Dr. Mariam Hanna:
I am Dr. Mariam Hanna. And this is The Allergist, a show that separates myth from medicine, deciphering allergies and understanding the immune system.
I have this love-hate relationship with every single eczema consult I receive. Please see, rule out allergy. I literally get goosebumps. I have to give myself this short pep talk before we walk into the room, take a deep breath and step into their story. I have so many eczema stories, they're all essentially a blur at this point. The themes are actually all quite similar, perfect skin, and then bam, it appeared an association with an event, a food, an illness, something else, and then spiral, spiral, spiral out of control. They're in the office. The itch-wake cycle becomes the new sleep-wake cycle of these patients.
The parents are stressed, the kids are often miserable. The teenager shrinks inside their sweater, all covering their scars. I see it. They wear their disease on the outside. The world sees it, and it immediately judges them and casts these anecdotes of advice on them faster than you can even say, "Stop." Unvalidated testing, food elimination diets, essential oils. You name it, I've seen it. The stories I essentially have a hard time remembering and deciphering, but the ones that succeed, the ones that actually gain control are my favorite stories. I've received home videos saying thank you, tears in my office at follow-up appointments, a card. And yes, the occasional smiling teen. Their confidence is back. Those are actually my absolute favorite stories.
So today's episode is all about atopic dermatitis, eczema, a condition that goes far beyond just the skin. The patients we meet literally pay hundreds if not more, getting the right products or the right testing to get to the diagnosis and along the way find many dead ends and they're itching to know more. This pun was intended. That's why I'm excited about this episode to set us all on the right track to the why of eczema and the how to get it under control.
We are very pleased to have with us today Dr. Vial Jain for our episode. Dr. Jain is an allergist and immunologist who did his internal medicine from Memorial University in Newfoundland. Thereafter, he completed his fellowship in allergy and immunology, where he also developed a keen interest in atopic dermatitis. He's got two busy practices based out of Niagara Falls and Stony Creek Ontario. He's the director with Allergy Research Canada, where he actively participates in numerous studies with a focus in atopic dermatitis, chronic urticaria, hand dermatitis, and asthma.
I'm also told, however, Dr. Jain is a diehard Buffalo Bills fan and is apparently praying that Josh Allen stops throwing more interceptions this season. We can all pray with him or alas, there's always next season. Dr. Jain, thank you so much for joining us and welcome to the podcast.

Dr. Vipul Jain:
Hi, Mariam, and thanks for having me on this podcast. What an honor. And you're speaking already like a true Bills fan. There's always next season.

Dr. Mariam Hanna:
Well, that's good to hear. Okay, Dr. Jain, this is an essential discussion for us as allergists, so we're going to get right into it. Let's start with what is atopic dermatitis? What is this condition?

Dr. Vipul Jain:

So atopic dermatitis is a chronic complex immunoinflammatory dermatosis, and it's more of a syndrome, and essentially it seems to be a complex interplay between barrier dysfunction, which is truly driven by the patient's genetics as well as a dysregulated immune system. And then of course, certain number of environmental factors that play a role like the itch-scratch cycle, as well as sweating, heat, stress, trauma to the skin. So all of these factors contribute to a compromise barrier function.
As a result, a patient's skin can start breaking down. You can get this sort of inflammatory dermatosis, you can get blisters, you can get papules, you can get excoriation, and of course lichenification, which is a leathery kind of a texture or change to the skin. Now, interestingly enough, the term eczema was truly described in the literature sort of in the early 1800s. So I believe in 1815 or 1817, but then the term atopic dermatitis was coined in 1933, atopy suggesting, or atopic, loose immunological association with various antigens and allergens in some capacity. And dermatitis meaning inflammation of the skin.

Dr. Mariam Hanna:
That's interesting because the word atopy has a loose association with allergy is what I heard you say. So is eczema or atopic dermatitis considered an allergy? Because what they're always asking me for is to rule out an allergy causing this.

Dr. Vipul Jain:
Yeah, that's a great question. So what we know is that many patients when we look at atopic dermatitis don't actually have any allergies whatsoever. However, many of these patients can have associated allergies such as allergic rhinitis or hay fever. You can see that in up to 40% to 50% of these patients, about 30% of these patients can also have asthma. And then depending on the severity of atopic dermatitis, some of these patients can have food allergies as well. Now, that's a very, very hot topic, very debated topic, and we can certainly get into that a little bit later on. But when you look at mild atopic dermatitis patients, about 1% to 3% of these patients can have food allergies. And then as the severity of atopic dermatitis increases, the likelihood of developing food allergies later on in life also increases. So severe atopic dermatitis patients, you may see about 30% of these patients developing food allergies later on in life. And that's really what the word atopy suggests. However, it doesn't suggest that your eczema is caused as a result of allergies.

Dr. Mariam Hanna:
Perfect. So that's exactly what I was going to tell you is we can't really get away with talking about atopic dermatitis without addressing this kind of age-old, is it a food allergy? So if I heard you correctly, you're saying that there eczema is not caused by a food allergy, but in the right setting, in the right person, they are at risk. Is that correct?

Dr. Vipul Jain:
Yes, that's absolutely correct. I think one of the controversies surrounding atopic dermatitis is what's the association with food allergies? What's the story? Every patient, and I think you can probably relate with this, is coming into our office saying, "Doc, what's causing my eczema? Is it the wheat and gluten? Is it shellfish? What is it? I need an answer."

And again, I think that we can all agree that the literature is quite dynamic. It's evolving, and there's a lot of conflict in our understanding of the association between atopic dermatitis and food allergies. But what we know as of today, again, based on high quality literature, is that food allergies do not necessarily cause atopic dermatitis, but a compromised barrier function in the skin can lead to food allergies later on in life.
And who's at risk? These are patients that have very severe eczema, typically before one year of age, and that is not typically controlled with topical steroids or topical calcineurin inhibitors. Well, some of these patients are at an increased risk of developing food allergies later on in life. And what sort of foods are implicated, typically dairy, egg, and peanut have been implicated. Now, when I'm saying allergies, I'm not saying that their atopic dermatitis flare is the allergy. I'm talking about IgE-mediated symptoms such as lip swelling, throat tightness, difficulty breathing. So those types of reactions.

Dr. Mariam Hanna:
I often end up in a discussion with families and saying, "I would much rather talk about all the different ways we can manage your kids' eczema or your eczema versus dealing with a life-threatening allergy where we have very limited options as to what we can do." It's an exciting time for eczema, and I like the fact that you're saying it is a dynamic space. We are continually learning about how this cycle works or how we can intervene to help. So as a segue, and there's a lot that's been happening in the space of atopic dermatitis, but what are some key things for you that have kind of stood out over the past two decades, let's say, that have improved our understanding of this condition? What are big highlight things that stick out for you that's changed what you do in practice?

Dr. Vipul Jain:
Yeah. So after 2014 where there was a paper that was published that highlighted the role of TH2 cells, our understanding of atopic dermatitis and how to treat this condition just exploded exponentially because we started looking at immune pathways and different components of a particular immune pathway. So the TH2 pathway, that's really used to treat atopic dermatitis at totally different levels now where we're getting into discussions around treat to target, we're aiming for 90% clearance of skin, we're aiming for 100% clearance of skin, and this is exactly how things happened even in the psoriasis space.
But before we even get into 2014, I think that the true revolutionary period for how atopic dermatitis is managed actually happened in the 1950s. What happened in the 1950s, that's where you had introduction of topical corticosteroids. This is when the practitioner started thinking about actually being able to manage an inflammatory dermatosis such as atopic dermatitis.
Now, since then, and looking back specifically in the last decade or so, you've had a lot of changes from a treatment algorithm perspective. In 2017, I believe that you had the first monoclonal antibody that kind of made it to the Canadian market. This is where you had dupilumab that was approved for treating adult patients with atopic dermatitis. Fast-forward almost six years later, and recently they just had an indication for treating severe atopic dermatitis in children six months and older.

And then if you look at what was sort of happening towards the fourth quarter of 2021, you had introduction of now oral agents such as small molecules and JAK inhibitors like upadacitinib or Rinvoq that came to the market for managing atopic dermatitis in adolescent patients as well as adult patients. And then of course you had a second monoclonal antibody that came to the market around the same time, so end of 2021, which is tralokinumab or Adtralza, which targets specifically interleukin-13 pathway.
And then of course you had another JAK inhibitor that came to the market, which was abrocitinib or Cibinqo. And now on the way you actually have lebrikizumab, which is another anti IL-13 that sort of works through decoy receptors. And what's cool is you're going to have another two molecules. I believe they target OX40 ligans, so rocatinlimab as well as amlitelimab. So there's just so much that's happening in the atopic dermatitis space and there's so much coming through the pipeline, but all of this can go back to 2014 when we understood what the TH2 cell actually does.

Dr. Mariam Hanna:
That's incredible. And I think this is what gives hope to a lot of the families that I talk to. I will say, let's start first with our treatments pre-2014. So let's talk about steroids first because I can't get away from talking about atopic dermatitis without touching on steroids. And the first thing I say is I say steroids really loud in the room so that I can dismiss all the myths and the phobia that exists in the room. But let's talk about it. So your skin's the largest organ and we're talking about using steroids. And then are they going to be dependent on it, Doc, is it going to cause steroid withdrawal? How do you address steroid phobia that still exists to this day?

Dr. Vipul Jain:
Well, I mean, what I remind patients is that your worries are shared worries. So as a provider, I totally get where you're coming from and there is a risk of skin thinning, there is a risk of telangiectasia with steroids, however that risk is minimal, typically speaking, when you're not using steroids for six or eight weeks consecutively. So typically the way that I tend to prescribe topical steroids is that I would recommend use it twice a day for three weeks and then give your skin a break for one week to 10 days in between sort of that three-week cycle. I also remind patients that we have a good understanding of where the skin is the thickest and where the skin can actually tolerate different potencies of topical steroids versus where we probably should use either low potency or we should switch over to a steroid bearing topical therapy.
So for instance, thin-skinned areas would be like your antecubital fossa or inside of your elbows, behind your knees or your popliteal fossa around the eyelids and the face. So this is where we can use topical calcineurin inhibitors, which are steroid-sparing topical therapy. I also remind them that look with steroids, when we're using the word steroid, there's a lot of phobia, but really traditionally they're speaking about systemic steroids like prednisone and dexamethasone. That's not the case over here. Yes, with those things, there is an increased risk of HPA axis suppression, infections, clots. There are short-term risks, and then of course there are long-term risks, but majority of those risks do not exist if you're using it in a prescribed manner. The way that a medication has been prescribed, chances are we're going to minimize that risk significantly.

And then ultimately, you also have to look at the practicalities. If you're looking at a moderate to severe atopic dermatitis patient to get them on a systemic therapy, pairs actually require for those patients to try topical steroids first before they can even have access to some of the newer agents. And that's just a practical reality.

Dr. Mariam Hanna:
Absolutely. Okay, so then let's move on to the, you said steroid, steroid-sparing. Let's move on to actually our TH2 addressing kind of pathways. So the role of biologics. How do you discuss biologics? How do you choose the biologic? How do you go about that?

Dr. Vipul Jain:
Yeah, this is maybe the $1 billion question is how you choose which therapy? And there's been a lot of discussion at various rounds around this. Look, when we use the EASI score, the BSA, and the IgA. And for our audience that aren't aware of what the EASI score is, it refers to Eczema Area Severity Index, where we're looking at how red the patient's skin is, how bumpy it is or indurated, and then how many scratch marks there are. And of course, how leathery the skin is. It's a standardized scoring system that we use to communicate how severe the patient's atopic dermatitis is with pairs as well as with other colleagues that we're co-sharing the care with.
So we look at body surface area as well. So what percentage of the patient's body is impacted by eczema? And then we look at kind of eyeballing on an IgA grading scale, is the disease mild, moderate, or severe, or very severe? And these are sort of the criteria that we use to say, "Is a patient a candidate for systemic therapy?" Whether it's biologics, which are injections typically, or whether it's an oral immunosuppressant. But keep in mind that these are pair requirements. How do you truly say someone that has a little bit of eczema on their face, neck, and chest is far worse than someone who has eczema on their genitals, which may be less than 1% of the total body surface area or on their face for someone that has a public-facing job or someone who has terrible, terrible eczema only on their hands, but can't go to work as a result of that because their skin is oozing, they're swelling, they can't close their fist. So these are all pair requirements, but you have to take several things into consideration when you're deciding on a systemic therapy.
Patient expectations, does the patient have underlying depression, anxiety, absenteeism from school and work as a result of their eczema? Does a patient have atopic comorbidities like asthma, like allergic rhinitis, like food allergies that you can target possibly with some of these biologics? Does the patient have non-atopic comorbidities like rheumatoid arthritis, psoriatic arthritis that you can target with some of these other immunosuppressants?
So you have to look at each one of these factors and have a very frank conversation with the patient and see if that patient is an appropriate candidate. I think EASI scores, BSA scores, and IgAs, these are all pair requirements, but you really have to look at your patient profile, have a candid conversation, understand your patient's expectations, and then make an informed joint decision with your patient.

Dr. Mariam Hanna:

When do you start talking about JAK inhibitors or oral versus injection? Does that factor into your discussion? Is it the efficacy? Is it their comorbidities? What swings you one way versus the other?

Dr. Vipul Jain:
Well, it's again, great question, but I think it's what swings the patient one way or another. I think as a, quote, unquote, "eczematologist," our job is to present all options to our patient. So if I'm speaking about, for instance, dupilumab or tralokinumab, I do make it clear to the patient that, "Look, it's an injection that you're going to be giving to yourself every two weeks. Are you comfortable giving yourself a subcutaneous injection or do you prefer a tablet? And oral tablets also sound excellent, but look, compliance tends to be a little bit lower when you're taking tablets. And from time to time, you may miss your therapy."
"With one therapy such as oral agents like the JAK inhibitors, whether it's upadacitinib or abrocitinib, you have to go in for periodic blood work." And I remind patients that, "You're going to have to go to the lab. We need followups every three to six months. Are you okay with that? Whereas with say, dupilumab or tralokinumab, you don't need blood work, but you're not necessarily escaping the needle in both therapies." So I speak to them about that.
Now, deep endpoints is an interesting discussion. We could speak about that for an hour just on that alone. But for some patients, 90% clearance is very, very important. 100% clearance is very, very important. You're going to get to those deep end points with these oral agents like these JAK inhibitors. But at the end of the day, they are immunosuppressants and studies have shown that there's a slightly higher risk of infections, clots, and the need to get vaccinated against shingles with majority of these agents.
Whereas with the monoclonal antibodies, they're slow to work, and the deep end points do come eventually, but it takes a really long time. Sometimes it can take eight months, sometimes it can take 12 months versus four or five weeks, six weeks you're there with the JAK inhibitors. So again, this comes down to patient preference. And then atopic comorbidities versus non-atopic comorbidities. Again, what does my patient have? Do they have asthma? Do they have nasal polyps? Then I may choose one particular monoclonal antibody versus does my patient have rheumatoid arthritis, psoriatic arthritis, enclosing spondylitis? I may go with an oral agent in that case.

Dr. Mariam Hanna:
So this space has been way more active in adults than in pediatrics. We're starting to see this come down into pediatrics. I don't know if you get this question much, but here's what I always get. I present the idea of a biologic or a systemic therapy. It sounds really, really good, and the fact that you can treat to clearance or 90% or 100%. But the age-old question is, and then for how long will they stay on that? Because they're usually quite pricey. So for how long? Like the six-month-old baby, for how long? Or the adult, for how long will they stay on it?

Dr. Vipul Jain:
Yeah. And again, another excellent question. A very common question. So typically once you see the patient, you know what they have, you've decided what they should go on with the patient. Before they typically start the treatment, we want to know how long is the patient going

to be on this therapy for? In fact, my daughter has eczema, and even when her family doctor is prescribing topicals, on the back of my mind, I'm wondering, "Well, how long does he want to keep her on a particular topical?" And the truth is right now we don't know because the studies we have long-term extension studies, we can comment on two years, three years, five years, but we don't know.

There's an important caveat that I want to address over here. I mean, you said that the space is exploding in the adult patient population. Actually, pediatric population is quite interesting. I mean, dupilumab, again has been approved in patients that are six months and old. But tralokinumab is now being investigated in patients that are two years and older. Nemolizumab, which is an anti IL-31 that we've looked at both for prurigo nodularis as well as atopic dermatitis, another monoclonal antibody is being investigated in children two and above. Upadacitinib, even a JAK inhibitor is also being investigated in children two and above. So there is a lot going on right now. Even the OX40 ligands, we have several patients that are 12 and above that are on that molecule and doing phenomenally well.

I don't know how long we can keep a patient on these molecules for, and I'm very honest and candid with my patients saying, "Look, this is as far as the studies go, but do we have 20-year data, 30-year data? We don't right now." Another very interesting concept that's emerging with the use of monoclonal antibodies is altering the trajectory of the condition and also associated conditions. So there was a meta-analysis done, not a great study, some flaws there where they looked at 12 studies essentially, of children that had moderate to severe atopic dermatitis. And what they said is, "By introducing dupilumab therapy early on in these patients, can we actually reduce the incidents or the severity of other type two atopic comorbidities such as allergic rhinitis, food allergies, asthma?"

And what they found was that in fact, all 12 of those studies showed that there would be about a 30% to 35% reduction in type two comorbidities in these patients. Again, a lot of issues with that study, which we're not going to get into I think right now, just in the interest of time, but long-term effects might be there. And we're also seeing that with some of these biologics, when you stop patients from taking these treatments, their eczema actually doesn't come back for a year, two years, three years in many of these patients. So are we inducing remission and how do we define remission? We don't know right now.

Dr. Mariam Hanna:

Yeah. I think certainly as these spaces expand, we start talking about remission and where that definition is. And for a long time in eczema, we weren't discussing that. We were saying, "It's a chronic condition, and this is the therapies we're on." So I'm always surprised with all of what we've discussed coming down the pipeline and even already available in future clinical trials, this tendency towards undertreatment.

I often am shocked the families will come in, yeah, they're doing great. Their skin is the best it ever is, and then when you examine them, they're moderate, at least moderate when you examine them. Or I get a referral and the physician's treatment or prescribed treatment would be kind of described as homeopathy in my mind, and no way would it address kind of the amount of lesions that we have. Why do we have this tendency towards undertreatment? How do you tackle that?

Dr. Vipul Jain:
Yeah, the AD patient or the atopic dermatitis patient is very different than a psoriasis patient. Atopic dermatitis is not about how it purely looks. It's about how it feels. So itch drives a patient insane just because it's such an uncomfortable condition. But the problem is when you look at these NRS scores, these are supposed to be validated scores of defining as a patient, itchy, very itchy, severely itchy. They're just not really well understood. To me, I don't understand the difference between NRS of eight and six. Theoretically, we understand what the difference is, but I don't know what the difference between itchy and very itchy truly is. I just don't. I don't know if any of us really do and we can't see it.
And for the patient, that becomes their sort of norm, that becomes their baseline. So sometimes patients are not necessarily reporting those symptoms, and that leads to undertreatment. I think that there is a little bit of kicking the can down the road where we just go higher and higher on our topical therapies in terms of strength, rather than pulling the trigger and saying, "You know what? Let's spend that extra time and let's treat this patient with these systemics and give this patient clear or almost clear skin." And that leads to a lot of undertreatment, just the amount of resources and time that's required for starting these systemic therapies.
I think access is a major issue. That's a bit of an uphill battle with pairs because let's face it, these therapies are not cheap. And I think that there's also a lot of phobia on the treater side as well. I mean, there's just a lot of misconceptions about immunomodulators versus immunosuppressants, like some of these older traditional biologics which suppress the immune system. We don't really see that with these newer biologics. They're just so much safer, but a lot of prescribers are not up-to-date necessarily with this data sometimes.

Dr. Mariam Hanna:
So if someone has atopic dermatitis, and your answer may or may not be biased, should they be seen by an allergist, a dermatologist, or they need both?

Dr. Vipul Jain:
I would argue that they need both. I would argue that they need, obviously their family doctor, their primary care provider to be actively involved. Because remember, these patients have a lot of other issues. 64% of these patients are anxious, 79% of these patients can't sleep. About half of them miss physical activity. So there's a lot of other issues going on in this patient's life. Many of these patients have atopic comorbidities. So as allergists, we're uniquely positioned to offer the atopic dermatitis patient a very comprehensive experience. We can address their food allergies, we can address their asthma and carry out spirometry or breathing tests.
Some of these patients can have underlying contact dermatitis. Again, another controversial issue, which we don't need to jump into, but at least patch testing is available through the allergist. And then of course, we should also start these patients on treatment. Oftentimes, when these atopic comorbidities are not playing a role, when we know that their anxiety, sleep deprivation, and absenteeism is related with their atopic dermatitis, treatment can be started either through an allergist or through a dermatologist.

Dr. Mariam Hanna:

I love that. And I think that's probably how we'll wrap up for today. So at the end of every podcast, we try to pick on the allergist of the day. So that's you today, Dr. Vipul Jain. And we ask for three key messages to impart either to patients and/or physicians on today's topic, atopic dermatitis. And with that, I pass it over to you.

Dr. Vipul Jain:
So, I mean, the three takeaways over here are, look, atopic dermatitis is a complex immunoinflammatory dermatosis with a dynamic treatment landscape. And I think that my message for the allergist is that we need to be more actively involved in treating patients with systemics that have moderate to severe disease. My second takeaway message is that the understanding between food allergies and atopic dermatitis is really not well-defined. However, in those patients and referring doctors that are requesting and insisting on food allergy testing, we need to be more aggressive about carrying out oral challenges because that is the gold standard, because up to 40% of these patients can have false positive reactions on skin testing, and therefore we're obligated to spend that extra time and carry out a food challenge to reassure the patient that typically it's not a food allergy that's causing their eczema.
And then this is for my primary care colleagues, and my third message is that allergists play a very, very critical and unique role in providing severe atopic dermatitis patients with comprehensive care. And as I was saying, for instance, the AD patient can get their coexisting asthma, allergic rhinitis, and food allergies addressed through the allergist, which isn't possible through most other specialists.

Dr. Mariam Hanna:
All right. Well, thank you so much, Dr. Jain for joining us on The Allergist. Atopic dermatitis always leaves us itching to know more. Itching to know more, anyone? No. We really appreciate your time and we hope to have you back again with us to tell us about the latest and greatest developments in this space.

Dr. Vipul Jain:
Thank you so much, Mariam. I really, really enjoyed speaking to you. And go, Bills.

Dr. Mariam Hanna:
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