Understanding Atopic Dermatitis and Treating It.

Atopic dermatitis, also known as eczema is a chronic skin condition that is estimated to affect between 10-20% of children but often appears in adults as well, particularly the elderly. Although there is no known cure for atopic dermatitis, flare-ups can nearly always be minimized and sometimes prevented, and recent research has identified factors involved in its development that may lead to new treatments to control it more effectively. We are exploring the different types of atopic dermatitis, discussing their unique causes, symptoms and treatments with Dr. Zelma Chiesa Fuxench from University of Pennsylvania.

Full Transcript:

Priya Menon: Good afternoon and welcome to another episode of CureTalks. I'm Priya Menon, your host and today the topic of our discussion is Atopic Dermatitis. We are joined by Dr Zelma Chiesa from the University of Pennsylvania. On the patient panel to discuss the patient perspective, we have patient advocates, David Stanley and Ashley Wall. If anyone has any questions for Dr Chiesa, please feel free to submit them on the page you're listening to the show or email them to priya@trialx.com. You can also dial in using (718) 664-6574 and ask your questions when we are live here today. I repeat (718) 664-6574. We would like to hear from you and would be on the lookout for the questions throughout the show. So to get the show started we have with us Dr Zelma Chiesa of University of Pennsylvania. Dr Chiesa is a board certified dermatologist with a focus on general dermatology, nonmelanoma skin cancer and inflammatory diseases. Dr Chiesa, great to have you with us and welcome to CureTalks.

Dr Zelma Chiesa: Thank you. Thank you for the kind introduction and for the opportunity to be here today as part of this wonderful panel. I will also like to take a moment to welcome the audience, and thank them for taking the time to tune into this program today.

Priya: Thank you doctor. So Dr Chiesa so what I have for you here are some basic questions initially as we try to understand what atopic dermatitis is, and then go on to some associated comorbidities and then talk about the latest research and treatments. This way I hope we can explore the impact of atopic dermatitis from multiple perspectives. So to start off, let's begin by defining atopic dermatitis.

Dr Zelma Chiesa: Yeah, so that's a great question. Now atopic dermatitis or Eczema, those are terms that are oftentimes used interchangeably. When you think about atopic dermatitis, we're thinking about a disease that's chronic, it's an inflammatory skin disease that presents with areas of inflammation. When we talk about inflammation, we talk about areas that are red, they can show increased thickness of the skin, scaling and dryness and perhaps the hallmark symptoms of atopic dermatitis is itching and itching is significant morbidity in this patient population because it can lead to impact in sleep loss, it can also impact and decrease the quality of life. Now in it's more classical form, particularly in children, it tends to affect the folds of the skin – interior to the elbows and behind the knees. However the clinical presentation can be quite varied in other patient populations. For example, in neonates, it might just present on the hands or you may also involve extensive surfaces, which are not the typical surfaces involved.

Priya: Dr Chiesa, so is atopic dermatitis different from eczema and if it's different then what makes it different?

Dr Zelma Chiesa: So it's again, as I previously mentioned, those are terms that are used interchangeably.

When we talk about Eczema, we're talking basically like an umbrella term. And there's different types of Eczema that could go within that group you could talk about Nummular Eczema, Dyshidrotic Eczema. You can also talk about atopic dermatitis, but for the most part, and I think for our discussion with our audience we will use both terms interchangeably, meaning atopic dermatitis referring as Eczema and either way, there's no clear diagnosis to distinguish atopic dermatitis or Eczema. There are certainly some criteria scores that are used, but those are basically used more in clinical trials or research, but they're not really used in clinical practice on a daily basis.

Priya: As you just mentioned that the condition is not restricted to children and it's an adult disease as well. So can you talk a little bit about the prevalence of atopic dermatitis?

Dr Zelma Chiesa: Yes, of course. So when thinking about atopic dermatitis or Eczema, most people, and even most providers will still think of this as a disease primarily affecting children. And that is partly true. We know that the prevalence of Eczema in the pediatric population is quite high. The prevalence worldwide has been reported to vary between 10% to 25% of the population. We know that in the United States the prevalence is closer to about 13 to 15% and we used to think that most patients with atopic dermatitis were pediatric patients who would outgrow their disease. However, this has been rather quite difficult to study and in fact what may be actually more common is that instead of actual resolution of the disease, what happens is that the disease severity will vary through time, meaning a patient may be more severe earlier during their lifetime and then as they get older, it might, kind of quiet down for a little bit.

And then as they continue to grow older, the disease starts to appear again and worsen again in severity. When you think about the prevalence of the disease or in the adult population, it's been found in one of the studies that we are participating in, the prevalence has been described to vary between 2 to 10% of the adult population. So it's less than the pediatric population. However, in our more recent study, we found that the prevalence in the population of the United States is about 7%. And so when you put things into perspective, if we use US-based census data, this would mean that we have about 16.5 million adults in the United States that would have a diagnosis or fit a diagnosis of atopic dermatitis with about 6.6 million meeting criteria for moderate to severe disease. So this would mean that atopic dermatitis is perhaps the most prevalent skin disease in the adult population as well.

And there's also the idea out there that are some things called Adult Onset Atopic Dermatitis. And it's atopic dermatitis that tends to occur in the adult population, different cut off ages have been used 16, 18 years of age or older, in patients who have no prior history of Eczema or atopic dermatitis as a child. And furthermore, there's another entity called atopic dermatitis of the elderly, which hasn't really been quite well defined yet, but has a similar clinical presentation and it tends to occur in patients who are older than 65.

Priya: What about the environmental effects on this prevalence?

Dr Zelma Chiesa: So yes. So the prior population based studies in the US have found that the prevalence of atopic dermatitis seems to be higher in either eastern states or states that have larger metropolitan areas. So trying to kind of explain why it could it be that patients who live in this type of environment are exposed to more environmental pollutants or air pollutants. Could it also be that patient that live in more metropolitan areas are less exposed to a number of antigens that they would get exposed to if they would live in the more rural areas? We don't really know how to best explain that relationship and certainly future studies need to address that. But there are certainly these and environmental components to atopic dermatitis. And we can see that in, for example, studies that have been done in countries that have been less developed in the past and now are being more developed such as Ethiopia where the prevalence of atopic dermatitis has also increased with time.

Priya: I have another question. We have already talked about the environmental effect on atopic dermatitis. But we also know atopic dermatitis is not contagious. But we've seen that more than one member of a family may be afflicted. So definitely, this condition seems to have a genetic component, isn't that right?

Dr Zelma Chiesa: Yes. That is true. And I'm glad that you talk about atopic dermatitis not being a contagious disease because I think it's very important to reiterate that to our audience that you can touch, you can hug, you can share a handshake with a patient who suffers from Eczema or atopic dermatitis and you will not develop this disease. Certainly patients with atopic dermatitis do have a strong family history of atopic dermatitis and this has been shown to be more consistent in the scientific literature. For example, approximately 70% of patients with atopic dermatitis do have a causative family history of atopic disease. And studies have also shown that the odds of developing atopic dermatitis are two to three, four times higher in patients in children that have one atopic parent, and up to three to five times higher in patients who have two parents who are affected with atopic dermatitis.

So it's important to understand that. And when you think about the genetic components of atopic dermatitis, perhaps the most well studied and known genetic risk factor for Eczema is the filaggrin gene. Multiple loss of function mutations in the filaggrin gene have been studied in the literature. So this gene, for those of you who are not familiar with it, codes for a protein called filaggrin or filament aggregating protein. Now this protein is an important component of the skin barrier and it's partly responsible for development of defects in skin barrier. So when you do have mutations in filaggrin, you have increased loss of water or transepidermal water loss. You also have exposure to antigens that can penetrate the skin and they can sensitize our immune systems through percutaneous exposure. It's also been shown that patients who have mutations in this, filaggrin gene have more persistent disease.

These studies, it's important to know that the majority of these studies were done in caucasian populations, populations of northern European descent and as well as Asians. And for a time we understood these to be less prevalent amongst other races or ethnicities such as African Americans or blacks. However, a recent work by one of my mentors, Dr Mercola and his team at the University of Pennsylvania has shown that African American children do in fact have mutations in the filaggrin gene. These are not the most common mutations that had been previously described but are nonetheless present. And interestingly, these studies also showed that these were also associated with particularly more persistent disease in pediatric patients or black or African American. So it's important to know that as well.

Priya: At this point I would like to take in one of the first questions that came in via email and it is like would it be right to say that Eczema is 80 % genetic and 20% environmental?

Dr Zelma Chiesa: I would be careful about attributing so much of the components to atopic dermatitis as a primary genetic disease. When you think about the pathophysiology of atopic dermatitis, it is an extremely complex disease. There's an interplay between genetic mutations of which I previously mentioned, Filaggrin, the environment as well. I think it's also important to know that there are a great deal of patients with atopic dermatitis who do not have filaggrin mutations and they still develop atopic dermatitis, and this would pinpoint more towards an immune dysregulation as the cause and not so much as a genetic component. And in addition to that, patients who have mutations in Filaggrin do not always develop atopic dermatitis. It's thought that about 40% of individuals with the filaggrin mutations do not go on to develop the disease. So yes, there is definitely a genetic component, but again, the pathophysiology is complex and it most likely involves an interplay between environmental factors as well as immune dysregulation and to whether or not, you know, to what point these susceptibilities are genetically predetermined. I think that remains to be seen.

Priya: We are on the topic of genetics here, I have a couple more questions related to it. It is said that allergies and asthma often develop in the same people, and that 50 to 70% of children with atopic dermatitis subsequently developed asthma. And I have a personal interest in this because when my kid was diagnosed with asthma, I was asked to keep a lookout for eczema as well. So it would be great to actually talk a little bit about this.

Dr Zelma Chiesa: I know, and, and I appreciate this question because this is a question that comes a lot during the discussion with patients. And I believe the concept that we are referring to is the concept of the Atopic March, or the idea that development of the atopic dermatitis early in life will often predate the development of other allergic disorders such as, for example, asthma or food allergies. And this is an interest an area of research and focus because it's trying to explain that. If you develop atopic dermatitis early in life, could you be in your way exposing that immune system by way of an intact skin barrier, to become sensitized to environmental allergens, right? And trigger other allergic diseases such as nasal allergies or asthma. And the idea is to try to identify, well, if we do early interventions, if we prevent the onset of atopic dermatitis, is there a way that we can prevent the development of asthma or nasal, seasonal allergies or food allergies as well.

Is there a way that we can identify what are those allergens that could potentially contribute to modify the atopic March in a way to prevent these other diseases, which can go on to become chronic lifelong diseases from developing in the first place. And I think that's a very interesting area of research that we're trying to get at. So it's not particularly strange to see in children both carry the presence of things like food allergies, seasonal allergies, asthma as well. I think with adult onset atopic dermatitis, the story is a little bit different. One of the questions that I typically get from my adult patients who come to see me for the first time is, I'm breaking out. I think this is Eczema. Is it something I'm doing wrong?

Is it something that I'm eating? And by the time they come in, they have been on these elimination diets and nothing is working. And when you take a step back and you look at those patients, you tend to realize that, the prevalence of food allergies goes down as we age. So I try to counsel my patients. If you are presenting now with symptoms of atopic dermatitis and you've never had this before, it's very unlikely that this is probably attributed to a food allergy. And that also brings I think a little bit of relief to the patients knowing that, we're not doing anything wrong. It's just a disease coming on and we don't really understand why it happens so later in life at this point.

Priya: In the same line of thought, I read that another indication that people with celiac disease are also more prone to have eczema. And relatives of celiac patients are twice as likely to have eczema and is this also related to the genes or familial inheritance?

Dr Zelma Chiesa: Yeah. So that's another interesting question that we also in new patients when they come to the office and ask the questions, could I have celiac disease? And I mean oftentimes, the answer is it depends on the patient and the age of its presentation. Right? We do know that atopic dermatitis, the way we think about the disease is changing a little bit, right, with the studies and comorbidities. We're not only thinking about atopic dermatitis as a disease just affecting the skin, but we're also thinking about atopic dermatitis as a disease that affects, that can also result in systemic inflammation. And associations that have been previously described include autoimmune diseases such as celiac disease, vitiligo, Alopecia Areata as well, or hair loss. With respect to the celiac disease, it's also being studied in more detail, but prior population based studies or systematic reviews and analysis have shown that patients with atopic dermatitis may in fact be associated with higher prevalence of celiac disease.

And there was a particular study that was done in the pediatric population in Estonia, which showed that pediatric patients who had a diagnosis of atopic dermatitis, had about even a four fold increased risk of developing celiac disease. So now the question becomes should we test everyone for celiac disease? And I don't think that the answer is yes at this point. Celiac disease is prevalent. It is out there, but it doesn't

affect our patients with atopic dermatitis. I would suspect more or raise suspicion in a patient who is presenting with symptoms of Eczema. But if it's a child who's presented with abdominal pain or intractable diarrhea or failure to thrive or other symptoms that could be indicative of a malabsorption, that's where I probably would pursue additional testing. That being said, there are patients who have celiac disease who have absolutely no symptoms. But again, I don't think that the data at this time supports that we screen all patients with atopic dermatitis for celiac disease, but it's important to know that this association has been reported and that we should keep it in the back of our minds whenever we have patients coming in who may present with any of these symptoms.

Priya: I'd like to move on and talk about the symptoms of atopic dermatitis, you did mention that right at the beginning of the talk. Could you please categorize it on the basis of early presentations and late or severe condition being presented to you?

Dr Zelma Chiesa: Of course. So, we're thinking about the clinical presentation of atopic dermatitis. There are studies showing that the distribution of lesions or the phenotypes of atopic dermatitis can actually vary with age. For example, in very young children or infants, the lesions of atopic dermatitis, the inflammation, the redness, the skin thickening, the scaling can be primarily localized to areas such as the face, the buttock area, sometimes the extensor surfaces. So we're talking about the interior aspect of the legs. And then as children grow older, if they'd present Eczema, when they're a little bit older, deletions can primarily be localized to what we consider to be the more classical sites of Eczema, which are the folds of the skin, the elbow falls or behind the knees, sometimes children with Eczema will also present lesions around the neck area.

Then adults, I think the presentation of atopic dermatitis in adults is a little bit more varied. And when we have a patient who's had Eczema for all his life, and you asked them – the question I usually ask them when you were a child, was your eczema primarily on the folds? And they'll say, yes, it was primarily in the folds. But now as I've gotten older, it's now appear in other areas. And that's something that's been described in adults. You can have eczema localized to not only the flexor areas, but also the extensor surfaces. Eczema can also be localized to just specific areas. For example, we have patients who present with Eczema only in the genital area or the breast, the nipple area. We also have patients who only present with Eczema on the palms, which can be very limiting because of the itching and can be very refractory to treatment.

And the diagnosis is sometimes not as easy to make. And so it's important to keep those considerations in mind because if we see a patient – an adult patient who comes to our office and we look at the distribution of lesions, then we find, well, this patient doesn't really follow the more classical pattern for the distribution of Eczema lesions. We may actually miss that diagnosis. So it's important to know that particularly now patients with Eczema can have a very wide presentation. I think one of the most important things to remember is that Eczema is very strongly associated with itching or itch. During my training, some of my mentors and teachers would say, if it's not itching, it's probably not eczema. So take a step back and reexamine your diagnosis because this is definitely a condition that's characterized by that. Other symptoms that I think need to be addressed when talking to patients with Eczema is that because of the widespread inflammation, because of the itching and these patients will experience impact in sleep loss.

They have also been shown to have higher rates of depression or anxiety. And a patient may not say that they're depressed unless you ask about those symptoms. So that is part of my questions when talking to patients, are you depressed – is the Eczema leading to depression? Is the eczema leading to anxiety because you cannot predict the flares? Are you sleeping? There are studies showing that patients with Eczema, may not sleep for five, seven nights out of the week, and that's basically not sleeping any night. And that can have a significant impact, not only in their psychological symptoms, but also in their overall wellbeing.

Priya: So what is the usual routine followed in diagnosis? You said of course the itch is there. And there's an audience question – she wants to know is that any blood work that is done to diagnose the condition?

Dr Zelma Chiesa: So that's another excellent question. So the diagnosis of atopic dermatitis is a clinical diagnosis. It depends, at this time there are really no specific blood tests or specific biomarkers which are routinely used to help establish this diagnosis. Typically a very thorough history is important to know that takes into account the onset of disease, the change of disease patterns through time – if there are any triggering or modifying factors, is there a presence of other atopic diseases such as asthma, seasonal allergies or food allergies as well as the family history of atopic diseases followed by a thorough physical exam with special consideration for current distribution of lesions on morphology of those lesions.

I think it is going to be critical for establishing the correct diagnosis. There are times when certainly you could use some of the criteria – diagnostic criteria that have been developed, including the Hanifin and Rajka criteria, the criteria developed by the American Academy of Dermatology and those criteria are freely available online. We don't typically will use them during clinic, if you're in a basic clinic because they might be extensive and they haven't really been validated in that way where we typically will be using them is for clinical trials. So at this point the diagnosis relies mainly on the history and the clinical examination. At times a skin biopsy may also be considered in cases in which the diagnosis is not clear or the presentation is atypical and this can help aid in establishing a proper diagnosis. And for example, I may have patients who present with severe flares of atopic dermatitis and I go about their history. There doesn't seem to be a strong history of atopic dermatitis in the past. And then I suspect, am I really dealing with atopic dermatitis or could this be something else? And a skin biopsy can sometimes help distinguish that. Particularly, if you have a patient who presents with erythrodermic psoriasis, which is that they're completely red from head to toe and patients with atopic dermatitis can present in that same way. So biopsy can often help to distinguish between the two. In addition to that – patch testing is a way that we can identify if a patient has a contact dermatitis. We do know that just for those of you out there, contact dermatitis or an allergic contact dermatitis is a dermatitis that develops from coming into contact with something in the environment.

It could be a perfume, a preservative, the laundry detergent, so on and so forth. Even the topical steroids that we're using. Atopic dermatitis patients are at higher risk for developing contact dermatitis and have a higher prevalence of contact dermatitis as well. So sometimes if I have a patient who comes to me and says, my Eczema has been very well controlled during the past couple of years and it hasn't been until recently that I just can't get it under control. And it's particularly in this area, it could be the neck, the hands, and it doesn't matter how much steroids I put on, it doesn't matter how much precaution I have, I just can not seem to clear it. So in those particular patients, before I move on to use a systemic treatments, I would say let's take a step back. Let's reexamine the diagnosis. We could consider doing patch testing to rule out the possibility of contact dermatitis. And we've seen that in clinic as well. And the treatment for that is avoidance and that could be life changing for our patients as well. So that may be another thing to consider. I did previously mention about food allergies and how the prevalence of food allergy decreases as patients get older. So at this time, my adult patients, I don't really recommend testing for food allergies unless patients present with other clinical symptoms such as, for example, hives, swelling of the face, the throat or lip to suspect that there could actually be some form of like anaphylaxis. And I also think it's important when you're evaluating your patients to get a thorough assessment of what their actual skin care regimen is because it's, this is probably considered one of the first steps in managing atopic dermatitis.

With respect to blood work, there's always the question about, well, should I get my IgE levels tested? And that's an interesting question. Certainly elevation in total or allergist specific IgE levels have been shown to be even in patients with atopic dermatitis and it seems that higher IgE levels are associated with more severe disease and the disease that has some more protracted course. However it still remains controversial. It's not something that I would typically do to establish a diagnosis or to manage response to treatment. We do know that about 20% of people with atopic dermatitis will not demonstrate changes in the IgE. So I really cannot use them in that population. And we also know that about 50% of the healthy population in the US, will have elevated IgE levels. So we tend to think about IgE changes as more of something happening more downstream in the inflammatory cascade and not something that's triggering the

symptoms. I will not typically test for that.

Priya: I have a couple more questions, but I think I should just open it up for the panel right now. With that I'll hand it over to David Stanley to begin with his questions. David is a writer, teacher, actor, narrator. He's a melanoma survivor. He has a book called Melanoma: It started with a freckle, which is available on Amazon, David over to you.

David Stanley: Yeah. Thank you. Dr. I have a couple questions. A couple of them are, kind of hard science questions and a couple of them are sort of self care questions, which would you rather address first?

Dr Zelma Chiesa: Hi David. Whichever you would like to start is completely fine by me. Whichever you think is the most important that you want answered.

David: All right. I want to go back to genetics because that's some of my science background as well. With one of the mutations that CARD11 mutation, that interrupts propyl glutamine, one of the amino acids that interrupts glutamine production. And there's some reading that I did in a couple of the journals that were showing some reasonable success with both glutamine and then using supplementation as a treatment for people who were positive for that particular mutation. Could you talk to that for a second?

Dr Zelma Chiesa: Yeah, sure, sure. David. So there's, I think it's an interesting point, right? And when talking about the types of supplementation, and there have been positive changes shown is some of the smaller studies, which could potentially be associated with the development of atopic dermatitis in the future. And it could be that supplementation may actually ameliorate some of these symptoms. However, at the present time, that the data is insufficient to recommend that for as, I would say as a more preventative approach or as a way to treat the symptoms of Eczema. And quite frankly, the most recent clinical trials are focused primarily on treating the immune dysregulation, and not so much the aspect of supplementation as well.

David: Okay. Let me ask again about some of the relationships between Eczema and Hay fever and asthma, as Priya said, I have a little bit of layman's expertise, just enough to be dangerous, on the gene linkage side and the pathway side because there's a huge amount of work and I'm here in Michigan being done at Michigan state on an RNA interrupter for the path for a melanomas pathway. Do you, in your judgment, do you see that as a possibility, something that should be explored, some sort of RNA, DNA-RNA translation, transcription pathway linking atopic dermatitis with some of those other cascade effects that come about?

Dr Zelma Chiesa: I think that would be interesting work to see. Right now the studies are primarily just looking at epidemiological associations primarily, between atopic dermatitis, seasonal allergies, food allergies, and also asthma. There is definitely work being done to see if there's something that may be more susceptible to patients that are particularly linked. We do know that the pathogenesis of atopic dermatitis and asthma has some interrelation with respect to things like interleukin four and interleukin 13. But I think our research is in an infancy. And I think what's also interesting to know that if you do believe that patients do follow the atopic March that's the way to go. But a lot of patients with atopic dermatitis do not follow the traditional atopic march where you have skin lesions developing first, and then you have asthma or food allergies as long as, so forth.

A lot of our patients will present them, they will say, I don't have seasonal allergies, or maybe I had the seasonal allergies before and now I have Eczema. So they don't all follow that pattern. So again, when you think about the etiology or pathophysiology of atopic dermatitis, it's very complex and I tend to believe that none of our patients are pretty much about the same. They all read a different book and in some the Eczema

developed first, then the asthma. And in others they have no history of asthma and now it's Eczema. So not all patients followed that March. But definitely I think that that's an avenue for research that's continuing to be done and that will probably get additional information in the coming years.

David: One of my good friends is a gastroenterologist and he treats a lot of IBS patients and he says almost the exact same thing about his particular, he said, look IBS is mouth to anus and nobody is following the same pattern because it's just this whole big cascading random effects is, does that kind of fit in with your worldview of Eczema, atopic dermatitis?

Dr Zelma Chiesa: Yes it does. It does fit into my worldview for atopic dermatitis, and I think it's also very important when we're having discussions with other patients and we try to come up with a treatment plan. None of my patients follow the exact treatment plan for the most part because they're very different. And I try to counsel patients that way to say, what works for you would not probably work for my patient who came before you and may not work for the patient who comes after you because you're all very different and your triggers are different, it is very hard to know what those environmental triggers are, and that's a very big question in our field that we're trying to answer. What is it about certain environments that tends to trigger the eczema in some patients more than others? Why is it that some patients can travel out of – I'm based in Philadelphia. So why is it that they travel outside of the country and they get better and then they come back and they get worse? Or what is it about some people who live in sunnier climates and then moved to what I would think would be drier climates and then they feel better. So there's definitely something out there that is potentially triggering this disease in patients who have some sort of genetic susceptibility as well.

So I think it's important to think about, and also I think it is important because then our patients don't lose hope. If one treatment regimen did not work for them, I try to explain a lot of this is going to be unfortunate at this point, trial and error because I have no biomarkers or no way, nothing to tell me beforehand to say this is what you should do next. And I think if we are clear with our patients, we take the time to explain that then patients are more on board and are perhaps more willing to try different alternatives and stay with me is that decision versus decide I'm just going to go to another physician because she's clearly not helping me, but then it's just there in this wheel that they can never get out of. So I think your gastroenterologist is perfectly right. I think no one follows the same path.

David: It sounds like what you wrestle with as a dermatologist is really the idea of, like we heard the other day Joe Biden saying we're going to cure cancer. Well cancer is pick a big number, 300 diseases, 400 diseases. They're all different. And what you have to face as a derm is almost the same thing where you have so many people presenting with similar symptoms, but with so many, with such a wide variety of underlying causes for those particular symptoms.

Dr Zelma Chiesa: Yes, that's absolutely true. And I'm glad that you also get to see it that way. When I was in my training, a lot of my education in Eczema, a lot of people can be for me would say, these are children, they will outgrow their Eczema, it's going to go away. And then if I can do to move forward with my training and now seeing that this is my specialty clinic, it's completely biased. I do get some of the worst of the worst cases, but I do see some patients simply do not outgrow their disease. And you're right is not just one single disease. So I would never say I'm going to cure eczema because how do, you're talking about so many different diseases at the level of immunology at the level of their clinical presentation.

I also do explain that to patients that and in some of my adult patients, those adult patients who don't have a strong history of Eczema in the past, clinically when you look at them that you are very strongly suspicious. So this must be Eczema or atopic dermatitis and you do a skin biopsy. It aligns with your clinical findings, but they don't respond to treatment. And so that makes me take a step back in saying, I am probably missing something here, that I will not be able to diagnose at this time because I just don't have the tools. Well the

tools haven't been invented yet for me to use. And those are the cases where I feel they should have a different name. They should not be called Eczema, or they should not be called atopic dermatitis. But for a lack of other options, we call them that, so it's a large group of patients with a heterogeneous disease, which can be quite difficult to treat it at times. But the times are changing and we can talk a little bit about treatments later on because I think the next few years it's going to be very exciting for our patients with atopic dermatitis.

David: I think it was someone….that said that science is always limited by its technology and it doesn't matter how good we get. They were very good at science in the 1600s but their technology was limited. We're pretty good at technology in 2020, our science is limited. I have one more question I want to ask you and then because the other person on the panel, Ashley, she's been wrestling with this for a long time. I was checking her bio and she's a long time Eczema sufferer. I want to turn it over to her and give her as much time as possible. But I do have a diet question and a couple of things that as I was doing some reading. A lot of the reading mentions trigger foods to avoid. And so this actually is kind of a three part question. So if you could talk about trigger foods, question two, one of the things that I saw in some of the literature was a nickel sensitivity, metallic nickel in the foods being taken up through vegetables in the ground. And lastly, if we have trigger foods to avoid, are there certain foods that people could be eating, if they have a flare up, might help allay some of that flare up. And then when you get done with that, let's pass it over and let her take the rest of the time.

Dr Zelma Chiesa: Of course. So again, the question about food allergies is very interesting and about trigger foods, so if we look at the data that's out there, there's some work showing that patients who follow more pro-inflammatory diets like a diet rich in fats and refined sugars and things like that can actually have increased an inflammatory burden and that could be triggering the eczema. We are not sure that that is entirely correct or right or wrong. And so, with respect to which food should patients limit, again it will depend on the history of the patient. For example, in some pediatric patients we do know that there are certain foods that could potentially be a trigger of the Eczema, it could be milk, sometimes they could be things like tomatoes and things like that.

I don't typically advocate for avoidance of food if they're not really associated with other findings in addition to do those that I talked about previously, like the development of hives or lips swelling or things like that. In the adult population, again, that's something that I don't really counsel patients because there's just not enough data to support doing that. Nickel free diets – yes. That is something that we discuss as well in clinic. And for some of our patients we might recommend doing a nickel free diet. That's not something that I will typically do unless again, there's no certain pattern to a patient and that goes back to the history of the patient or a patient may say, I haven't been able to identify any potential triggers. And so when I go over and review their dietary intake or we talk a little bit about the things that they consume and most of them, will either say their diet is very varied and it's not I always counsel them or you should probably be cutting down and eat well, it's not so much because they will trigger eczema because overall it's not good to be eating that much amount of refined sugar or sodas or things like that.

So I'd be careful about making those recommendations. And oftentimes what I've found in the majority of my patients, and I get, again, this might be the bias of my practice because they see the worst of the worst is that those types of dietary interventions, while they may help to calm the symptoms in some cases, the itching may not be as bad, inflammation may not be as bad, they don't really cause remission of the disease. The disease doesn't seem to go away. The eczema is still there and they can still see it. So it would be very difficult for me to surely say to someone go off on this and that and I really do try to limit the amount of elimination diets that my patients are doing. Oftentimes when they come to see me some of them have only been eating water or bread for the past month and it's like, no, that's really not healthy overall. Or some of them decided to go on very strict paleo or gluten free diets and they haven't really seen any change. So I try to counsel them and say, if you don't think that there's anything that you can exactly pinpoint and your eczema seems to flare just at various times throughout the day or the weeks or months, I

would say there's probably no relationship there. So really would not advocate for that at this point.

Priya: Thank you David. We will move over to Ashley now. So as David was saying, Ashley, is a long term eczema sufferer, freelance writer and blogger of Itchin Since 87, which highlights skin conditions with a particular focus on eczema. So Ashley, please ask your questions.

Ashley Wall: Hi, thank you so much for having me and good afternoon everyone. I could talk about this all day. I'm so excited. I can't even mention like how these conversations are making me so excited. You have no idea. But my first question, which you kind of answered a little bit, but as a patient and Eczema advocate, I've had it since I was diagnosed when I was two years old and I hear so many, so many issues and concerns within the Eczema community and there's just so much information going on. As a dermatologist, what do you think would be the biggest challenge when treating patients when it comes to like a moderate to severe Eczema?

Dr Zelma Chiesa: Excellent. Yeah. I think Ashley, thank you for taking the time to be here today and for the questions, I think one of the biggest challenges I face as a provider and especially for patients who have been dealing with Eczema for a very long time, is having that initial discussion and understanding, what they think about their disease. And what has been the struggle for so long and when patients come to see me for this first time is there is a lot of information out there, like you just mentioned that a lot of this, that is misinformation or information that may not apply to them and it's not accurate. So patients typically come in with all of these questions and all of these thoughts about their disease. And I think the most important or perhaps the most challenging step for me is finding the time to have that first conversation about what do you know about your disease as the patient is travelling with us.

What do you think it is that you have? What are your expectations? Do you think that this disease that should be gone by now? And trying to explain to patients that this is a chronic disease in many cases. And as soon as I mention the word chronic, if you can see how there's semblance, changes a little bit into, oh, you're telling me I'm going to have this for the rest of my life. It's a little bit kind of like we can hope that but I think it's important that I'm very clear with them that if you have had this disease for such a long time, it's very unlikely that this will be outgrown. And we'd need to start thinking about it as a chronic disease. And it's not just about treating the symptoms with an oral course of Prednisone and that's it. It's also about coming up with a long term treatment plan. And that might have been something that was a little harder to do in the past because we really didn't have many great treatment options. The world is changing for Eczema. So, the struggle I also see is when patients come in to see me and I ask them, what we've been doing with respect to treatments in the past and a lot of them will say, Oh, you know, I just go to my dermatologist Dr or my primary care physician, because I can't get into a dermatologist and I'll get a course of steroids and then I'm fine for a few months and then comes back and it comes back worse. And when I go back I get more steroids or I go to the emergency room and they're in this loop of constantly being treated with steroids and not being able to get off of it.

And that is challenging. Trying to convince my patients to see the disease as a chronic disease that cannot necessarily be treated, on and off and we need to come up with something better than that. Just because with the side effects, so it's just dealing with, with steroid culture long term. So I would say that's the biggest challenge. Having that first honest conversation with our patients. And I think that if we take the time to do that initially, then it makes all the other conversations a lot better, a lot easier as well. So that I would say is the biggest challenge. I think one of, in addition, one of the other challenges, particularly in the adult population is making sure that I have the correct diagnosis. That I was briefly talking with David. There might be some patients who just don't read the textbook for eczema and their distribution of skin lesions are not where you would expect to find them. They don't seem to respond to topicals or orals the way other patients would. And in those types of patients, that's when I do take a step back, go back, review their history, review what their biopsies and make sure that we have the correct diagnosis before moving forward.

Ashley: Absolutely. It's so interesting that you mentioned steroids because right now in the Eczema community it's kind of split and there's a huge movement towards people not using steroids and the long term effects that it had on people. Probably my age, maybe a little bit older, a little bit younger who have taken it for years and years and years when we should have never taken it for so long because it did so much damage. So I find that very interesting that you talk about steroids and now I feel like a lot of pharmacies are realizing that people that have taken steroids for so long are really, the side effects are just so bad that they're trying to come up with different treatments that don't include or involve steroids. So that's very interesting. You previously talked about mental health with Eczema and last May was mental health awareness month and I think Eczema and depression and anxiety go extremely hand in hand. And I think a lot more people have been vocal about how they'd been suffering and how Eczema is debilitating and it's really taking control over their lives if they haven't had it managed. What are some suggestions for people going through this? What do you think that they could do to maybe help with their anxiety and whatnot? And you mentioned the word avoidance, which I find myself having that problem as well. Sometimes when you have such a flare up, you kind of just avoid doing certain activities that you would normally do. But what would be your best advice for somebody that's, or a group of people that are maybe going through things with Eczema and they really have nobody to turn to?

Dr Zelma Chiesa: No, I think it's great that you actually bring that question on the topic of depression and anxiety and Eczema and, and just to briefly provide some background information. There is a recent Meta Analysis, which is basically a review or systematic review of the literature of the studies that are out there that looked at the risk of depression and suicide in patients with atopic dermatitis. And the results were actually quite alarming. And from my perspective, it shows that about one in every six patients with atopic dermatitis met a clinical diagnosis of depression and one in four had symptoms suggestive of depression and about one in eight having symptoms of suicidal ideation, particularly in those patients with more moderate to severe disease. So this is definitely something that I think as physicians we do need to address more frequently in clinic. And as part of my discussion with patients, going over their symptoms, I do open up the question about depression and anxiety and you will be surprised by the number of patients who don't volunteer that information when you just ask them, how are you doing today?

And then their answer is, I'm fine. But then when you specifically talk to them about any symptoms of depression and anxiety and suicidal ideation, they'll mention it to you. Yes, this is having an impact to me on that level. There's studies showing that patients with atopic dermatitis, particularly those with moderate to severe disease actually do experience lifestyle changes or do lifestyle modifications and we can talk about avoidance not being involved in social interactions, even changing their line of work sometimes or choosing an occupation that may not be their preferred occupation, but it's something that they feel they can do despite having Eczema. So it does have an impact on their quality of life and that needs to be addressed. I do recommend that patients who have Eczema and are struggling with the symptoms that you do need to provide that information to your provider in case your provider or doctors are not asking you those questions.

You need to let them know. We do try to keep the avenues of communication with our patients pretty often initially, I will see patients very quickly in clinic, especially if they have moderate to severe disease and they're not very well controlled. Because it's a way for me to establish a relationship with our patients. And then as I feel that their symptoms are improved and that their mood is also improved. And then I would say, okay, we're ready to stretch our visits farther out. But it's important to bring those symptoms to your physician's attention if they are not asking you the question. What's interesting is that, what we don't really know is the association between depression, and atopic dermatitis if there is a biological association, a pathophysiological one, if it's because of the inflammatory burden or if it's because of the impact that itch and sleep loss has in our patients' quality of life. Studies have shown that once you can improve the signs and symptoms of Eczema, you can actually control the disease and improve the symptoms of depression or anxiety. So it might be that that's the reason why that's happening in the first place and that if we can work towards achieving disease control those symptoms should also improve as well. But definitely mention it to the physician, opening up the conversation is critical.

Ashley: That's great advice. Yeah, I have to say, I've sat in panels and I've read things online where kids have been taken out of activities from school or just avoid going to school altogether together cause there's gonna so bad and it really affects their mental health. I read things about people not wanting to have kids so that they don't pass their Eczema just really sad things and it's so unfortunate. So that's a great answer. I know we're probably kind of running short on time. I just have one last question. The Eczema community right now is just thriving. Like so many people are coming out of the woodworks and all supporting each other and talking about like what they've been going through and just excited for the opportunities that are upcoming. And so my biggest question would be what do you think the trends are going to be for I guess, the rest of 2019, 2020 and within like five to 10 years within the atopic dermatitis community?

Dr Zelma Chiesa: Now I think that's an excellent question. Before I just want one mention about what we were talking about patient support groups. And I just want to say the National Eczema Association is a patient advocacy group. So if patients are looking for someone to reach out to, some guidance and some recommendation, I would say that that's a really great association to reach out to, in case you need to establish rapport with other patients who are suffering from atopic dermatitis, I think that that would be a great forum to reach out to. So it's the National Eczema Association. I don't work for them, but I'm just thinking about our patients who are out there thinking about who to reach out to. They can reach out to them.

With respect to treatment. You're right, the next coming years, people are talking about this being the decade of Eczema and it's because the more that we've gone, we start to understand the pathophysiology of the atopic dermatitis, the more that has led to development of more targeted treatment approaches. So in the past in your treatment options were either oral courses, steroids, topical steroids.

Then we got the calcineurin inhibitors like Pimecrolimus – brand name Elidel or Tacrolimus brand name Protopic. And then we had systemic agents that were not really FDA approved, but we would use for a lack of other alternatives like cyclosporin, methotrexate. In 2017, we had the first biologic approved for atopic dermatitis, which is called Dupilumab which blocks the action of interleukin-4, and interleukin-13. And that has actually changed the way we treat our patients with atopic dermatitis because it's been aligned, particularly me to get patients off of steroids, not even having to use topical therapies. So that is my goal to wake up one day and not have to use oral steroids, topical steroids to treat any of my patients. And the research is actually focusing on that immune dysregulation and restoring skin barrier defect. And there are going to be newer targeted approaches that are currently either in phase one, phase two, phase three clinical trials that offer a targeted approach meaning they will block different molecules that are driving the inflammatory processes such as interleukin-13, Interleukin-19, Ox40. And the results look very promising. In addition to that, there are other molecules that are being studied in clinical trials, such as the JAK-1 inhibitors, or JAK/STAT pathway inhibitors that have been showing great results so far. And we think that once those medications do get approved, they are going to be life changing. So right now we are currently in the process of doing clinical trials and getting started on a trial with a JAK inhibitor. So we hope to offer that to our patients as well as well as doing trials with other more targeted cytokines like IL-33.

So that will definitely, I think would be exciting for our patient population. And again, as I mentioned, my goal is that one day we're going to wake up and we're not having to use oral steroids anymore, just like we don't do steroids by mouth, orally for psoriasis patients anymore. So that would be my goal for our eczema patients. And it is a very exciting time. And we're also seeing the development of new topical approaches to treatment, which also includes topical JAK inhibitors so that patients don't have to be using this topical steroids for such a long time and avoid the detrimental effect in the long run.

Priya: Thank you Ashley. And thank you doctor, I have to just take a couple of questions from the audience. Why does eczema flare up at night?

Dr Zelma Chiesa: Yeah, so that's an interesting question. And there's studies being done on Eczema, sleep pattern and the circadian rhythm. When you ask patients within particular patient population, when is your itch worse? And a lot of them will say it's when I go to bed and start to fall asleep and we don't know if it's because our minds are not as occupied during the day. Yeah, we were not at work, we're not rushing around or if there are actually some physiological changes in the circadian pattern. We don't really have the answer to that question yet. But I don't think so much that it's Eczema and that's getting worse at nighttime. I think it's more the itching that's getting worse and that triggers us to scratch and as we scratch, then we cause more inflammation of the skin and so on and so forth. But there is definitely a study showing that know alterations in sleep patterns are associated, the relationship, we don't know in which direction it goes yet, whether if it's the Eczema is not allowing me to sleep better or if it's like the sleep alterations that I'm experiencing also could have maybe some form of pro inflammatory effect that's affecting the skin. So it'd be interesting to see the results of those studies that are currently ongoing.

Priya: Thank you doctor. Can you touch upon use of monoclonal antibodies in drugs for treating atopic dermatitis? She has given a reference to the Novartis trial.

Dr Zelma Chiesa: Yes. Perfect. Okay. So know with respect to other inflammatory skin conditions, I mean, when you look about, I had psoriasis, we have about more than about 10 biologics give or take that we could use to treat the designs of psoriasis. And before 2017 we had nothing for atopic dermatitis. And at that point, a new medication came about called Dupilumab. It's a human monoclonal antibody and it blocks the action of interleukin-4 and interleukin-13. We do know that those two cytokines, interleukin-4 and interleukin-13 can promote inflammation. And this clinical trials show that patients who were treated with Dupilumab about 4-6 out of 10 patients actually achieved clear skin or minimally active disease and about maybe 40 to 50% saw about a 75% improvement in their skin from baseline.

So it has definitely resulted in a game changer for our patients. It's a medication that's safe and tolerable. I do counsel my patients on risks versus benefits and we have a discussion, but compared to the other currently available systemic agents such as Cyclosporine and Methotrexate, or mycophenolate Mofetil, the side effect profile is definitely better. Current clinical trials that showed the most promise in results are in biological agents and monoclonal antibodies and they included antibodies as they previously mentioned – 2OX40 ligand, interleukin-17, interleukin-33, interleukin 31 and those are molecules that are known to be important in the pathophysiology of Eczema. We may have some patients in which lL-4 and IL-13 are as important and it is only by blocking maybe one of the other ones that we can get their disease to improve. So that goes back to our discussion with David about the heterogeneity of the disease. So the results do look promising. The same goes for the JAK inhibitors. So JAK inhibitors are smaller molecules, which also help control the production of proinflammatory molecules and they've also shown promising results in early phase clinical trials. And we do think that they will be a game changer for our patient population as well.

Priya: Thank you. Doctor. I'll just take one more question before we wrap up. Would improved or controlled atopic dermatitis mean no dementia or lower risk of dementia?

Dr Zelma Chiesa: Yeah. So it's great that you asked that question. Recently during the meeting for the Society for Investigative Dermatology, one of the researchers, Dr Katrina Abuabara, a wonderful colleague and she is doing great work on atopic dermatitis. She did a study, I think it's approximately using a primary care database of approximately 1 million patients, and as the lead author for the study, they did find that adults with atopic dermatitis, compared to those who don't have atopic dermatitis, have higher risk for dementia also Alzheimer's dementia and vascular related dementia and these associations were still present when they control for other factors such as age, sex. And there was also a trend that they saw in that patients who have more severe disease, had a higher risk compared to those with lesser disease. So it's interesting to think about how that's changing the way about how we think of Eczema or atopic dermatitis,

not just as a skin disease, but also as a disease that can, a systemic disease, right, where the inflammation is not only on the skin, but it's also going inside the body as well. And so now the question becomes, well, if we can further prove that those associations with these types of systemic diseases like cardiovascular disease, dementia, celiac disease. If those associations are true and then the question becomes, if we treat patients with atopic dermatitis, if we're able to control their inflammatory burden, can we somehow be able to modify their risk for developing dementia in the future or developing cardiovascular disease in the future? So I think that's going to be a question that needs to be answered in future studies.

Priya: Thank you doctor. I think it's a wrap now. Poor disease control plays a major role in the disease burden reported by the atopic dermatitis patients. The condition has social and economic repercussions as well. We've just heard Dr Chiesa explain how atopic dermatitis can be managed better though. Dr Chiesa thank you very much for your time and information shared. David and Ashley, thank you for participating and bringing the patient's perspective into the discussion. We also thank the University of Pennsylvania. The talk will be available on curetalks.com – please visit our website for details on upcoming talks. Thank you everyone and have a great evening.