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Pediatric Psoriasis in Focus: Emerging Insights on Immune and Obesity Drivers

Announcer:
You're listening to *On the Frontlines of Psoriasis* on ReachMD. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *On the Frontlines of Psoriasis* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss immunologic and obesity-driven mechanisms in pediatric psoriasis is Dr. Amy Paller. She's the Walter J. Hamlin Professor and Chair of Dermatology and Professor of Pediatrics at Northwestern University Feinberg School of Medicine in Illinois. Dr. Paller, thanks for being here today.

Dr. Paller:
My pleasure.

Dr. Turck:
To start us off with some background, Dr. Paller, is there anything that makes pediatric psoriasis unique compared to adult-onset disease, especially in terms of underlying biology?

Dr. Paller:
Well, I will say that most of the pediatric patients who develop psoriasis develop it in their adolescent period in contrast, for example, with something like atopic dermatitis, where we see most of that onset very early on. There are some differences morphologically, and I think one of the huge problems in pediatric dermatology with respect to psoriasis is under-recognition. The majority of patients probably come into our offices with a misdiagnosis, and that's why the numbers, if you look at ICD codes, are so low compared to the percentage of adults who say that they had its onset during childhood. So what we see is lesions that sometimes are not as distinct as what we see in adults, and they are very often on the face, for example. Many of these children are misdiagnosed as having atopic dermatitis or fungal infections.

In terms of the underlying pathogenesis, though, it's largely the same. Sure, there are kids who have genetic disorders that present looking like psoriasis, particularly something like CARD14-activating pathogenic variants, but that's the small number, and most don't have this as a monogenic genetic disease. And it's very similar to what we see in adults. That's why we've been able to basically take biologics, for example, that are very targeted and work so well in adults and just move them into pediatrics once safety is shown.

Dr. Turck:
Now, obesity is increasingly recognized as both a risk factor and a disease driver in psoriasis. What else can you tell us about that in children with the disease?

Dr. Paller:
I would say that there's no question that obesity is a driver in the pediatric population. In a study that we did internationally more than a decade ago, we were able to show that there is that shift towards the association, especially of moderate to severe psoriasis, with being overweight or obese. And we went a step further and looked in our own population of children who were overweight or obese, and we looked back to whether they were overweight or obese at the time of the onset of their psoriasis. And we also looked back through pediatrician records at whether they were overweight or obese two years before the onset of the psoriasis, and we showed in 92–93 percent that this overweight or obese state preceded the onset of psoriasis by at least two years and then, of course, was perpetuated. We know how hard it's been—at least in the past, without some of the newer medications—to lose that weight, and so the psoriasis had to be treated in the face of the ongoing obesity.

The impact of that obesity may be not just that they have more severe psoriasis, but also there may be a little bit more resistance to the medications that we tend to treat it with in terms of effectiveness. I would say that we all know that obesity is associated with the increase in certain circulating cytokines—that makes sense that it can be a driver of psoriasis. We don't know that there's anything different in children or adolescents versus adults who are obese and have psoriasis, but we do know that there are certain chemicals that are put out or reductions. For example, adiponectin is a fat-produced cytokine that is reduced in those who are obese, and we and others have shown in the laboratory that we can turn that around by introducing adiponectin mimetics to increase T helper cells and to reduce the Th17 signaling that drives the psoriasis.

Whether in the future that means that there will be some new adjunctive agents to treat our patients with psoriasis who are obese, I don't know. But right now, I'm really excited to see the impact of the GLP-1 agonists in helping some of our adolescents who are obese to lose that excess weight and the impact that will have on the severity of their psoriasis, not to mention their cardiovascular risk factors.

Dr. Turck:
What can you tell us about biologics and the role they play in the treatment of pediatric psoriasis?

Dr. Paller:
We are so lucky to have biologics now and a growing number. Unfortunately, only half of the biologics that are available for adults are available for children, but there are ongoing studies, and we keep seeing new ones come out; in the last month, guselkumab became available for adolescents and children down to 6 years of age.

What we are seeing with these biologics is a pretty good response. So those who are obese are doing quite well with them whereas in the past, we might have had some trouble with some of our traditional immunosuppressants. We're doing better with biologics.

Dr. Turck:
And if we look ahead before we close, Dr. Paller, where do you see research heading in this space? Are there any particular pathways or treatment strategies that look promising to you?

Dr. Paller:
We're really excited about the increasing numbers of effective and safe agents available for our patients with pediatric psoriasis. We do have several biologics that are approved by the FDA down to 6 years of age, but the only problem with these is that they are injections. We've gotten better ones to the point that we're getting better than PASI 75 in the majority of patients with some of the newest agents, particularly targeting IL-23 and IL-17. In fact, there were studies done in the adolescent population showing that it makes a statistically significant difference in their quality of life if they're able to achieve better than PASI 75, so we're really excited about new agents.

What I'm seeing in the future, though, that I think will be very impactful for our patients is two possible scenarios. One is that we're going to be seeing biologics that don't need to be given as often. We've already seen that. I remember the enthusiasm when we published on etanercept many years ago—the first biologic in the pediatric population—and how incredible it was that 57 percent of them were achieving PASI 75, but this is a once-a-week medication, and now we have medications that can be given every month, every two months, and every three months, and that's made a big difference. In the future, we're going to see agents that are given every six months or even every year, and that will be a game-changer, including for our adolescents going off to college and the parents don't have to worry so much about are they getting that injection on a regular basis. So that's one aspect.

I think the other, though, is that we're going to have available oral agents as well. Now, those have to be taken daily, but nevertheless, we now have icotrokinra, which is targeting IL-23. Side effect profile looks great, and it's oral. We have the TYK2 inhibitors. There are several of them now that are moving forward, and those also will be able to be taken orally. And that's, I think, going to make a difference for many of our families where we have a hesitation or a struggle to be giving the injectable.

Dr. Turck:
Well, as those forward-looking comments bring us to the end of today's program, I want to thank my guest, Dr. Amy Paller, for joining me to discuss how immunologic pathways and obesity may influence the development and expression of pediatric psoriasis as well as its treatment. Dr. Paller, it was great speaking with you today.

Dr. Paller:
Thank you so much.

Announcer:
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