Itch Related to Atopic Dermatitis
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Diego Dasilva, MD, FAAD, interviewed by Deirdre Hooper, MD, FAAD

DEIRDRE HOOPER, MD, FAAD: Hi, everyone. I'm Deirdre Hooper. I'm a board certified dermatologist. I practice in New Orleans and in private practice and I'm also volunteer faculty at LSU and Tulane departments of dermatology. I'm here today with Dr. Ruiz Dasilva. He is an Ivy League-trained dermatologist, practicing in Virginia Beach, Virginia. He was born in Brazil and raised in south Florida, where he attended the University of Miami. Dr. Dasilva then attended the Perelman School of Medicine at the University of Pennsylvania and subsequently completed his internship and dermatology residency at the Hospital of the University of Pennsylvania, where he ran a pruritus specialty referral clinic.—

--There, he developed an expertise in chronic pruritus, inflammatory skin disease, psychodermatology and dysesthesia, also skin of color skin cancer, and aesthetics. Welcome, Dr. Dasilva. Thanks for coming on today.

DIEGO DASILVA, MD, FAAD: Thank you so much for having me, Dr. Hooper. I'm really excited to talk to you guys today.

DEIRDRE HOOPER, MD, FAAD: Tell us about yourself. In your bio, your history of learning about itch is pretty impressive, so just tell us a little bit more about you.

DIEGO DASILVA, MD, FAAD: I've always had a passion for dermatology, just finding it interesting, the breadth of diseases we see and that we treat and how every patient on any given day can be different. In residency, I was really encouraged to find a niche or a specialty or just try to learn a lot about one topic, publish, etc. I wasn't really sure that I only had one thing that I cared about, but I happened to see a few itchy patients that were very interesting in clinic and in the ER who were essentially driven mad. It just seemed that they were in a way much

more disturbed and bothered by their disease process than even a patient with skin cancer, melanoma, other conditions that are serious.—

--So I feel like that made me feel that it was a worthwhile endeavor, that was something that patients cared about, that I could make a big impact on their lives. I was fortunate at Penn, of course, to have titans in that field who had trained there or were there. So Brian Kim is one such person who has done amazing research in the world of itch and neuroimmunology. He came and gave grand rounds and spoke to the residents afterwards and inspired me even further to pursue that.—

--Atopic dermatitis, mostly I think what we'll be talking about today, and that's one of the most common itchy disorders that we see, but just itch in general is a symptom of pretty much almost any disorder that we see that's a skin disorder and a symptom of a lot of other things, as well, and something that patients care about sometimes more than the way that the skin looks.

DEIRDRE HOOPER, MD, FAAD: That is fascinating and I agree with you, I'm always advising my residents to find their niche and I guess your niche is itch. You're making such a good point, they can kind of stop thinking about their basal cell and wrap a bandana over it on their head but they can't stop thinking about their itch. So itch is one of those things that lots of people talk about, but what do we know about the basic science of itching? I know that in your itch clinic, you probably can get us a bit more onto the cellular what's going on.

DIEGO DASILVA, MD, FAAD: It's changed a lot, the dogmas and the thoughts, even only over the last 5 to 10 years, but certainly over the last 20 to 30, where people have been thinking more and more about this. I'd say that was the impetus for creating that pruritus clinic also was just the fact that a lot of people, our colleagues, not that they don't care too much, it's there's so many things to focus on so it's hard to have a dedicated clinic for that. Unfortunately, part of it is just the world that we practice in now, a lot of people are having to see a lot of patients. There's

a huge demand for dermatology and those itch visits can sometimes take a long time and they don't necessarily reimburse well.—

--That is not what we do it for but it's a time suck and an energy suck for a lot of our colleagues. So I thought this was a perfect time when I was in academia to say I think we had 70 dermatologists working at U Penn and they don't really want to see the itch patients. We didn't have an itch expert per se at that time working there, so I became that person. I got to learn a lot, practically speaking in treating patients and we'll talk about that. But to get back to your original question which is just about the science of it all, I think in the beginning, our rudimentary knowledge was like histamine, antihistamines, histamine, and other pruritogens essentially affect the sensory neurons and cause that sensation of itch to go the brain and then you scratch.—

--That was like a very basic thing we thought about. Then it's kind of evolved, IL-4, IL-13, IL-31, these all have receptors on sensory neurons and they activate itch. So as the inflammation comes and allergic stimuli, etc., and then it's activating the nerves, and then leading to that itch process. I think at that point we started thinking, so there's an inflammatory itch. Somehow your immune system is either overactive, whether an innate thing or whether it's due to some kind of exposure activating the neurons that cause itching and that causes that intense sensation.—

--Or a neuropathic itch, which is like you have a hot nerve and that nerve is hyperexcitable. We don't really necessarily know what is activating it, is it just that it's being pinched in the wrong way? Is it some other neuropathic process and then that's causing itch, but you don't really have the immune system involved? Even just a few years ago, that's the way it was thought of. Now, the field of neuroimmunology has really developed and we're at a level beyond that, where it seems like many things in medicine, it's a catch-22 or a cycle that feeds each other. So it's

essentially yes, the neurons can be affected by inflammatory cytokines, like we just talked about, and activated.—

--But the neurons themselves are not simply sensory. They have motor function in a way, not necessarily in the traditional way we think of activating muscle or anything, but they actively release neuropeptides. And those neuropeptides can actually activate inflammatory cells to produce inflammatory cytokines, which in turn feeds back into that cycle and affecting the neuron. Basically, it's all connected is the best way to put it. And we're still learning a lot.

DEIRDRE HOOPER, MD, FAAD: So that's absolutely fascinating and I appreciate you putting that all together, because sometimes you think people are itching because they're anxious. Or sometimes they're itching because of disease, sometimes it's sensory, sometimes it's motor, but it sounds like it's sort of all of it. So let me ask you, when you have your itch clinic and a patient comes in itching, I guess that's their primary complaint, what is your approach? How do you start talking to them to make the diagnosis and treatment plan?

DIEGO DASILVA, MD, FAAD: My very first question is length of time. Number one, chronic pruritus would be over six weeks, which is kind of just of course an arbitrary time cut that we've had for a lot of disorders in dermatology. But the personal cutoff that I care a lot about is actually a year. So there's been some great publications out of Shawn Kwatra's group, looking at basically if your itch was present for over a year, it was very unlikely that you had some kind of severe, pressing issue: lymphoma, other cancers, other dangerous processes like cholestasis from something compressing the liver, etc.—

--To have something like that, it would be discovered before then. You're not just sitting with that for over a year.—

DEIRDRE HOOPER, MD, FAAD: Right, like kidney, right.

DIEGO DASILVA, MD, FAAD: Exactly, kidney, etc., so these are things people would know. Versus shorter than that, you do have to cast a wider net and test for all those things. The second crossroad is, is there a primary rash? If they just have excoriations, they're scratching all over, and there's not really an eczematous patch or plaque or papules or nodules, then you're thinking more of those disorders like prurigo nodularis, chronic pruritus of unknown origin, neuropathic itch. Again, these things all connect to each other but when you're reading in textbooks, because they're not necessarily that updated, these things have their own categories.—

--So that would be like notalgia paresthetica, brachioradial pruritus, scalp dysesthesia, or general itch, those type of things which don't usually come with a rash, it's more of the sensation is just there. Versus when there is a rash, that's what we all love and are used to in dermatology. That's your atopic dermatitis patient, your psoriasis patient which of course can still be itchy, seborrheic dermatitis, other inflammatory conditions. That's usually what I start with.

DEIRDRE HOOPER, MD, FAAD: So history of duration and then primary lesion. We want to talk about atopic dermatitis and you realize that your patient is an itchy, atopic dermatitis patient. I know everyone wants to know what do we do with those patients. We've had so many new medications. I know there are a lot, but let's start talking about how you manage itch in atopic dermatitis.

DIEGO DASILVA, MD, FAAD: Now we have an embarrassment of riches. I just feel so lucky to get a young attending dermatologist practicing in this time with all these resources to be able to help these patients feel better and in a less dangerous way, too. I think just to keep it basic in the very beginning, it's alright, what are they using in terms of non-prescriptions. Are they using lots of fragrances and scents. A lot of people are naturopaths these days, so there's tea tree oil

and black soap, just like these interesting ingredients that appear to be safe or clean but can be very allergenic or irritating to an atopic patient. So that's number one, I want to make sure they're using basic, bland emollients, minimizing irritants.—

--Then I'm curious about what prescriptions they're using and then discussing the options. So when we start with topicals, there's topical steroids that we're all used to, low potency, mid potency, high potency, and how often they're using them. I think topical steroids are here to stay. I'm certainly not steroid-phobic, although society is going towards that a little bit. They have their proper use but again, we've all seen those patients that they come in, they don't look that bad. You think they're in a good regimen but it turns out they don't look that bad because they've put triamcinolone on their whole body every single day for the last year.—

--You're surprised they don't have terrible atrophy or sometimes they do. I had a gentleman I saw the other day, a young man, and his hands were like literally, he was a Caucasian guy but it was like ghost translucent, you could see all his blood vessels and everything. Of course, what do they do when they see that? They put more clobetasol on it, because they think it's flaring, so they've got to keep treating it. That's a challenge. At that point, we talk about the prescription topicals that are nonsteroidal. Now we have excellent options, like roflumilast, which is otherwise known as Zoryve. Or tapinarof, which is VTAMA. These are both nonsteroidal, once daily topical creams that can be used for atopic dermatitis, with excellent efficacy and tolerability, so those are good options.—

--Again, it just depends on what body sites the patient is using it and how often they're needing to use their steroids in terms of how you're going to mix these in there to minimize the steroid use. And then we kind of go into systemics. This is where it gets kind of tricky, because we have of course oral systemics, we have injectable biologics, both of which work excellently, that are beyond what we had in the past. In the past, we had our aggressive immunosuppressants:

methotrexate, cyclosporin, azathioprine, mycophenolate. And these are things that of course we needed them at the time, but we know that they suppress the immune system.—

--We know they cause serious infections, cancers, a slew of other problems, so it's nice to have these newer options. But the challenge to me is more in determining who is the moderate to severe atopic dermatitis patient. So traditionally in a lot of these systemic trials, you have to have at least 10 percent BSA of your atopic dermatitis. But some patients, they can have 7 percent, 6 percent, and they could be on the brink of suicide or so miserable that they don't go on dates, they don't go to job interviews, they can't function appropriately in their daily living. For me, a lot of times it's asking a patient, "How much is this impacting you?"—

--"Can you sleep okay? Do you have trouble at work or in your personal relationships with friends, family, going out? Do you limit what clothing you wear because certain fabrics or certain colors you feel like are going to have blood on them." Basically, you're wearing white, if you're scratching a lot, etc. Flakes if you're wearing a dark shirt. So I try to get at those questions because it's not always concordant. A patient can have 20 percent BSA and feel relatively like, "Oh, this is no big deal," although I guess we wouldn't feel that way, and vice versa. So I try and get that information.—

--And then that's when we're talking about, just to briefly mention some of the options, stuff like the orals which are abrocitinib, Cibinqo; or upadacitinib, Rinvoq; oral JAK inhibitors that come with a little bit of baggage because of a boxed warning but have a lot of safety behind them, both years in dermatology and outside of dermatology. And then we have our biologics, which started with this revolution of dupilumab or Dupixent, which has changed a ton of lives, I think over a million people treated at this point, and very safe and well tolerated.—

--But then you have the new generations, like tralokinumab, an IL-13 blocker which is Adbry; lebrikizumab, another IL-13 blocker which is Ebglyss. And then finally the newest mechanism of

action which is quite intriguing, which is nemolizumab or Nemluvio. So that's an IL-31 blocker. IL-31 has been long known as the itch cytokine, just directly and very targetedly, basically triggers itch. They know this actually on a dose-respondent basis. Like when they inject mice with IL-31, essentially based on the amount they inject they get a direct itch response from that. So it's an immediate pruritogen.—

--That drug is an injection that folks can take once a month or even once every eight weeks, depending on what condition they have. But for atopic dermatitis specifically and can majorly improve their quality of life and their itch.

DEIRDRE HOOPER, MD, FAAD: You and I were talking before this interview, and I practice in New Orleans and I treat a ton of skin of color. Pearl Grimes taught me very kindly early in my career to always address hyperpigmentation in my skin of color patients, because often even though I'm counting their pimples or looking at their rash, what they hate and it's true is their pigment. I think you said something so profound to me and I'd love for you to talk just a little more about when you're making the determination of how sick that this person has to be (s/l or this) patient, how do you weigh looking at the skin lesions versus talking to the quality of life about itch? Because I think that's such an important pearl for us to share.

DIEGO DASILVA, MD, FAAD: I feel like this is almost taboo to say as a dermatologist but it's almost that I don't care what the skin looks like in that exact moment. I'm having at that point just an earnest conversation about tell me about your itch. Tell me what activities that you like doing for fun, in your professional life, travel, clothing, work relationships, and how itch affects that. And then sleep, of course, and I think I kind of use sleep as a proxy because it's just hard to function mentally speaking, mood speaking, if you're not sleeping properly. I get a sense from that how much their itch is bothering them.—

--Sure, I care a lot about the skin and I tell them, “That’s something we can get better with time, but I want to make sure I can address your itch in the quickest, most efficient way possible, and also at your discretion,” meaning some patients say, “Doc, I want the thing that’s going to make me itch-free the absolute fastest. I don’t even care about side effects, risks, or anything. I’m at this level that’s near suicidality,” which is just crazy to think that we see patients like this, but we do. And then you’ve got some of those patients, they go, “Doc, just tell me what’s kind of a good regimen.” I have patients like this is not a huge deal, although I do want to address it. And these are just two very different patients.

DEIRDRE HOOPER, MD, FAAD: Would you walk through your typical treatment algorithm for that severe, I’m almost suicidal, all I’m thinking about is my itch? Do you always go right to a systemic with them?

DIEGO DASILVA, MD, FAAD: I sure do in those cases, and it really depends. So I think systemic corticosteroids have been used of course since what, the 1950s, a long time for all inflammatory things, and can help an atopic stop itching pretty fast. So that’s never a bad idea, it just depends at that point a bit on comorbidities. A lot of our patients have hypertension, diabetes, significant heart disease, etc. I think that makes things a little bit more challenging because I’ve seen a ton of patients referred to me. Also earlier in my career when I made mistakes, yes, you may fix that itch quickly with that but then now they’re in the ER with sepsis or a fracture or some kind of major hyperglycemic episode, hypertensive urgency, strokes, those sort of things.—

--So we want to make sure that you’re picking the right candidate. So younger healthier, no medical problems, that might be a good idea. But even in those younger, healthier, if I get an idea that this is a chronic thing, then I’m already talking about the advanced systemics. So at that point, it’s very much for me pill versus injection. I say the pill medicines, oral JAK inhibitors

kick in very quickly. Efficacy is fantastic, because you want to stop itching like yesterday. But comes with a few issues that can be seen with it. Number one, has a warning, although I don't necessarily believe the weight of those warnings, which are cancer, malignancy, venous thromboembolism, and heart disease, and that sort of thing as part of the baggage, and serious infections.—

--You can pick that but then you're going to have to take a pill once a day, every day. You're going to need bloodwork monitoring and that's okay, we can do that in a safe way. But some people prefer to do a biologic and then that's an injection. You might take that every two weeks, it might be once a month, it might be every eight weeks now that we have Nemluvio approved. You may do great on that, sometimes it kicks in remarkably fast. Nemluvio, for example, has a very good, or nemolizumab has very good 48 hour itch data. They all have a little bit of that itch data anyway, but certainly they work well long term.—

--You don't need bloodwork monitoring and you don't have those warnings associated. So it just kind of depends on what fits their lifestyle. And I try not to be paternalistic in the sense to say, "Hey, this one has the best data," best in quotations, because we can't compare head to head "and is the safest, so that's the one I want you to use." I really like to take a couple of minutes, it doesn't have to be a super long conversation, just lay that landscape out. And then I immediately follow it, "Do you feel like you're more favoring the pills that I just talked about or the injections?" And you'd be surprised, patients, they're either one way or the other. "Oh, Doc, those injections sound cool but absolutely not, I want the pill medicine."—

--Other ones are like, "Oh, I don't know, it's kind of scary. You said it's not that bad but there are warnings and stuff, give me what's safest." And then it kind of makes the choice a little bit easier for us.

DEIRDRE HOOPER, MD, FAAD: That's a fantastic roadmap. I want to make sure we keep us on time, so I would love to just close out and ask you, for our listeners, what are your top tips as such an expert. And thank you so much for sharing your expertise on itch and itch in atopic derm. What are your top tips that we should all take to our clinic tomorrow?

DIEGO DASILVA, MD, FAAD: The top things I would talk about, some of them I mentioned already, so I'll just briefly say, is ensure that the patient is not actively putting on irritants, whether that's soaps, detergents, etc., or exposed because that's something easy that we can do to minimize. Have an idea of how your patients are using their topical steroids because I think it's easy to gloss over that, especially in a chronic patient. Make sure they're not using them in an unhealthy way. Don't assume patients are well controlled just because the skin looks better. Even at follow up, you started that drug, biologic, whatever it is, and they look better and sometimes it's that you want to walk in and walk out of the room.—

--The reality is you've still got to ask those itch questions and how it's impacting their quality of life and their sleep because it's not always concordant with how the skin looks. Utilize these advanced topicals and systemics that are safer, more effective, and well tolerated. Don't try to lean on your steroids and your old drugs. Even if you like to, again not saying, there are appropriate times to use those but we have safer options. That kind of ties into the last thing I was going to say, try to treat these patients like you'd treat your favorite family member or your close friend. Because I think we should all do that as physicians and providers.—

--I think sometimes it's challenging. I've literally had providers tell me, "Oh, you're showing me all this stuff but the healthcare system, and that's expensive, and this. And methotrexate has worked fine for me. Why do you need to be EASI 90? Why do you need 100 percent clearance or itch of zero or one? That will work fine." And I say, "Would you do that to your own child? If I was your cousin, or your mother, or father, you're going to give them methotrexate instead of

dupilumab, instead of nemolizumab?" I feel like if they say yes, that's you, some people may feel that way and be the steward of the healthcare system. But I think most people would give that type of person the best, safest treatment that they believe in, so I want us to treat patients like that.

DEIRDRE HOOPER, MD, FAAD: That's very admirable. Thank you so much for your time today and for your expertise. Thank you, listeners, for listening to another edition of *Dialogues in Dermatology*.