Congress Interviews

The AMJ team had the pleasure of speaking to Amy Paller and Yagiz Matthew Akiska, who summarized their abstracts that won first and fourth place, respectively, in the 2024 American Academy of Dermatology (AAD) Annual Meeting Poster Award. The pair also outline the future direction of their research, before summarizing the most exciting sessions at AAD 2024.

Amy Paller

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Q1 Congratulations for receiving first place in the 2024 American Academy of Dermatology (AAD) Annual Meeting Poster Award for your submission, 'Growth Analysis in Children Aged Less Than 12 Years with Moderate-to-Severe Atopic Dermatitis'. Can you summarize the research presented in your poster?

The poster summarizes results to date of a 10-year observational study called PEDISTAD, which enrolls children under the age of 12 with atopic dermatitis (AD) that is severe enough to need systemic medication. There are many parameters that we're studying as we follow these children through the various visits. But one of the parameters that we're studying is growth. We know that individuals of this age group who have AD have chronic inflammation and that they don't sleep well, primarily because of their itch. In addition, many of them have used relatively potent topical corticosteroids, and courses of oral corticosteroids. These are all factors that we know can affect linear growth.

Indeed, what we showed here is that when we followed 1,329 of these children aged under 12 years of age, we found that the weight and BMI were above the means for children of same age using the Centers for Disease Control and Prevention (CDC) percentiles. But the heights were below the average for age for both males and females. While database analyses have suggested that height in children with more severe AD may be low, this is the first real-world study through a registry.

I think that the results raise some very interesting questions, not just to further dive into what is driving this change, but also whether we can reverse this with effective management at this critical time of linear growth.

We now have an improved repertoire of medicine that's very safe and is being used increasingly in this 6–11 years of age patient population. It will be important to track not just the impact on inflammation, but ideally on sleep as well, and whether these improvements translate into improved linear growth for these children younger than 12 years of age.

Q2 Why did your research team choose to focus on AD in young children, and how do you hope your research will change the lives of these patients?

I happened to be the primary investigator of the PEDISTAD study, which is multi-center and sponsored by Regeneron. Children who are enrolled may stay on topical therapy based on shared decision making – and many have, while others may advance to a biologic or conventional systemic therapy. All are tracked, and there are no limitations on what the doctors prescribe – so it reflects real life practice. This gives us a change to compare responses and potential risks of use of our group of available agents, now and in the future. I hope that our data will help doctors and families compare among options for treatment, and will give us perspective about the answers to questions that may not have come up during trials of new medications, such as responses to live vaccines – as we are now enrolling another 500 children under the age of 5 years – and long-term safety of a variety of topical and systemic medications for AD.

Q3 What is next for your research team?

With respect to PEDISTAD study and its research team, having a longitudinal 10-year study presents an opportunity to study each participant in terms of the disease course. There are still many enrolled children who are on topical medications, providing the opportunity for a wonderful "control group" to compare with those who advance to systemic medications. I think it will be really key as this population grows to track their courses in response to various interventions, including of the development of comorbidities, which will be particularly interesting with respect to allergic disorders in those enrolled who are under 5 years of age.

We can look at durability of response, as well as long-term outcomes and risks. With respect to linear growth, recent data was presented from studies of dupilumab in 6–11 year olds that those on medication had signs of improved bone health, such as increased levels of alkaline phosphatase levels and bone biomarkers. Tracking linear growth in relationship to these biomarkers and AD improvement will be exciting.

Q4 You moderated a session at AAD 2024, focusing on AD. Could you tell us about this?

Well, this was a wonderful session, that really took the participants through all of the basic epidemiology, comorbidities, alterations of the barrier, immune system, and microbiome, and finally available and emerging topical and systemic therapies for AD. It's a huge topic that is rapidly evolving. With respect to epidemiology, Aaron Drucker showed evidence that the prevalence of AD is now stabilizing after a period of increasing occurrence. Some more recently recognized comorbidities are autoimmune diseases and a link with cardiovascular disease in adults with AD.

> **"The prevalence of AD is now stabilizing after a period of increasing occurrence."**

It is so clear that AD is a heterogeneous group of disorders with a similar phenotype, driven by Th2 immune skewing in the skin. Understanding biomarkers of subclassification that predict responses is going to be very important as we start to personalize therapies. Perhaps these will emphasize barrier issues with filaggrin or lipids – focus on different immunophenotypes (e.g. increased Th17 or reduced Th1 cells and products, in addition to the shared skewing towards Th2 pathway activation). The microbiome, with its reduction in commensal organisms and increases in *Staphylococcus aureus*, especially with flares, is another avenue of investigation with therapies in development to combat the shift in the microbiome without antibiotic use. To date, we do not know how variations in biomarkers affect responses.

But we do see certain changes in specific populations, such as the increase in Th17 pathway expression in children, individuals of Asian communities, and in lesions of nummular dermatitis. Would these groups of individuals benefit more from concurrent suppression Th17, or even an anti-microbial approach, since these surface organisms can be a driver of high Th17 responses?

I think what's most exciting to the participants is the new treatments, and how they differ from what is currently available. We talked about new topicals that have recently become available for psoriasis. One is a PDE4 inhibitor, and the other the first aryl hydrocarbon agonist; both really look like they're doing well for psoriasis and demonstrate very promising data for AD. Topical application of commensal organisms with potent anti-*S. aureus* effects are in development as well. New systemic medications are also emerging. Tralokinumab is most recently available for children as young as 12, lebrikizumab is coming out in the next year (already in Europe), and there are other biologics and JAK inhibitors in development. I think that the new kid on the block in terms of pathway is targeting the OX40 receptor and its ligand. Some long-term data in adults suggest potentially a more prolonged improvement off of these medicines after a treatment course, but more work is needed.

Q5 As the title of your abstract would suggest, you have dedicated a significant portion of your career to pediatric dermatology. What are the unique challenges associated with this specialism?

There are many challenges to treating children and bringing them new treatment options. Of paramount importance is safe management, especially for chronic diseases of the skin in which medications, whether topical or systemic, need to be used long-term, and potentially for a lifetime. I'm glad to see new medicines that have been very carefully studied in younger children. But we still have questions. The fact that we're going to have children on drugs for decades longer than adults raises questions about long-term safety that we cannot answer easily until decades have passed.

Of course, there are issues with drawing blood, and we're delighted to see some medications that do not require this that are very effective. There are also issues with injections. Many families, unfortunately, either cannot deal with doing the injections, or even coping with their children screaming while getting the injections in a doctor's office. Some of these children then are treated with agents we've had for decades, like low-dose methotrexate – and we have to remember that these are still effective, largely safe agents, even if they

require more careful monitoring, and should be used with caution long-term.

We also have to pay close attention to the psychosocial impact of chronic disease in children - the effect on stigma, on peer relationships, the potential development of anxiety and/or depression, and the impact of having a chronic skin disease on family dynamics, which also can profoundly affect a child long-term, beyond the disease itself. School-aged children and adolescents are very vulnerable to psychosocial impacts.

Q6 Reflecting on your extensive research career and substantial body of 650 publications, which areas of dermatology do you think require greater attention?

My personal areas of high interest are inflammatory and genetic skin diseases. I've been so thrilled to watch my patients who suffer from AD and psoriasis become clear, or virtually clear, and have a dramatic change in their life and its quality. Areas among my patient population that require the greatest attention now are the rare diseases, for which there are often no treatments, and certainly not targeted treatments. Because they are uncommon, they receive very little attention from the scientific community, industry, and regulators. But that is changing. I am seeing a new interest in helping this needy population, whether it's topicals or systemics, and I am so eager to repurpose medications or work with developing new options, particularly as we discover new targets based on the underlying mechanism of disease. Anything that can help children who are suffering from chronic inflammatory diseases is very important to me, and I will continue to enjoy spreading exciting news to patients/families and the scientific community. It is especially important to develop safe medications that are easily embraced by the families we serve. ●

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