EPISODE 1
MODERATE-TO-SEVERE DISEASE BURDEN, DISEASE PROGRESSION, AND TREATMENT CHALLENGES

Peter Lio, MD, FAAD: This presentation is "Gaining and Maintaining Flare Control in Atopic Dermatitis: Enhancing Patient Quality of Life." Hello, I'm Dr. Peter Lio. I'm a Clinical Assistant Professor of Dermatology and Pediatrics at Northwestern University, Feinberg School of Medicine and the Founding Director of the Chicago Integrative Eczema Center. I'd like my colleague to introduce himself.

Mark Boguniewicz, MD: I'm Mark Boguniewicz. I'm Professor in the Division of Allergy-Immunology at National Jewish Health in the University of Colorado School of Medicine in Denver, Colorado.

Dr. Lio: So let's begin with the pathophysiology of atopic dermatitis, and I think this is incredibly exciting because we have learned a lot about what is going on under the proverbial hood and in just the past few years. There is a figure that I'm in love with, and I love this figure because it encapsulates all of this complex pathophysiology in a very, very compact space; and it puts them together in a relationship that shows us there really is a vicious cycle that can start. And we know that no matter where you begin on this cycle, you can bring all the other players involved along very quickly.

So, if we look at the top of this figure, we have the skin barrier; and we know that if the skin barrier is not up to snuff, we will get water leaking out, and we can measure this in one way as transepidermal water loss. But more importantly, we can get allergens, irritants, and even pathogens that can then penetrate in an abnormal way.

If we follow around counterclockwise, we then realize that this barrier disruption can lead to dysbiosis, an alteration of the microbiome. That often results in *Staph aureus*, one of the bad actors in this condition, to become much more dominant; and in so doing, it releases a number of toxins, things like alpha toxin and delta toxin and V8 proteases that can then drive inflammation. But they also can directly damage the skin barrier, and you can actually see that that arrow is bidirectional. They also, it turns out, we can even draw an arrow across the whole figure because they can directly drive itch.

The next part here at the bottom, at the 6:00 position, is the inflammation. We know the immune system is activated. It then releases a whole bunch of factors like IL-4, IL-13, IL-31, the master itch cytokine, doing a lot of things as well, bringing more inflammation, damaging the barrier, driving itch.

And then the last piece is the behavioral part, the scratching behavior which physically damages the skin barrier and creates another behavioral cycle.

So when I meet a patient, I'm thinking about all of these things. And one of the most exciting parts for the severe patients is when I send them to Dr. Boguniewicz at National Jewish, they're able to address a lot of these factors at once.

Mark, when you're thinking about this in terms of a patient and bringing it to life, how are you interacting with these ideas? How are you inquiring about which aspects are damaged and then, ultimately, we're going to get to how you're thinking about treating.

Dr. Boguniewicz: That itch that you started out with, and the scratch that follows, you know, in some ways the immune dysregulation contributes because it turns out that there are receptors on sensory nerves for some of these pruritogenic cytokines. I think that this provides potential identification of therapeutic targets that will be new therapies and where they fit.

But one of the things I would point out that maybe this figure doesn't quite show is a key lesson that it took us a while to appreciate and that is that normal appearing skin in our atopic dermatitis patients, so the nonlesional skin, is really not normal. And that also has translational implications.

But for the patient, I certainly try to simplify things and say, "Look, there's the immune dysregulation, the skin barrier abnormalities, and bacteria." Think of your skin as Disney World. They want to come and set up camp or colonize it and so a lot going on there.

Dr. Lio: It's such a great point, and I do think that the most exciting thing is that now we have treatments that we can actually apply to different areas. So we're learning. I call this the virtuous cycle of drug development. We learn a new aspect of the disease. That often leads to a new treatment, and then that in turn gives us new insight in the disease. And we know that talking to our patients, there's a huge burden of disease and a lot of unmet needs.

One of the things I'll talk about is that it's not just skin deep, that there really are other comorbidities, both atopic and nonatopic, that can come along with eczema that's untreated or undertreated or maybe even if we do our best job treating it, we don't really know. But I think of no better person in the US to talk about this than you. What are your thoughts on this atopic march, and can we alter it? Can we affect it in any way, or do we just sort of have to let fate run its course?

Dr. Boguniewicz: Yeah, for sure. Many of us who work in these tertiary referral centers, it appears that every patient we see is, you know, on this atopic march. It turns out that so, first of all, to sort of better, you know, define that, that is that progression from one atopic disease, typically atopic dermatitis to asthma and allergic disorders.

You know, when you look at large birth cohort studies, that are skewed towards more mild patients, it seems that only a small percentage of patients follow an atopic march. But the more severe patient is certainly more likely to do that. Part of the problem is that when you put things up not in a linear way, but you draw like incidence curves, the curves for food allergy and atopic dermatitis almost mirror each other. And to so many, typically caregivers, but occasionally even older patients, you know, they become consumed with that idea that food allergy and atopic dermatitis are one in the same.

Dr. Lio: When we think about the diagnosis of atopic dermatitis, this is interesting because we know it's changed a little bit over the years. And I do think that probably it's not one disease that we're probably lumping. It may be 10 or 20 years from now when we have better genotyping and we understand a little bit

more of the exosomes and are able to figure all this out, we're probably going to say, "Boy, there really are some distinctive subtypes."

But right now, it's very straightforward. All we really need is it to be itchy. It has to be itchy. It has to be eczematous in one of the patterns that we recognize, and it has to be chronic. And that really is what most clinical trials use as well.
Do you, again you guys see a lot of different patients? Do you feel like there are certain patterns that come back? I'm sure you see also a lot more erythrodermic patients who kind of everything is involved.

Dr. Boguniewicz: Yeah, since you bring up erythroderma, I would certainly, you know, share with our colleagues that if we see an adult because we discuss actually the high numbers of adults that are presenting, to me it's always a question of is this new onset because if you present with new onset eczema, especially with an erythrodermic pattern, I really feel you need to be biopsied because I don't want to miss that rare but potential cutaneous T-cell lymphoma that can manifest in a very sort of nondescript eczematous rash.

The thing that is much more common that I think some of us, especially our younger colleagues who haven't seen many of these patients struggle with is just, you know, a patient who has darker skin pigmentation, an African American patient. And I think that, you know, unlike that, a pale, freckled, Irish sort of child where that erythema is screaming at you from across the room to "help me, help me," you know, some of those patients you don't appreciate the amount of inflammation. They already present with more advance lichenified skin and so on. So is that a common problem for you too?

Dr. Lio: Absolutely, and I think the biggest risk is exactly as you're alluding to, that you can underdiagnose somebody or, you know, underrate them. You think, oh, it doesn't look that red. It doesn't look that bad; and meanwhile, they're pretty severe. So I'm a big proponent for, of course, a close examination but also some of those patient-reported outcomes. Ask how they're sleeping. Ask their level of itch.

Dr. Boguniewicz: Earlier you had mentioned, you know, the usual atopic ones that we sort of discussed in the context of an atopic march with asthma and allergic disorders. But in recent years, people have been paying more attention to nonatopic comorbidities. So, is that something that you sometimes see with the behavior like ADHD as part of the complicating the course of atopic dermatitis?

Dr. Lio: Absolutely. The psychological comorbidities are really scary. The ADHD, the depression, the anxiety, and even suicidal ideation, you know, these are not, fortunately not that common in the general population of atopic dermatitis patients. But in our group, these more severe patients, I see it a lot; so I end up screening for depression and anxiety quite a bit. And many patients will endorse this diagnosis, and I think that part of it is that the disease is terrible, directly. They're miserable, they're often itchy, and they're in pain. Part of it is that even second piece with sleep disturbance, and I often feel that one of the most sensitive questions for control is just about sleep. You know, "how are you sleeping?"

Dr. Boguniewicz: A super important point because, you know, as I teach my younger colleagues, the fellows that are training with us, you know, you see what it's like to have disturbed or interrupted sleep. Not for days or weeks but sometimes months or years.

And I'll often have a parent say, usually a mom, who has come to us; and it seems like I'm the first clinician to really address that issue. And they often, at that point, break down and cry because, you know, you could make those clinical diagnoses of how much erythema, excoriation, so on so quickly. And yet dealing with the psychosocial aspects of a chronic pruritic relapsing disease is so important. And, I'm so happy that with the new drugs that we're studying, they often now incorporate those different measures of assessing how much, you know, the disease is impacting quality of life of the patients and their caregivers.

Dr. Lio: It's so true. And I think this really gives us a sense of, when we are approaching a disease, we realize that it is a rollercoaster. There are often ups and downs, these flareups, and then maybe some intermissions between them. But we know from some of the surveys that even between a flare, patients are really worried about it. They're anxious about it. So, even if their skin looks better or they're in a relative remission, they're still often not okay. There's still activity going on; and as you said from the very beginning, even if the skin looks normal, it probably is not normal. There's probably still barrier damage and low-level inflammatory activity.

So, when we think about this, I often break it down into two components, and this is really just a way of thinking about it. But I like the idea that we have a rescue treatment for when they flare up because we want to try to do everything we can, use all the tools in our toolbox to quickly dampen that flare down. But more importantly then, just as we would with asthma, if somebody's having more than a couple flares a year, we want to get them on more of a maintenance or a preventative protocol so that we're not having to keep trying to fight these flareups as they come because they take a huge toll on disease.

Dr. Boguniewicz: Right, you waved your hand like that; and to me, that brings up that perfect analogy of we need to get our patients off this crazy rollercoaster ride that atopic dermatitis takes them on and not be chasing after these flares in this typically reactive manner but to try to stay ahead of it.

Dr. Lio: And I kind of break it down into those three hurdles that I call, the three great hurdles. Getting the patient clear; usually we can do that. I feel like we have enough tools in our toolbox to get almost anybody clear. I have a couple of patients that keep me awake at night where I can't seem to get them clear in the first place.

But then keeping them clear safely, to me, that's really hard. You know, these are the patients that say, "Boy, I'm using a tub of triamcinolone every week, and that keeps me under control." But then you say, "But, boy, this is not good for you. I can't have you putting this all over your body. It's not safe." Or people getting prednisone or prednisolone all the time, you know, four, five, six times a year. It's like this is not going to work.

And then they have to be able to maintain it, and I think that's the other piece. I love phototherapy as a dermatologist, but I also fully realize that it is a pain in the neck; and very few patients can actually do it.

I'm trying to always balance these with that opposite pressure of not wanting to be chasing flares. When you see patients, do you often feel that sense of frustration about their regimen in trying to put everything together?

Dr. Boguniewicz: Yeah, absolutely because, I mean, there are the practical things that you're limited in the amount of time. So you have exhausted, sleep deprived families that often can't absorb all the information. Like if you're talking about the complexity of the underlying disease. You're talking about the natural course, the prognosis. You know, right now we're hampered by the fact that we don't have biomarkers that can really tell us with certainty, you know, what is going to be the natural course for any given, you know, patient.

The good news is that it is a big pyramid – would you agree? – with lots of little infants and fewer patients as they get older. But, you know, that's good when you're talking in generality. For that parent who says, "Well, when is my child going to get off that pyramid?" you know, now we're sort of, you know, stuck and limited. And then to try to convince them that a proactive approach makes more sense than a reactive approach to chasing the disease when they are, in a way, hoping that maybe when that child's finally clear, that this is the end of it. And so until they convince themselves that there is a relapsing aspect, you know, and who knows with the new therapies that it's systemic therapies intervening early, you know, we may change all of that. But that remains to be seen.

But I think that, right, sitting down with them and giving them those options of, you know, a written action plan and what to do during a flare versus what to do when you maintain, I think, those written step care plans or action plans are really critical when you're dealing with patients who either have trouble understanding the disease, the complexity, the chronicity, or just, you know, they haven't slept well.

EPISODE 2
CURRENT AND DEVELOPING SYSTEMIC AGENTS FOR TREATING M-S AD IN ACCORDANCE WITH CLINICAL GUIDELINES

T.J. Chao, MPAS, PA-C: Hi, I'm T.J. Chao. I'm a Dermatology Physician Assistant with 24 years' experience. I work at Atlanta North Dermatology.

Peter Lio, MD, FAAD: I'm Dr. Peter Lio. I'm a Clinical Assistant Professor of Dermatology & Pediatrics, Northwestern University Feinberg School of Medicine, and the Founding Director of the Chicago Integrative Eczema Center.

T.J. Chao: And I'm very thankful that we have not only products that are highly effective that can stop these flares from even happening, but also minimize the use of some of those more dangerous medications, like immunosuppressives and oral steroids that we used in the past.

Dr Lio: I totally agree because, you're right, that's the other side of the coin; the treatments that we have can help, but they always come with some price to pay and some potential adverse events. And we're always looking to maximize that balance and make it as most favorable as we can for the patient.

And this is reflected, I think, in the clinical practice guidelines. Now, some of these guidelines are a bit older that we're looking at and they're finally getting updated after quite some time. I mean I think the American Academy of Dermatology guidelines were pushing a decade of age, and so finally they've been updated. But what's really interesting and, I think, wonderful but also a little bit tragic at the same time is that things are happening so fast that the guidelines can't keep up.

T.J. Chao: Yes. And I'm very thankful for the guidelines now because I've had a number of patients over the years who really prefer or lean on oral steroids or maybe they've come into the practice from another practice where they were receiving IM Kenalog every three months. And with these guidelines, it's a good way to show the patients that we're not treating this disease that way anymore and, really, we need to treat the disease more comprehensively and less broad and more targeted.

And I think that's what these guidelines now reflect is there's a change in the way we're treating the disease overall, and it's going to be safer and more effective for patients.

Dr. Lio: It's such a great point. And the more people we can get to at least get into the guideline concept that there is a therapeutic ladder, that we're trying to have shared decision-making, that we're, of course, trying to build from doing as little as possible that would be easy – things like good education, avoiding triggers, good moisturization, gentle bathing – like that's always going to be the basics.

T.J. Chao: What I tell my patients now when they come in and they ask for steroids, systemic steroids I tell them, "You don't need to live this way, that we're in the middle of a renaissance of the treatment of atopic dermatitis and we don't have to rely on the old agents to treat this disease anymore. We don't have to put you at risk. We don't have to destroy your body like we may have in the past with some of the options that

we had available." So I do try to really reorient those patients and if they still push back, I still push back even harder to make sure that we get them off the systemic steroids and get them on one of these newer agents that work so well.

Dr. Lio: It's such a great point. And how do they work? Well, of course, you know, systemic corticosteroids are doing a lot of things, right. They're affecting the immune system extremely broadly. Of course, they're even used in transplant patients and all sorts of different diseases. Because they shut down the immune system broadly, they also have effect on the blood vessels, they have effect on the eye, on the gut, you know, all these different things because they're so broad.

When we look at some of the more targeted treatments, of course, the first big systemic, I think, entry into the market was March of 2017 in the United States. That was dupilumab and that's a fully human monoclonal antibody. It binds to the IL-4 receptor alpha. It blocks both IL-4 and IL-13 signaling. Really exciting. And then, of course, shortly after we got tralokinumab, which is another biologic agent, binds directly to IL-13. Lebrikizumab was already released in Europe and other markets. Hopefully, will be coming to the United States some point soon. That's another IL-13 direct binder. And then we have nemolizumab, which is being developed right now. That's an IL-31 inhibitor, kind of neat, the master itch cytokine.

And then the other side we got one layer deeper because we know when the cytokines bind to the receptor, those receptors come together and the JAK system then activates and activates the STAT molecule which goes into the nucleus. So if you affect the JAKs, then we can also block some of this cascade. And that's really where our JAK inhibitors come in, and we have in the US upadacitinib, abrocitinib, and then a topical agent, topical ruxolitinib, and then in other parts of the world there's baricitinib for AD as well. In the US, that's only for, right now for alopecia areata. Have you had some experience? I'm sure you have.

T.J. Chao: It's gotten very easy, I think, to treat this disease now. And the patients that I've seen on all of these agents overwhelmingly are happy. And the good news now is if they are not responding to one agent, I always tell the patients, "If you're not happy with what we're doing right now, it's okay. We have other options, and we've got a lot of other options coming for the treatment of atopic dermatitis. And you'll have endless options going forward into the future so we don't necessarily have to settle if you feel that you're not doing well."

But overwhelmingly when patients respond, they almost can't believe that their atopic dermatitis is this well-controlled. Some of them say, "I've lived my whole life with this and all of a sudden it's gone. I don't know, you know, I don't know how to think about this or feel about this because I've never had this level of freedom from this disease." So it's exciting as a provider to also get that kind of positive feedback from patients. You know, it makes us feel good that we're able to have such a great impact on our patients.

Dr. Lio: I totally agree and I love that sentiment that when we have better tools in our toolbox, we're actually better at getting people better and it's more fun to actually use these things instead of struggling and everything seems like a terrible tradeoff. And when you look at what we now have in our toolbox, so,

for example, dupilumab, the first biologic, now we have four-year data on its safety and efficacy. We have an indication all the way down to six months of age.

When we look at the four-year data, we can see just incredible stability of people just staying quite, quite in good shape. In fact, you know, the numbers for EASI-75, so the patients who were able to get 75% or better improvement on their Eczema Area and Severity Index, over 90% of the patients. It's kind of crazy to be able to maintain that because I often say, "The three big hurdles are we got to get you clear, we have to keep you clear safely, and then you have to be able to keep it up." And that really speaks to some of the issues with topicals or side effects with them, you know, people can't keep it going and here we're seeing multiple years of maintaining this really good improvement with a relatively compact side effect and safety profile.

You know, we know we have to talk about the conjunctivitis in particular, so the conjunctivitis, blepharitis, keratitis, but apparently in some patients that we can see that, we have injection site reaction. We do maybe have a little bit of a signal for increased oral herpes reactivation but, in general, pretty tolerable. And, similarly, with tralokinumab, its cousin, you know, the IL-13 inhibitor, we can see the 52-week data and, again, we're seeing a very, very nice improvement. In fact, it almost seems like for some of the indices it continues to creep up. Like they're continuing to get better in some ways even at that mark and that's kind of fascinating. We've seen this sort of slow progression. The first month or two they're doing better, but it continues to creep up slowly. We don't seem to hit the plateau maybe even as long as year.

I'll conclude by saying lebrikizumab, kind of the third of our biologics, again, hopefully to be approved soon, approved in some parts of the world already, very similar. Again, excellent data even all the way out through 52 weeks both in terms of safety and efficacy. And one nice thing about these, this trio of biologics – dupilumab, tralokinumab, lebrikizumab – they're all very similar in terms of efficacy and safety profile. And that makes it nice because if one agent didn't agree with somebody or if an insurance company preferred one or the other, we now have a few options even within this same relative class. They're not all identical and I want to be clear on that. They are distinct entities and they work a little bit differently each one, but they are same pathway which is kind of nice.

T.J. Chao: Yeah, and I believe that all of these agents are great and then the ability to be able to toggle between, you know, various dosing schedules every two weeks, every four weeks, potentially every other month in some cases, you know, we have the opportunity to have or offer our patients the freedom from the disease that they're looking for like never before. You know, in the past, obviously, they used topical steroids and would have to essentially treat it every day; and then today, other than moisturizing, really they can feel that freedom from their disease by using these products. And as more and more of these products come to market and the dosing starts shifting more and more, it's just going to offer a lot of relief and feelings of freedom for the patient.

Dr. Lio: I couldn't agree more. That last one is quite different, which is nemolizumab, and that's the IL-31 inhibitor. And that's kind of neat because it seems to be more focused on the itch, which we know is one of the most common complaints of patients. So, again, to even have another totally different pathway for biologics, hopefully in the next year or two we'll have that, we're going to really have quite a menu to show

patients. We're going to be able to say, "Listen, there's a number of different ways we can go here. We can talk about these very early on."

We'd be remiss if we didn't talk a little bit about the potential side effects because, you know, the systemics are amazing and they do have a lot of benefits. Some of the side effects, I think, that come up especially for the IL-13 inhibitor, so dupilumab, tralokinumab, lebri, all seem to have this eye issue. So this ocular surface disease I think is kind of the maybe the most broad way of putting it because it can be conjunctivitis, keratitis, blepharitis, eye pruritus, dry eye, sort of this whole group of things.

Now, the most important thing that I've had to tell patients, I had a few patients who were very worried that this would cause blindness or, you know, something much more dangerous. And, generally speaking, that's not what we're talking about here. This is really ocular surface issues. And one of the thoughts on how this happens, and this is, I think, just squarely in the realm of a theory, but it's that the goblet cells in the conjunctiva they actually require IL-13. So any agent that can decrease IL-13 causes them to kind of shut down and maybe even undergo apoptosis so that the eye becomes dry and irritated.

So the most important thing I think we can say about this is just tell the patients to be on the lookout. I always make the dad joke, "Keep an eye on your eye." They roll their eyes, but they remember. And then if they have dryness, itching, conjunctivitis, then we just want to get them to see a specialist.

T.J. Chao: Well I think you're great at dad jokes, by the way; I just wanted to mention that. When the patients are actually coming into the office, in many ways and many times, they are talking about this as an issue, right. They've gone online, they've read. Maybe they've been on blogs and read whatever anyone can type on there about this. And I've had patients come in and, just like you said, they think that these products are going to cause blindness or, you know, blurred vision or some sort of permanent damage.

So, you know, it's good to really go over this and then explain, and I loved your explanation of the goblet cells because that's a theory that I've heard over the years as well. And to explain to them that for most, for the most part when patients have this, you, they could be referred to an ophthalmologist. In many ways, it's treated and the patients, the condition resolves and they move on and they continue the therapy. And even in the clinical trials, we saw dropout rates be very low for this particular problem. So I think education is key with the patients regarding this concern.

Dr. Lio: We'll shift gears again a little bit and talk about those patients on a biologic therapy. One of the big questions that comes up is, "What do I do about vaccines?" And this is a little tricky because the first point I think is easy. The easy part is saying, "We don't want anyone to take any live vaccines while they're on a biologic or any kind of immunomodulatory drug." And the reason there is just that if we're tinkering with the immune system, ever very gently as we've, as we intimated, there is a weird chance that that live vaccine, which is a pathogen, right, it could activate in their body and cause disease. So that, that's generally a no go.

But what about the inactivated vaccines, which are the majority of things adults are going to get? This would be things like the COVID vaccine, influenza vaccine, the newest zoster vaccine, pneumococcal vaccine. These are inactivated so, in general, these seem to be not only safe because they can't cause

disease, they're truly inactivated, but also, at least the data that we have and we can see in the dupilumab studies they looked at tetanus, diphtheria, pertussis, and meningococcal vaccines that the response rate was good. They were able to mount that immune response. So it seems like we can go ahead and do those nonlive ones. In general, how do you counsel your patients when you're talking to them about this?

T.J. Chao: So to expand on that a little bit, one are that I've identified where there could be some issues with this is in kids and babies because they are being exposed to some of these live vaccines. So it's important, I think, to reach out to the pediatrician, let them know that the patient is on dupilumab because we've had a couple instances where they were not told and the vaccine was administered and it, while it's probably unlikely to cause any problems, it created a high level anxiety for everyone, including the pediatric practice and the parents. And so everybody was worried for a while. Thankfully, nothing every came of it, but I think that's an important place to make sure we're talking to our patients.

You know, with adults, it's a lot less likely that that's going to be an issue. And I think there's a lot of misperception out there. I think patients come in thinking all vaccines can't be administered. So a day doesn't go by that I get a call about a different vaccine and if it can be administered, especially during the fall and winter, with dupilumab. So educating those patients I think is key.

Dr. Lio: It's a great point. And we're still learning, right. We're still going to learn. Some of these real-world experiments will happen, so we'll kind of keep following.

Well this has been fantastic. Thank you so much for chatting. I really enjoyed this and I'm looking forward to continuing the discussion.

T.J. Chao: Awesome.

EPISODE 3
UTILIZING QOL AND PRO ASSESSMENT TO ENHANCE CLINICAL OUTCOMES IN M-S AD MANAGEMENT

Mark Boguniewicz, MD: I'm Mark Boguniewicz. I'm Professor in the Division of Allergy-Immunology in the Department of Pediatrics at National Jewish Health and the University of Colorado School of Medicine in Denver, Colorado.

Victoria Lazareth, MA, MSN, NP-C, DCNP: I am Victoria Lazareth. I'm a dermatology certified nurse practitioner, and I practice at Contemporary Dermatology on Cape Cod in Massachusetts.

In dermatology, we see so many rashes, but atopic dermatitis is completely different from others in that it affects the entire person. Atopic dermatitis tends to persist even when we as clinicians don't appreciate a great deal of cutaneous eruption. Our patients are struggling because they can't sleep, because they can't stop scratching, because socially they're embarrassed by the presentation of their skin, and it affects their overall mood and very directly the quality of their lives.

Dr. Boguniewicz: I think that, you know, this is such an important aspect to address. When you approach a patient with atopic dermatitis, because it's one thing to recognize the typical clinical signs of redness and swelling and skin thickening and excoriations and maybe even secondary skin infections, weeping and so on, but to see how that is actually impacting the life of that patient or their caregivers when, as you pointed out, they may not have slept well for many weeks, months, sometimes years. And they scratch in their sleep, and you know, then they feel embarrassed by how their skin looks or they're unhappy when they look in the mirror. So, unless we take that on and appreciate what our patients and their caregivers' lives are like, I think we really can't expect successful outcomes.

Victoria Lazareth: But I think one of the most concerning aspects of this disease is patients with skin of color have been underdiagnosed or not diagnosed because clinicians may not be so quick to recognize the patient's experience. It is incredibly difficult for patients, African American or Hispanic descent, to really be able to seek care from clinicians who have a longstanding experience with the entire disease.

Unfortunately, a lot of patients end up with repeated visits to primary care or repeated visits to the Emergency Room. Too many receive a prednisone taper which when they complete the course, then they flare again. So in a way, they are seeking more and more care but having less and less effective disease control.

Dr. Boguniewicz: Yeah, you make such a great point, Victoria, because I think that it adds to that patient or their caregivers' or family's, you know, frustration. And I think that they sometimes sense that some of those clinicians really aren't comfortable with, you know, appreciating what is going on in their life when we look at the bigger picture, not just like looking at their skin because even that very basic thing we often get it wrong because we don't appreciate the amount of inflammation and how sometimes patients develop those more chronic changes with lichenification quite early.

And so unless we really take the time to be empathetic, to really try to communicate some of the key messages and win those patients and their caregivers over so that we can establish really long-term meaningful relationships, knowing that we're at this point certainly not solving things with, you know, a few quick visits.

Victoria Lazareth: I had really a heartwarming experience a month ago with a 17-year-old. She struggled for years and years and years with the itching and scratching and really became somewhat of a social recluse. After her initial injections with a biologic, she came back in absolutely beaming – skin cleared, eyes bright, making great eye contact and smiling. And I looked over at her mom, and her mother had tears in her eyes. And I just thought, huh, and I said, "How you must wish to have back all of those sleepless nights." And she just nodded. And I think that helps us to remember that atopic dermatitis is a disease of the family. It's not just the patient.

Dr. Boguniewicz: Yeah, I love that point because we need to have that whole family engage because they're the ones that are often up with that patient. They're helping them with their skincare.

But to your previous point and to actually have a real patient behind some of these teaching points or pearls is really so powerful in telling that story that our patients want to share with us. And I think we, sometimes it goes both ways because sometimes we underappreciate because we see that, ah, your illness doesn't appear to be as severe to us. And yet to that patient or family, they're still experiencing the itching, the sleep disruption, or that parent looks at that child and to them what we would consider mild erythema, let's say, is still, you know, looking terrible in their eyes.

Conversely, as you pointed out, some of our patients, especially with some of our new systemic therapies, you know, are experiencing disruption of sleep has improved, that the pain that they sense, that it's not just itch but sometimes painful sensations have disappeared, even while we still see a fair amount of maybe chronic changes that will eventually resolve. But to that patient, you know, they are, you know, that's impacting their quality of life so quickly that it's so gratifying to see. So, I really appreciated your clinical vignette.

Victoria Lazareth: I have often relied on journaling as a means to help patients with a variety of different inflammatory dermatoses, help to share with me their experience. As far as I'm concerned, any time I have to take the car to the garage, it looks and sounds fine, right? And our patients will often say the same thing, "I'm absolutely fine today."

So, I have found that asking them to journal their experience and to track what may be common triggers for them. It could be stress, of course, but it could also be diet. It could be certain medications, if they had to be on an antibiotic or others. And I do find that journaling does help me to better appreciate the frequency and the severity that my patients may be experiencing with their atopic dermatitis.

Dr. Boguniewicz: You know, I have to smile as you discuss this important aspect because, you know, on the one hand, I have families that come because they're coming to a tertiary referral center in Denver. And they have, you know, these extensive diaries or journals of what's gone on in that child's life since birth.

And it's literally hundreds if not more pages. On the other hand, I have people who now communicate with one-, two-, three-word texts. And for them, you know, they really keep it very brief. So the two extremes.

You know we have tools that assess different aspects of atopic dermatitis severity because oftentimes in clinical trials we have to do these fairly elaborate scoring systems. It's kind of ironic because some of them were actually developed to help clinicians, but clinicians have pushed back and said, "Look, I'm too busy to do these complex scoring such as using tools such as SCORAD, which was primarily a European scoring atopic dermatitis tool; EASI, so Eczema Area and Severity Index; and then something much more simple like an Investigator Global Assessment where you basically walk in and are able to tell a patient, you know, or to score a patient saying are they clear, almost clear, mild to moderate, or severe? So I'm curious, do you incorporate those in your clinical practice?

Victoria Lazareth: For me as a clinician, it actually helps to have the guidance of a validated tool that suggests that, well, if the patient's responses indicate that the disease severity or the disease frequency is actually increasing, then that's a red flag and, of course, helps us to identify that they're really not nearly as well-controlled as they may appear to be that certain day in clinic.

Dr. Boguniewicz: Here I think the important thing to recognize is we're trying to help busy clinicians. So that patient or caregiver could fill that out while they're waiting to see you. So, we're not trying to add to the burden of seeing patients. We want a simple tool that a patient can fill out and you can look at it and know the scoring and have a sense of how the patient or caregiver, at least, perceives things are going. You want to pick one that you're comfortable with and probably stick with it rather than trying to throw too many of these tools to better understand their illness.

And we know that none of them are perfect, but it's interesting to me that I just recently learned about one that the National Eczema Association developed called Eczema Wise, so this is using an app, so a little bit maybe more technologically advanced.

Victoria Lazareth: My experience, I agree with you that the more focused questionnaires are a little bit easier to manage in a busy clinic.

Dr. Boguniewicz: As you were presenting that Eczema Wise app for the person who's able to download it and use it effectively, you know, the beauty of that approach is that you could capture a lot of data that a clinician, I suppose, could look at and quickly synthesize if they brought it with them to that busy appointment because sometimes a patient only can spend a certain amount of time with their clinician; and sometimes it's hard for them, you know, to recall all the important points that they're trying to make, especially if they haven't slept well for a while. And this really helps both the patient and the clinician in understanding better like what is going on in the life of that patient in between those visits.

EPISODE 4
INCORPORATING SHARED DECISION-MAKING IN ALL FACETS OF TREATMENT SELECTION TO ADDRESS QOL

Victoria Lazareth, MA, MSN, NP-C, DCNP: Hello, my name is Victoria Lazareth. I'm a dermatology Certified Nurse Practitioner, and I practice at a private practice in Massachusetts called Contemporary Dermatology.

T.J. Chao, MPAS, PA-C: Hi, my name's T.J. Chao. I'm a Dermatology Physician Assistant with 23 years of clinical experience in dermatology. I practice in the Atlanta area at Atlanta North Dermatology. I'm also Past-President of the Georgia Dermatology Physician Assistants.

The days of administering systemic steroids and only using topical steroids are things of the past, yet many patients have been using those products for years and are comfortable using those products. With all the new technology we have now with biologics, small molecules, novel topical nonsteroidal agents, it's going to take a lot of educating to help the patients understand why these new products work, why they should continue using them for the long term, and what are their actual goals for success.

Victoria Lazareth: I think that one of the things that we've learned more recently about the disease itself is that it is so multifactorial that it requires really a team, as you were discussing, of not only healthcare providers but also, you know, personal caregivers, family members, dietitians may be helpful, especially behavioral health workers. Patients have disease flares that are associated not just with their skin or their allergies, but they may be associated with an infection or with a malignancy. So, our broadening our horizons to incorporate as many as appropriate into the individual patient's team is really going to ultimately be able to work with that shared decision-making that you were referencing and ultimately to help prevent those flares.

T.J. Chao: I also think, Victoria, that the social network of the patient is an interesting and important factor. We have and understand that social determinants of health have multiple impacts on the patient from their willingness or ability to do things like moisturize the skin. Are they able to afford those products? Are they able to afford the good products, or are they, do they have difficulty with access to those? Do they live in a home where taking a shower and then applying moisturizer is something that can be? And I think there's a lot of questions surrounding this.

And then you have, also, questions about the ability for, of patients to pay for medications. More and more patients are being saddled with the burden of paying large portions of medications; and as newer technology comes, becomes available, that seems to be getting more difficult over time. There may be some social economic issues there. Patients may not make enough income to be able to pay for some of these products or be able to sustain the utility of those products for the long term.

But then there's also factors such as if we're dealing with children, are there caregivers at home that are actually going to help treat some of these problems like atopic dermatitis that require a lot of intensive treatment for both the patient and the family?

Victoria Lazareth: Yeah, I think, by definition, atopic dermatitis is a disease of the family. I absolutely agree. And I recently had an experience with an older patient, she was almost 80 years old, and it's a patient who has struggled with her disease her entire life. And she lives in a nursing facility where the staff conscientiously were concerned about her scratching and the state of her skin and her discomfort.

But unfortunately, in a setting like that, people start treating with anecdotally what they think might be best. So when I met this patient, her caregivers were applying a myriad of different prescription and nonprescription treatments, talcs and powders, and all kinds of stuff to the point where probably was allergic to many of them. She was just digging her skin raw, and then, of course, had secondary infection. So, it's just a cascade of events. In that setting, she was not able to come into the office for phototherapy which can be very effective with that kind of severe flare.

We were able to address that individual's concerns by working with her whole team of caregivers and convincing them that less was going to be more. It took a lot of encouragement, but we finally got them to stop applying anything but a moisturizer to her skin. And I had the opportunity to determine that it would be absolutely appropriate and safe for her to have a biologic therapy. And for the first time in her life, literally within two weeks of starting the biologic, she was no longer scratching.

So, we do know more than we ever did before, but we can't do it in a vacuum. It really takes a team to work together to get that kind of outcome and benefit with a patient.

T.J. Chao: I try to involve not just the patient but potentially their family members as well because they're going to have an input into this decision-making.

Victoria Lazareth: T.J., I think you're absolutely spot on. I think it's clear that as providers, all of us are looking at efficacy and safety as pillars of treatment decision-making. But in the shared decision-making, I believe that NPs and PAs really shine at this level. We tend to have really meaningful conversations with our patients. Maybe we have the luxury of a little bit more time. I'm not sure that's true, but I think we make the time, we take the time because NPs and PAs are very, very focused on patient education.

And, therefore, when we are communicating with them, and it goes back to what you were previously saying about, you know, cultural concerns or financial access to insurance, to healthcare providers, that we tend to take all of those factors into consideration. And we'll discuss the accessibility of a treatment, and we'll access, we'll discuss with the patients what they can expect in terms of tolerability. And if they don't tolerate a treatment, and I think that's really our strong suit, is to be able to create that open dialogue so that the decision-making really is shared.

T.J. Chao: One factor that plays a role in this is diversity. There's a big push now in the dermatology education community to focus on the more diverse population. We know that there's an issue with clinical trials, for example, of having diverse populations. Many times the patients in the clinical trials are predominantly Caucasian. So getting patients of color to come into these studies is going to be an important task for the future because the United States is becoming more multicultural. It's changing. It's going to be more brown than Caucasian in time. And so it's imperative for us to be able to get those

patients in clinical trials and understand how they respond or how they will perform with different treatments.

Victoria Lazareth: That's so true. I was preparing a lecture earlier this year, and I came across the statistic that dermatology is the second least diverse specialty in all of medicine. Second only to orthopedics. It's really staggering. So statistically, Latinos make up 16% of the population but only 4% of dermatologists. African Americans make up 13% of the population but only 3% of dermatologists. So this is extraordinarily important we understand that because we have to understand these concepts of just, you know, race concordance and discordance. And some patients are going to feel more comfortable with a female provider. Others with a male. Some patients are going to feel more comfortable with a provider who shares their ethnicity or their cultural background.

And it really has, I mean this has been studied, and it makes a huge, huge difference. The American Academy of Dermatology has a group called the Skin of Color Physicians, and they are in the process of creating 100 modules of education for dermatology physicians and residents in order to help with this understanding of diversity and in the potential barriers to care. Unfortunately, that's not yet available to NPs and PAs, so this, again, this type of program is really valuable to us to consider and incorporate those concerns, you know, openly with our patients.

T.J. Chao: So there is something that we could do. It's called the VIBE Framework. It provides questions that should be asked throughout conversations with patients to make equitable decisions regarding treatment and management choices. VIBE stands for views, inclusion, benefits and burdens, and equity.

With views, you know, we're asking is the patient's view, is their view, their outlook on this current problem that they're having, is it being considered by the medical provider?

Inclusion, the next, the I in VIBE, is has the necessary time been taken to hear concerns? Are we listening to our patients? Are we rushing from room to room? Are we actually sitting down and having that conversation with our patients to find out what their needs truly are? And I think that is an important piece that dermatology nurse practitioners and dermatology PAs focus on when they're treating their patients.

The B of VIBE is benefits and burdens, and how will the patient benefit from this shared decision-making or this decision about treatment? And if there's a risk to the patient, what harm might be done by making this decision? What are the risks? What are the benefits for those patients?

And then finally, looking at equity, the E in VIBE, does the decision lead to an equitable situation for the patient? Is this a fair treatment for the patient? Is the patient going to get what they're looking for out of this treatment decision?

Victoria Lazareth: I think that this type of tool is extremely valuable for us just to maintain the patient as the focal point. So I think there is some value. Certainly there is for me in scheduling follow-ups pretty quickly after the initial encounter to give patients a chance to digest with the initial information and then to come back and be able to really enhance that shared decision-making process.

T.J. Chao: And to further expand on that, I also think it's important when the patients come back that we reeducate or remind the patients of what that shared decision was and then evaluate what were the results of that shared decision. Was it the right decision; was it the wrong decision? How can we make better decisions going forward, and what are the options?

The first thing is sitting down and talking to the patient and giving them a say in the treatment and not dictating what the treatment should be and hope the patient just does it. Those times are gone and really talking to the patient, making shared decision-making is really the way to go into the future.

Victoria Lazareth: And as a result, a huge number of new modalities available for treatment that we just didn't have before. And that's why I bring up the older patients. I met a gentleman last week who said that he spent half of his childhood in tar baths and not able to participate in all the rest of the fun that his friends were having. And he was astounded to learn that we actually have modalities now that can actually manage this disease and not just wait for flares, then prednisone as you referenced earlier.

So again, working with our primary care colleagues, being able to see the patients in specialty clinics whenever possible, at least for baseline, is really, really valuable to the ultimate management of the disease.