

## PEDIAPOD APRIL 2024 TRANSCRIPT

### **Geoff Marsh**

Hello and welcome to PediaPod for April 2024. This month is the first of one of our new episode formats where we explore what's hot within a specific field of pediatric research right now. This month I'm delighted to be joined by Section Editor for Endocrinology, Jeanie Tryggestad. Here she is with her full introduction.

### **Jeanie Tryggestad**

I'm Jeanie Tryggestad. I'm one of the pediatric endocrinologists at the University of Oklahoma Health Sciences Centre in Oklahoma City, Oklahoma. I also serve as the Section Editor for endocrinology for Pediatric Research.

### **Geoff Marsh**

Would you describe yourself as a physician-scientist?

### **Jeanie Tryggestad**

I absolutely would describe myself as a physician-scientist. I spend probably about 65-70% of my time actively involved in research. My research focus right now is primarily on Type 2 diabetes. I have been involved with the TODAY study, which was the Type 2 Diabetes in Adolescents and Youth study, looking at treatment options for youth with Type 2 diabetes and we didn't find any great treatment options. Most of them progressed to treatment failure within five years, some of them as soon as six months into the trial. So it kind of raised the idea that we need better treatment for Type 2 diabetes, but even before that, trying to understand how it even develops. I'm currently involved in a newly formed consortium called the Discovery Consortium to try to better understand what predicts Type 2 diabetes in youth. Why do some kids with obesity and insulin resistance and risk factors for Type 2 Diabetes progress to diabetes and others don't. We don't fully understand that and we need to understand that to begin to prevent diabetes, or at least Type 2 diabetes in youth.

### **Geoff Marsh**

You must have quite a unique vantage point on all this as someone who runs clinics and is involved in research and is a section editor for Pediatric Research journal. You must have a really good global view of where we're at with all this.

### **Jeanie Tryggestad**

I feel like I do. And I feel very privileged to be able to do the research that I can then take directly to my patients and better inform their care and provide them with the best and top care. And that's the whole goal.

### **Geoff Marsh**

Is it fair to say that hormone disorders are relatively rare?

**Jeanie Tryggestad**

So let's think about diabetes for a moment. So Type 1 diabetes is about one in 300 youth. Other things like congenital hypothyroidism, so that's a baby that's born either without a thyroid or not able to make thyroid hormone, that's about one in 2000. So, yes, more rare than diabetes, say, but still not uncommon. There are different things, especially when we get to problems related to the adrenal gland that are much more rare. But there's quite a spectrum in endocrinology with regard to how common things are.

**Geoff Marsh**

And certainly, the impact can be really quite severe with some of those things that you've just mentioned.

**Jeanie Tryggestad**

Oh, absolutely. When we think about someone who has panhypopituitarism, so they have none of the pituitary hormones, they're dependent on the replacement. The great thing for us is that we have replacements of those hormones. But it's critical that they do replace them because if not, they are in danger.

**Geoff Marsh**

I just want to get a sense of where the major advances have been in the field of pediatric endocrinology over the past few years?

**Jeanie Tryggestad**

Let me start with diabetes because the biggest breakthrough this year in diabetes has been the approval of Teplizumab. Teplizumab is the first treatment for the prevention of diabetes, or at least trying to preserve some of that function of the  $\beta$ -cell, the ability of that cell to make insulin. And what they saw in that pivotal trial was there was a significant increase in the time to needing insulin for patients that were treated with this. And so this is really the breakthrough that has happened this year. There's ongoing trials right now to look at patients who are clinically diagnosed with diabetes. What's approved right now is stage two, so they have antibodies but not symptomatic diabetes. They're looking now at symptomatic diabetes and if we have someone who already has symptomatic diabetes, if they get this treatment, does that keep their  $\beta$ -cell working? Does that mean that they can come off of insulin for some period of time?

**Geoff Marsh**

This sounds like a bit of a sea change in how we tackle Type 1 diabetes, because it's getting at the root causes. It's an immunotherapy, not just trying to deal with symptoms.

**Jeanie Tryggestad**

Exactly. We know that the underlying pathophysiology for Type 1 diabetes is an autoimmune attack. So if we can begin to modulate the immune system to prevent that attack, preserve some of those  $\beta$ -cells, that's game-changing. There has been some movement in Type 2

diabetes as well, trying to get additional medications approved, because just a few years ago we had two medications approved for youth in Type 2 diabetes and now we're looking at five or six coming up very soon. So that's been a huge huge increase as well.

**Geoff Marsh**

Is there a quick answer to what the mechanism of action is for those Type 2 diabetes drugs?

**Jeanie Tryggstad**

So right now what we have tried for preserving  $\beta$ -cell function in Type 2 diabetes isn't working well. The Restoring Insulin Secretion (RISE) study was a really excellent example where they tried metformin, they tried glargine and metformin- it did not preserve the  $\beta$ -cell function. Now, in adults they've looked at GLP-1 agonists and they do maybe show some promise. Those studies haven't yet been done in kids but those are some of the areas that we need to investigate further of how we can keep the  $\beta$ -cell working in the patients with Type 2 diabetes as well.

**Geoff Marsh**

So they're exciting areas associated with the pancreas. What else is going on in the world of pediatric endocrinology?

**Jeanie Tryggstad**

Yes, so there are two other areas that I think I'd like to highlight. One is in growth hormone deficiency or short stature. With the advent of better genetic screening, better testing, we've been able to identify the etiology of more and more cases of short stature leading to growth hormone deficiency, or some other mechanism that leads to short stature, aside from growth hormone per se. And in conjunction with that, there have been multiple studies now looking at longer-lasting growth hormone therapies. We now have at least two on the market that are weekly preparations and that have indications for growth hormone deficiency that are looking for new indications, including those small for gestational age, Turner Syndrome, Noonan syndrome, and those studies are ongoing with hopes to have those indications in the next year or two. So it's very exciting for patients, especially for convenience going from something that they're having to do daily to something that they can now do weekly. So very excited on that front for therapy, as well as being able to understand better, we've used this term idiopathic short stature for so long, but now we actually have diagnoses that we can nail and say yes, this is because your stature is related to this gene. So being able to do that has really progressed that field quite a bit. And thinking along the lines of advances in diagnosis and new genes associated with disease, we've also had some really great progress in central precocious puberty in the last couple of years, with new genes identified helping to understand why some people, particularly girls, go through puberty early. Again, the treatments haven't necessarily changed but in the last years we've had longer and longer-acting GnRH agonists that have made treatment easier for those children as well. I think one of the last areas that is still up and coming is also with adrenal insufficiency, specifically thinking about patients with congenital adrenal hyperplasia. There have been new preparations of cortisol and things to try to block ACTH as well, again, trying to improve therapies and try to decrease side effects from long-term steroid use in those patients

as well. So there are lots of exciting things happening in the world of endocrinology.

**Geoff Marsh**

When you mentioned those long-acting growth hormones, are the recent breakthroughs in synthesizing those hormones or is it in the molecular diagnosis of some of the etiologies of various diseases?

**Jeanie Tryggestad**

It's really both. There are new preparations and research within the pharmaceutical realm trying to modify the growth hormone to allow it to be used as a weekly dose rather than a daily dose. And there's ongoing efforts to extend that even beyond a week to two weeks or longer as well. But also new molecular diagnoses are getting at different mechanisms of short stature beyond just growth hormone deficiency.

**Geoff Marsh**

So which topics are advancing the most rapidly would you say, out of everything we've just been discussing?

**Jeanie Tryggestad**

It's probably on the diabetes front with the Type 1 diabetes, looking at ways to preserve that  $\beta$ -cell. I think right now, that is definitely moving the fastest in all the fields of endocrinology.

**Geoff Marsh**

And in your opinion, what if anything is limiting endocrinology research?

**Jeanie Tryggestad**

I think it's moving fast enough from the development phase in the lab and into the realm of being taken up by pharmaceutical companies. Then getting it through the FDA process, that unfortunately is a laborious process. If there were ways to move that faster I think it would bring therapies and treatments much faster.

**Geoff Marsh**

And finally, is there any advice for anyone listening to this who might want to follow in the footsteps of you as a physician-scientist?

**Jeanie Tryggestad**

I think the biggest thing that I can encourage you to do is find good mentors and find them early. That really was key for me in getting on this path and having the success toward being a successful clinician-researcher. You have to have that early support and backing by your mentor, by the department, by the setting or the university that you're in. And if you have that support, you can really be successful.

