having you shed some light on what is going on in this area. First, I was wondering if you could tell us how common is diabetes in children and what are the different types of diabetes in children that can be diagnosed?

SM: There are two major types of diabetes and a few more rare causes as well. The most common type of diabetes to happen during childhood is type 1 diabetes. It used to be called juvenile diabetes, but we don't use that name anymore. It's caused by the body attacking its own cells that make insulin, and those kids do not make enough insulin. The other type of diabetes we are seeing more and more of is type 2 diabetes during childhood, which used to be seen almost always in adults. But with the increases in pediatric obesity, as well as other environmental factors, we're seeing more and more during childhood. There are some other, more rare types of diabetes, but I think for the purposes of today, we can focus on those two. And maybe Dr. Wolf can talk a bit about how common they are.

RW: Absolutely. It's estimated that there are just over a million children worldwide with type 1 diabetes. And that translates to about one in every three to five hundred kids will have type 1 diabetes. Type 2, as Dr Magge said, historically was very rare in kids, but has been increasing significantly in the incidence and prevalence and now accounts for approximately 5 to 10% of all kids with diabetes, but about 50% of new cases in adolescence, so in the teenage years, and accounts for essentially one in every 1000 or 2000 kids. And in general, for both type 1 and type 2, the incidence has been

increasing really over the last two decades. At a very steady rate, a slow and steady rate for type 1, but really at a much higher rate for Type 2 diabetes is estimated as the incidence has increased by 30% over the last decade or two.

SM: And it seems to be increasing year over year. The most recent data from the search for diabetes in youth study shows if you adjust for race age, sex, An incidence increase of about 4.8% per year increasing for type 2 diabetes during childhood. And it seems to affect much more commonly youth of color or racial and ethnic minorities with increased prevalence in our African American, Hispanic youth, Asian youth and Native American youth as well. Although in certain populations, it's more rare, it's more common in others.

RK: That's so amazing to hear about; the changes in the patterns really of the types of diabetes in children. And it really sounds that while both types have been increasing, type 2 diabetes has just taken off in terms of the numbers of children, especially in adolescents, it sounds like being diagnosed.

Dr. Wolf, I think you mentioned that 50% of new cases in adolescents are type 2 diabetes. And that seems pretty remarkable when you think about, as recent as a decade or a few decades ago; were we even talking about type 2 diabetes back then? What has caused this increase, especially in type 2 diabetes over the past few decades?

RW: It's interesting because if you look at the diagnosis of adolescence two decades ago, in the early 2000s, the numbers that are reported in literature are less than 3% of cases were type 2. So now we're seeing if it's an adolescent, it's a, a 50, 50 chance it's type 1 or type 2. The biggest factors that have contributed to the type 2 increase have really been the obesity epidemic; changes in lifestyle, more sedentary behavior, unhealthy diet, and then, really just all contributing to, obesity that we're seeing in childhood.

And, even before type 2, there's also been an increase in prediabetes. It's estimated that one in every five adolescents will have prediabetes. There really has been a tremendous increase. With type 1, it's been a little bit of a slower sort of slight incline, but the sort of contributions to that might be just the genetic predisposition. Obviously, if you have a family member with diabetes, you're a little bit more likely to develop type 1 diabetes. There might be some environmental risk factors that are really hard to pin down, but just this sort of trend in the autoimmune disorder that we're seeing with type 1.

SM: By and large, during childhood type 1 is the most common type of diabetes. When you think about the percentage among teens, I think it's important to look at the population that you're looking at. In some parts of the country, it's going to be mostly type 1 and that's true, across the board. I would say, though, that if you look at certain populations, like Native American kids, where you see much higher prevalence of type 2 diabetes, and if you're looking at a very ethnic and racially diverse population, like we have in Baltimore, among older teens, we see more, we still see a lot of type 1, but you have increased rates of type 2 in those populations. I think one thing that people also can get confused about is the genetics of it. So, for a child with type 2 diabetes, generally 75 to 100% of those kids have a 1st or 2nd degree relative with type 2 diabetes. Whereas with type 1 diabetes, we often get kids diagnosed with diabetes where families will say nobody in our family has it, right? And even if a parent has type 1 diabetes-- it's in the range of 5% chance that the child might get it. The genetics are complicated and play a role in both. As Dr. Wolf said the environment is a big part of why we think youth onset type 2 has been increasing. And that's really complicated and can be difficult to change.

We try as much as we can not to put blame on anybody because much of it's the built environment. All of us are walking less. All of us are eating more processed foods. If you look, when you go to the grocery store, the least expensive foods are the processed foods. How expensive is it to buy all those when you go to the salad bar? That's more expensive than going and buying a cheeseburger. I think it's very complicated. And when we see these kids, we try to take the blame out of the situation and see how we can work with them to see what personal goals we can set with them, what they can change in their lives as individuals.

RK: Yeah, I think it's interesting what you both talked about that. This is a general societal trend, right? It affects people of all ages that increase in obesity, that decrease in physical activity. The accessibility of more processed foods, especially when finances might be limited. All of these things really impact risk at any age. But it is interesting that now we're seeing that age of onset, especially for type 2 being pushed down even lower into those childhood years. What is the average age of onset for type 1 versus type 2 diabetes in children?

SM: Type 1 diabetes often happens during preschool years or adolescent teen years. Those are the two times that you often see. In youth onset type 2, it's largely a phenomenon that's seen during puberty. During puberty, our body makes growth hormone, which causes increased insulin resistance. It's just physiologic-it's a normal part of all of us growing up. And what that means is that our body makes insulin, but it is harder for that insulin to work. So whatever we eat, our body makes insulin and brings blood sugar back down to normal after it increases when we eat. So if you have insulin resistance, that insulin isn't working as well. So your body tries to make more and more insulin to keep that blood sugar down.

We have a physiologic increase in insulin resistance during puberty. It's never every single person, but by and large, this is a phenomenon we see as people start entering puberty. We've had kids as young as 8, but girls can start puberty at age 8 also. Puberty is the key part of it, usually it's teenage years,

RK: That's really interesting to hear about the spectrum that type 1 might be more of the preschool early adolescence and type 2 really in the adolescence late teen years.

Dr. Magge, you mentioned ethnic minorities as being populations where we've been seeing increasing numbers of type 2 diabetes, and you talked about insulin resistance as well. I know this has been a focus of some of your research. I wonder if you could just talk briefly about how that relates to body mass index or obesity in children. How is that measured in children? We know the cutoffs in adults. We talk about them often in terms of BMI of 25 to 29. 9 in the general population for overweight and 30 and above for obesity, maybe lower in Asians. But how do you define obesity in children?

SM: Kids are growing, and so we don't have absolute cutoffs as they do in adults. For kids, we go by the BMI percentile. There are percentiles for age and sex. Most of your listeners out there are probably familiar when they take their child to the doctor, their pediatrician, they'll be plotted on a growth chart. And there are good charts for height, for weight, and for BMI or body mass index. Generally, a normal BMI is between the 5th and 85th percentile, 85th to 95th is considered overweight. And greater than or equal to 95th is considered consistent with obesity. And, those terms, I tell families, sometimes they'll hear these terms, and I don't want them to feel labeled or stigmatized by them. They're more epidemiologic terms. So that when you look at populations and various cutoffs, we can define what groups are at higher risk for medical complications. We even have a cutoff for what's called severe obesity of greater than the 99th percentile. Or you can get more complicated about greater than the 120th percentile of the 95th percentile. It's BMI percentile to answer your question, but BMI isn't everything for sure. And in terms of type 2 diabetes, very much, just anecdotally, I will say that I many times have patients that I see who may not have as much excess weight as another patient,

but their parents were diagnosed with diabetes in their 20s [or] 30s. Those kids show up with either prediabetes or diabetes much sooner and then sometimes I have kids that have a lot of excess weight, but they might be metabolically okay. So the genetics does play a role, environment plays a large role, and BMI is not a perfect measure. If you have somebody who is an athlete, a runner, a bodybuilder, they could have a lot of muscle mass that can throw off your BMI. And actually, when you mentioned my research, a lot of my research has to do with body composition and how different areas of fat accumulation can affect your risk. We know that some populations accumulate more fat inside, centrally around the belly and around your internal organs, which is considered to be more metabolically unhealthy compared to subcutaneous and lower fat around the thighs and such. Sometimes there are genetic predispositions, ethnic racial predispositions. So, all of that can play a part as well.

RK: It sounds like the risk factors for type 2 diabetes in children are very similar to those in adults, but perhaps defined in different ways. For obesity, looking at percentiles or where children might fall on their growth curve in respect to other children of their age. And also, the family history, ethnic minority status, physical inactivity. As an adult endocrinologist, these are things I often talk about with my patients as well. With type 1 diabetes though, Dr. Wolf, are there risk factors that parents would know about to look out for? You mentioned that not everyone, in fact most, may not have a relative with type 1 diabetes. What are the risk factors, in contrast, to type 2 diabetes that we might look for in type 1 diabetes

RW: If you have a family history of any autoimmune disorder, it could be something that you might think about as a risk factor for type 1 diabetes. Oftentimes we'll see families where there's a lot of people with thyroid disease or celiac. Any of these sorts of autoimmune disorders can be a risk factor for other autoimmune disorders like diabetes. That's one thing to think about. Obviously having a family member or, we talked a little bit about not having a family member, but if you do have a family member, you are at increased risk and the risk is probably up to about 5% compared to, probably less than 1% in the general population.

There is now the first medication that has been approved to delay the onset of type 1 diabetes was FDA approved last year. Because of that, people are starting to look a little deeper into finding out when people are actually at risk for developing diabetes. There are several research studies or other statewide initiatives that if you have a family member with type 1 that you can screen other family members for the diabetes antibodies that might be present and indicate that you are at risk.

And then if you're found out to have at least two of these antibodies. It means that you are your risk of developing type 1 actually in your lifetime approaches almost 100%. With that we know that having two antibodies for diabetes is a risk factor and it's something that we actually will follow kits for just so that it's not a sudden onset of clinical symptoms when type 1 diabetes does actually develop.

We call this an early stage of diabetes. We provide anticipatory guidance or advice to families of symptoms to look out for, which would be peeing a lot, drinking a lot. I always tell families to think about what about at night? You hear the child getting up in the middle of the night to go to the bathroom. Are they coming to you and asking for a drink in the night? Because that's not typical. You might be eating more, but also losing weight or just seem a little bit more tired. And those are some of the symptoms that we guide families to think about and to look out for that we would know type 1 diabetes onset is imminent; that risk for autoimmunity, and having a family member, and then this opportunity now to actually get screened to find out if you're at high risk. And in addition to the one FDA approved medication that potentially can delay the onset there are other clinical trials that are ongoing around the country. They are looking at other interventions to try to delay the onset, if not prevent the onset of type 1 diabetes.

RK: Thanks for going over those exciting trials and having that approval for early stages of type 1 diabetes over the past few years. It's just so exciting. You did mention some of the symptoms, so thanks for going through those. The symptoms of diabetes tend to be similar, wouldn't you say, between type 1 and type 2, but are there specific symptoms that in a child, parents should be thinking about that might be different than adults?

SM: I think as Dr. Wolf said they are, urinating excessively, drinking excessively, weight loss-- those are similar.

I think a couple things are a little bit more problematic. For example, if you have a teenager who is overweight, and they're trying to lose weight, but they're drinking a lot, urinating a lot and losing weight, a family member might be happy that they're losing weight, but it's losing weight for the wrong reasons. They're actually losing a lot of calories through their urine. So I would say that drinking a lot, urinating a lot is important to keep an eye out for. Dr. Wolf mentioned that, in type 1 you're trying to avoid having children present really sick. There's a condition called diabetic ketoacidosis where kids can get very sick and hospitalized, often in the intensive care unit for that. Whereas in adults, generally, they don't really see that onset happening with type 2 diabetes. We do see that in youth onset type 2 diabetes, which kind of leads me to one of the big differences between type 2 diabetes in adults and in childhood. The most recent data has been somewhat frightening in that youth onset type 2 diabetes, glycemic control seems to deteriorate faster and children seem to develop complications quicker than in adults and can even have complications on diagnosis. That's why when we diagnose kids with type 2 diabetes, we are quite aggressive with treatment. Sometimes I have parents saying "why is my daughter on more metformin than I am?" And it's for this reason, we want them to live a very long, happy, healthy life.

The "Today study" was the only clinical treatment trial for youth onset type 2 diabetes. We've been able to learn a tremendous amount regarding type 2 diabetes from that. One of the disturbing factors in their complications follow up was that as these kids grew up at an average age of about 26 years when they had diabetes on average for about 13 years, 60% of them had at least one complication, and 28% had at least two complications. That's really significant, much worse and more rapid than we see in adults.

RK: Wow, that is certainly alarming! You know, even after 10 years of diabetes in adulthood, with proper preventative measures, we may not expect to see that high burden of complications. Do you think those numbers reflect not having that aggressive identification and treatment of diabetes early on? Or do you think there's something about being diagnosed at a younger age that puts individuals at a greater risk of complications?

SM: I'm not sure that we know the answer because for the same duration of diabetes, youth onset type 2 seems to have more complications, not only than adult type 2, but also of pediatric type 1. We don't know why, and that's why there's a lot of research going on in this area to find out.

It seems like the cells that make insulin, the beta cells, you have a deterioration of their function faster. So it seems to happen at a much more rapid rate during childhood. But we also wonder whether other things could come into play, like social determinants of health, systemic racism, poverty, all these things, because youth onset type 2 diabetes not only disproportionately affects our ethnic and racial minorities, it also disproportionately affects kids of all ethnic and racial backgrounds who have socioeconomic stressors. Some of the research that we're doing now is having to do with social determinants of health and how they can impact your physical health and might play a role. It's a question that we don't really know the answer to.

RK: It sounds like irrespective of the type of diabetes in childhood, the risk of complications is really the primary driver of why we focus on identifying and treating so soon, and that's a very high-risk population to begin with. Dr. Wolf, you talked a little bit about antibodies and testing, and I wonder if you could go into a bit more detail about how we diagnose diabetes in general, and what additional tests might be done to differentiate type 1 diabetes from type 2 diabetes in children.

RW: Type 1 diabetes is typically diagnosed when a child presents with clinical symptoms, and it's usually made with onset of symptoms, and those symptoms we talked about urinating more frequently, being more thirsty, losing weight, but eating more, and at that time that would generally prompt a physician or provider to check the child's blood sugar. If the blood sugar is elevated, then it might indicate that there is diabetes. The other tests that we typically do are something called the "hemoglobin a1c," which is essentially a measure of your average blood sugar over the last 3 months, and it gives you an indication of what that is. An A1C level that's over 6.5% is diagnostic of diabetes. Both type 1 and type 2 use the same cut off. That's typically the tests that are done when somebody is newly diagnosed with type 1, or you suspect that there might be type 1 diabetes. We do other tests at the time of diagnosis to screen for other autoimmune disorders to see. One of the things that we can use to help us – a great example of an adolescent who's overweight, who's presenting with diabetes and sometimes it's not really clear whether they have type 1 or type 2. Typically, the symptoms of type 1 are usually happening more acutely, meaning that they happen, and then deterioration is more rapid, whereas with type 2 diabetes, sometimes it can be a very long-standing slow process but it's hard for people to recognize those symptoms. One of the tools that we have to help distinguish between type 1 and type 2 are these diabetes antibodies that I mentioned earlier. They are typically present in type 1 diabetes, and there are 4 that we can send as a lab test and do when somebody is diagnosed. It is possible to have type 1 diabetes and not have any antibodies and that makes up about 10 - 20% of the type 1 diabetes population. And the flip side is also true that you could be somebody with type 2 diabetes, and about 10 - 20% of them will have some very mildly elevated or abnormal type 1 diabetes antibodies. So that makes it a little bit complicated, but we generally use these antibodies to help guide us to distinguish between somebody with type 1 and type 2, particularly if it's an adolescent, which is when it becomes a little bit trickier to figure out. Usually, younger kids [who are] pre-pubertal are going to be type 1 and it's not an ambiguous thing to determine at that point.

SM: Also, since 20% of children are overweight or have obesity, and we know that type 1 childhood diabetes is much more likely to be type 1 than type 2. You are going to have many kids with type 1 that just happen to have excess weight as well.

RK: It certainly sounds like it can be challenging to make the diagnosis of which type 1 versus type 2. In adults, we are recognizing that type 2 diabetes is the most common, that type 1 diabetes can also be seen. And as you mentioned, Dr. Wolf, sometimes it's not as acute as it is in children; they may not present with that complication ketoacidosis right away. But it's interesting that in childhood, from what I'm hearing, it sounds like it can be quite a focus to try and figure out whether it's type 1 or type 2, especially with this rise in type 2 diabetes that's being seen in childhood and that sounds like it's an important point both for families to be aware of and also health care providers to be aware of that really the symptoms and the signs can be confusing and it may perhaps take a few visits, wouldn't you say, or it might take a little bit to figure out which one it is.

RW: Sometimes it takes us a little bit of time away for the antibodies to come back. Sometimes we'll also monitor what the insulin requirements are. If the lab results are indeterminate for the antibodies, sometimes it just means that we have to look at how much insulin somebody is using and needing to maintain blood sugars in the goal that we set. That is really established by the American Diabetes Association and the Pediatric Endocrine Society for what we want our goals to be. Needing a lot of

insulin won't even help us figure it out. But if you need less insulin, sometimes it can help us determine which one it is. But it still can be challenging.

SM: And I will say that because type 1 diabetes is not only more common, but those kids need insulin to survive. So, if we have somebody in the hospital who's sick, we treat them as if they have type 1, and then if it becomes, the labs come back, and it becomes clear they don't, it's an easy kind of transition. But we wouldn't want to do the reverse, and not treat somebody with insulin when they need it.

RK: Yeah, that makes a lot of sense. You talked about treatment, and I wonder if this would be a good juncture to kind of shift to talk about what are the treatment targets in terms of glucose goals and both type 1 and type 2 diabetes. Are they the same or different? Then the medications we know the medications that are used or are similar, but as mentioned, type 1 tends to be insulin and type 2, there may be other options. So, I wonder if you could talk a little bit about treatments for type 1 diabetes and then type 2 diabetes.

RW: For type 1 diabetes, the treatment is insulin, and you really cannot survive without taking insulin. Insulin is generally provided as an injection. When children are newly diagnosed, they're usually doing that with shots that they have to do generally four to five times a day, sometimes more. The only way that we can give insulin is as a subcutaneous injection. That would be something that you can do at home.

We do have insulin pumps, which are a small device that holds a cartridge of insulin and can be programmed to deliver insulin. As a substitute for doing shots every day, you can put a pump on and then tell the pump to deliver the insulin the same four to five times a day that you would do with an injection. A lot of our children choose to do this because it's a lot easier to put a pump on and change your pump site every three days. It's one needle every three days as opposed to five a day. So many will choose to do that. Then the other component of the diabetes management is glucose monitoring. At minimum, you need to know what your blood sugars are at least five times a day- before every meal, bedtime, and often in the middle of the night. We recommend checking to make sure that the blood sugar is not going low. Checking a blood sugar takes a few minutes when you're using a meter and a little test strip and, pricking your finger. So, we also have continuous glucose monitors, which are very small devices that have a very tiny wire, the breath of two hairs, that sits under the skin and gives a reading of the subcutaneous blood sugar. Those machines, the continuous glucose monitors, can read out a blood sugar every one to five minutes, depending on the brand of device that you're using. This allows continuous monitoring and measurement of blood sugars to help guide the insulin treatment and help us keep our children in the goal blood sugar range, which is set to be between 70 and 180 (mg/dL) for the target goal blood sugars for the day. It is possible that people will have blood sugars below that and above that, but our general recommendation is that we try to achieve about a 70% time and range between that 70 and 180 (mg/dL).

That's not possible for everybody and it can be challenging to reach that goal. It's easier if you use a hybrid closed loop or automated insulin delivery system, which means that your CGM and your pump talk to each other and the pump insulin delivery will automate adjustments to the insulin delivery, which can help you achieve a time and range close to 70% or greater. But if you're on injections, sometimes it's more achievable to reach a minimum of 50% time in range. But those are the goals that we set because the goal is to try to keep the A1c below 7% for children with type 1 diabetes, because we know that if we do that, we can prevent the complications of diabetes, which, include eye disease that can lead to vision loss and blindness; neuropathy, which is nerve dysfunction, so you don't really

feel things as well as you should; as well as kidney disease. Those are some of the most common, what we call microvascular complications of diabetes and we want to prevent that. We don't want any of our kids to end up with any of these complications. So, we as a diabetes team, work very hard to help our families achieve the goals set forth really by the American Diabetes Association to try to keep the time in range at the goals that we would like.

SM: And I would just echo, when Dr. Wolf talked about some of these technologies, they've really been game changers for families with type 1 diabetes. For example, the glucose sensors, oftentimes I would hear stories of parents would be up all night checking their child's blood sugar because they were afraid that they would go low and have a seizure. And when I was a fellow, we'd get calls about somebody heard rattling, and they went and ran into the room and the child had a seizure. Having a monitor that's going to alarm has allowed many families to get a lot more sleep and improve quality of life significantly. So, the technologies that Dr. Wolf mentioned are really life altering, I think, for our families, because having type 1 diabetes really is a big adjustment for everyone. In terms of treatment for type 2 diabetes, it depends, at what point they present themselves to medical attention. As Dr. Wolfe said, our target is to keep the A1C less than 7%. But I try to, if possible, eventually get it even much lower than that, or as close to normal as possible, because we know that beta cell function seems to deteriorate quickly, and we want them to live a long and happy, healthy life. And in addition to those microvascular complications, we worry about things like stroke and heart attack in the future. If you think about somebody having type 2 diabetes as a 70-year-old and when they're going to have complications, if I have a 10-year-old patient with type 2 diabetes, are they going to have a heart attack in their 30s? We don't want that to happen. So, we are quite aggressive. If somebody presents with an A1c that's quite high, like over 8.5%, we will often start insulin first. That is to quickly bring down the blood sugar. We also, at that point, might not know whether they have type 1 or type 2 and quickly bring down the blood sugar because having high blood sugars also has a toxic effect on some of the different metabolites in the body. And we allow the beta cells, the cells that make insulin to get a rest. But then we know, if somebody presents with a lower hemoglobin A1c in that setting, we often will start the first line medication. First line medication for obesity, prediabetes and type 2 diabetes is lifestyle management. So, exercise, nutrition, healthy diet, but for children with type 2 diabetes, we do start them all on metformin. We automatically will start even if the child's A1c is 7%. So as Dr. Wolf said, it's 6.5(%) and above that's considered diabetes. And even if it's 6.8%, we start metformin. That's the first line. It's a medication that's been around for a long time. Other medications we also have, if we need to, let's say that we're not getting optimal control with metformin, we now have some exciting new medications that we can use. The GLP 1 receptor agonist medications that people may have heard of for in adults, talk about Ozempic and all these different things. For kids, there are fewer medications that have been approved. But liraglutide or Victoza has been approved for youth onset type 2 diabetes if you are 12 or older. And the same thing with dulaglutide or trade name is Trulicity, also approved for 12 and older. And then in addition, we have another class, the SGLT2 inhibitors, that's empagliflozin or Jardiance can be used in type 2 also. This is super exciting because when liraglutide was first approved in childhood it was I think 2019, prior to that, the only treatment that was FDA approved for youth onset type 2 diabetes was metformin and insulin.

And all these medications you would see for the adult forms of diabetes, they were not approved in kids. Having these GLP1 receptor agonists are also small injections, but they are either once a day or once a week. And then the empagliflozin is oral. Having these other options can really make a big difference for these kids.

RK: It's just so amazing to hear how much technology has revolutionized really the treatment, especially in children who need multiple injections of insulin, such as in type 1 diabetes, and then for type 2 diabetes, just having all those other options that perhaps on the adult side, we're used to having.

But now having the availability of more than one or two classes of drugs for type 2 diabetes really seems to be something that will contribute to being able to address this rising number of children with diabetes. What more do you think is needed? Both of you have spent a lot of time in this field. You've seen a lot of children with diabetes. This, I expect, is going to continue. The numbers are going to continue. What more do you think needs to be done? We haven't talked about the role of caregivers or family members. I wonder if you might want to touch upon that as well.

SM: Before we get there, I just do want to also put in a plug for the fact that we really need advocacy to increase accessibility of some of those medications that I mentioned to our patients, to children, because those GLP1 receptor agonists, those medications like Victoza and Trulicity are very expensive. And insurance companies put a lot of restrictions on using them. Often, they get rejected for kids with prediabetes or before they get diabetes. Sometimes it feels like you're almost waiting for them to get diabetes. Then sometimes we can't start them on children unless they're on insulin already, or some other restrictions. I think these are all things that we want to avoid and avoid disparities in care amongst our kids.

RW: With all childhood chronic diseases, I think the family unit is really important and having a lot of support in managing this - diabetes is a burdensome disease. There's a lot of things you have to do every day in terms of monitoring and taking medications, and it's not something that any child can do alone. I think it's really important that caregivers in the home are supportive and helpful. It may not be that they need to do anything. It might be a teenager can do everything themselves, but having a little bit of support or oversight could really go a long way. And sometimes even just some gentle reminders about the things that need to be done. I think also, in general, and maybe more particularly for type 2, we often will recommend lifestyle modifications, changes in the diet, and I think it's really important that this is something that the whole household embraces. And it's not just something that one child has to do, because it's really hard to be a kid and, not eat something specific that the rest of your family is eating just because you have a condition that says you can't.

I'll just clarify that in type 1 diabetes, we don't really say you can't have something, we just say you should just make sure you take insulin with it. But, we do generally recommend avoiding a lot of excess sweets, especially in type 2 diabetes. And we don't want it to be that one child allowed to have it, but the other sibling is allowed to. We have to be very thoughtful about that. As Dr. Magge alluded to, making sure that everybody is getting rest, everybody feels supported. So, these CGMs (Continuous Glucose Monitors), have helped a lot in that realm, because by having a device that's going to alert you if the blood sugar is going low or too high, then at least you can get some rest.

I think, obviously, that's an important thing, because it's a marathon, it's not a sprint. This is the thing that is going to be continuous day in and day out and making sure that you set up a good framework for managing it in the home, helping the school, making sure things are settled and comfortable at school is also really important, because you don't want any sort of specific environment to be stressful for the kids. Even in summer camps, there are camps for children with diabetes, so that they can go and have normal camp experiences while there's a medical team to help manage the diabetes and they can take a little bit of a break. It's an all-in for everybody in order to feel supported throughout.

SM: It's also as Dr. Wolf said, it's a lot for a family because even with the new technologies, when somebody has a closed loop system, it's a advantage that they can get those frequent blood sugars through their CGM. But the family members, like the parent might be at home following remotely the child's blood sugars and the child's at school and they might see that they're going really high or they're going low and they're nervous. And so it's important to have good communication between the medical team, the school nurse, the parents, in terms of what's going on and the child too, depending

on the age of the child, of course, because we have some very young, preschool age kids who obviously can't play as big a part in their care.

RK: Yeah, thanks so much for talking about the role of the family and the caregivers. It really does take a team, especially when it's a child who's with a chronic condition such as diabetes. You mentioned the school as well and some of the advocacy that is important to continue to ensure that children get access to the medications they need. What about access to services at school? I wonder if you could talk a little bit about that for children with type 1 diabetes that might need frequent insulin injections and monitoring. And then even for type 2 diabetes, I feel like I've seen physical activity become less and less unfortunately, emphasized during the school day. So, I wonder if you could talk a little bit about the school environment in contributing to what we're seeing in terms of the rise of diabetes in children.

RW: I'll start by just mentioning that any child that's in a public school and has a condition like diabetes, the school is actually required to provide some onsite nursing services because somebody does need to supervise the insulin administration. This is really important for young kids, preschool, kindergarten, lower school age, elementary school age children, obviously, as the kids get a little bit older and more independent when they're in high school. Sometimes they can do things on their own. But I think the partnership between the parents, the school nurse and the medical team is actually really important and really can make a very big difference.

I know that our team has done a lot of work with school nurses. The technologies, as we said, are changing all the time and there [are] new pumps out every few months. Just in general, the fact that we now have these, hybrid, closed-loop systems is different than what we were using 3 to 4 years ago. So there's definitely been a big learning curve for everybody involved and making sure that everybody is informed on how to use the technologies. And we definitely play a large part in that. But making sure that there's a team approach really from everybody. One- it makes it safe for the child, but also, definitely more feasible and comfortable, but there's also a partnership and, the school nurse can help if there's a need to provide additional support in the school day, they can actually do that because there are constant every day for all those meals that they're eating in school, whether that be breakfast and lunch and checking in at gym. So there is some, routine and consistency to that can be very helpful also to the child as well as to the medical team. I think it's important also for parents to work directly with the school nursing staff because, they're in the ones who are going to be the first call when something's a mess, sometimes even before they call the medical team.

I think it's a really important relationship to establish up front. And if there are any gaps in knowledge, obviously reaching out to the medical team to help fill those gaps and everybody feels comfortable and on the same page.

SM: I would say, about the decreasing physical activity in schools, definitely we've seen that. For anybody with excess weight it's a challenge. To remain physically active, we recommend at least an hour a day of what's called moderate to vigorous physical activity. And for some kids, their main source of physical activity is at school and they would talk about PE (physical education). If they don't have that, it is not ideal. So we try to work with families to see what they could potentially do in their own environment, but it can be difficult. We can't tell somebody to go play outside if it's not safe to be outside. So, I think, meeting a family where they are is important. And the other thing is in terms of family interactions with type 2 diabetes, often children, if they have excess weight, they may also be very tall and they may look older than they are. It's important to remember that this is still a child with the maturity of a child. And sometimes teens don't want to do what they're supposed to do. So we've partnered with school nurses to help make sure that kids are taking their medication by having the school nurse checking on them or help them check their blood sugar before lunch or see if they

can help with medication adherence because there are times where, families can have a tough time with if it's a single parent household and the parent is at work, they may not be there to supervise. They might not be able to be there to supervise medication. So, partnering with the school can be helpful as well.

RK: It sounds like education is just so key. In terms of the partnership with the school, the partnership with the medical team and then family education as well. It's an ongoing process and there are certainly things that can be done to enhance the care of people with diabetes, children with diabetes at the school, but also, as you mentioned, things that might be limitations that need to be addressed as well during the health care visit.

We talked a bit about complications, and I don't think we need to go into great detail about them as I think they're pretty common also with adults with diabetes. I think it might be of interest to our listeners to hear about, do children with diabetes develop complications in childhood? We think about longer duration, the longer you have diabetes, the more likely you are to have complications that Dr. Magge, you mentioned the study where even in the mid-twenties people who'd had diabetes for 13 years had complications. Can children actually in childhood have complications? And which ones do you see in your practice?

SM: Yeah, we do sometimes see complications. Sometimes youth onset type 2 kids can have some of these microvascular complications even at diagnosis. So, seeing some kids with retinopathy, we have seen kids develop nephropathy or protein in their urine. Obviously as a complication, it's further down the road. Oftentimes they might present with this after they've transitioned toward a middle provider, but we sometimes see the starts of complications as well during childhood.

RW: I think overall, it is unlikely that children will develop these complications, particularly for type 1 diabetes with the improvements and technologies and advancements in diabetes management that we've had over the last decade. And, really, we can see that the hemoglobin A1C level, which is a measure that we use to guide, glycemic control and where, meeting those targets. We've seen a decline in the last few years, particularly with the advent of these newer technologies, such that, in the teenagers, the average A1C is not generally a goal, actually fewer than 20% actually meet that goal, but we're seeing people getting closer to that with the use of these technologies. So, the hope is that with continued improvements in management, that we can delay or prevent the onset of complications.

I think as Dr. Magge mentioned, in the type 2 population, we're more likely to see them at a younger age, and that's definitely why we worry more about them. That's why there are screening guidelines in place that say that we should be; for type 2 screening from the time of diagnosis and on a yearly basis. And for type 1 from the time of diagnosis, usually after about three to five years, you start to screen for all of these potential complications. We're happy to see that we don't see too many of them, but some of the more recent reports do suggest that really by mid, 20s, 25, 26 years old, if you've had diabetes for more than 12 years, there is a risk of having some of these complications. The more that we can do in the younger years to help improve glycemic control, hopefully we can prevent that.

RK: It is encouraging to hear that technology has really helped, perhaps with that management of glucose levels and diabetes in children and really helped give some rest to parents and caregivers as well. Dr. Wolf, I wonder if you want to briefly talk about some of the work you're doing looking at the use of technology in screening for complications such as retinopathy.

RW: We are the first pediatric diabetes center to use something called "autonomous AI" for diabetic retinopathy screening. That is an artificial intelligence software system that can view images that we take of the retina, of the back of the eye. And make a decision, so it's autonomous. It makes its own decision without oversight, to say whether the patient has diabetic retinopathy or not. So, this is something that we do at the point of care. Actually, at a clinic visit, it takes about five minutes. We take four pictures of the eye and the camera doesn't touch you. It just takes two pictures of each eye. We run those images through an algorithm and then it says the patient has diabetic retinopathy or the patient does not have diabetic retinopathy.

And that suffices to take care of that diabetic eye exam that patients historically had to go to an eye doctor to do. Of course, there are some people who should still go see an eye doctor, especially if you wear glasses, but if you just need it done because you have diabetes, it's the kind of thing that we can now do at the point of care. And we have done a lot of work in this area to show that has good diagnostic accuracy. We've also demonstrated that it improves access to completing and getting your screening done. Compared to saying, "please go see your eye doctor" and, it's another visit on top of your quarterly visits with your diabetes team. That's a big ask for people to do because it's another day off from school and work. So, this has been really instrumental in helping us make sure that all of our kids are getting screened for complications. We're currently looking at whether the use of this technology can also mitigate disparities in screening because we know historically that our minority youth are less likely to get their screenings done, and we want to see if we can close that gap with use of this technology. So that's some of the work that we're doing with autonomous artificial intelligence. We've also done a lot of work looking at the use of CGMs, pumps, and hybrid closed-loop systems in our population, again, looking to see whether this can close care gaps that exist for our minority youth in our population here in Baltimore.

RK: That sounds so exciting, and it sounds like there's many more technological developments to come, and I'm sure we'll continue to see even more technology integrated, not only into the monitoring, but it sounds like even the screening of complications in children, which is very exciting.

I wonder in closing, if you both might have some parting words for our listeners who either are parents of children who might be concerned that their child has diabetes or are parents of children who have diabetes, who might be struggling or really getting used to having a child with this disease. What would you say to them? What advice would you offer to them? And what resources would you suggest might be helpful?

RW: Let me start with type 1. So there are a tremendous amount of resources and community supports out there for families of youth with diabetes. And, the younger kids, when your child is diagnosed and they're under five, it really can be very challenging especially if they're one, two, three years old. And there are a lot of resources, one through the Juvenile Diabetes Research Foundation, now known as JDRF. Through the American Diabetes Association there are a lot of family groups that provides support and support groups that actually are out in the community. I would really encourage people to access these resources because I think having a community is really important when you have diabetes. It's not only important for parents of kids, but it's also really important for our teenagers to know that there are other kids like them that also are having to face the same things that they have to do every day, in addition to their regular lives. And I think looking for these supports and leaning on them can be very helpful for families.

SM: And I would say, similarly for children with type 2 diabetes, you can do this. We can really partner with you. I think there are a lot of exciting new treatments that we can use to really control blood sugars and bring them down hopefully to almost normal. So that we try to do the best we can to ensure that our kids live very long, happy, healthy lives and do everything that they want to do.

I would just encourage people to partner with your doctor, talk about any limitations you have, don't be embarrassed about anything. If there are issues, you don't have access to certain things, we can help. And our clinics for both type 1 and type 2 diabetes, we have multidisciplinary teams with nutritionists, behavioral health, diabetes educators, social workers, because we really do partner with the family as a whole to try to help them where they are. Sometimes it might be that the doctor is the least important person that needs to see a patient at a particular visit, because it might be the social worker that's going to help that family get their electricity turned back on or something else. So, I think working together as a team is so important.

RK: Thank you so much, Dr. Wolf and Dr. Magge for being on our podcast today and sharing your expertise on this growing burden of diabetes in children, both type 1 and type 2 diabetes, your perspectives on partnering with not only the families and the parents, but also the school system and everything that you do to champion and advocate on behalf of your children.

Thank you so much for being here today.

SM: Thank you for inviting us.

RW: Thank you.

RK: I'm Dr. Rita Kalyani, and you've been listening to Diabetes Deconstructed. We developed this podcast as a companion to our Patient Guide to Diabetes website. Our vision is to provide a trusted and reliable resource based on the latest evidence that people affected by diabetes can use to live healthier lives.

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Thanks for listening. Be well and see you next time.