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If you or someone you love is living with the primary immunodeficiency, you know that the journey can feel isolating. But this June, you can see for yourself that you're not. Join us for the world's largest gathering of the primary immunodeficiency community at the immune deficiency foundations twenty twenty six PI Conference in San Antonio, June twenty fifth through the twenty seventh. Whether you're newly diagnosed, a longtime advocate or a family member, your story matters. From life changing educational sessions to meaningful new friendships, this is where our stories come together to form a beautiful Mosaic. Head over to primary immune dot org slash conference to register now, and we'll see you in San Antonio.

**Emma Mertens:** Alright. Good evening everyone and welcome. Thank you for joining us as we kick off the immune deficiency foundations twenty twenty six education series. Our featured speakers for tonight are doctor Alexandra Freeman and doctor Heidi Kong from the National Institutes of Health. Who join us to discuss dermatological issues in primary immune deficiency.

My name is Emma Mertens, and I'm the Program Manager for Education here at the Immune Deficiency Foundation. On behalf of our organization, we thank you for tuning in to this virtual event. Throughout this series, guest speakers provide a deep dive into clinically advanced topics from the world of PI. If time permits, the session will be followed by an audience q and a with our presenters. In offering these programs, we aim to engage and empower the PI community through education.

During portions of tonight's talk, we will offer audience polls. When a question pops up in your screen, you may submit a response by clicking one of the presented options. As always, closed captioning is available. This webinar is made possible by our wonderful sponsors. It is due to their partnership and contributions that we can provide programs like this for the PI community.

Please join me in thanking our sponsors. Before we get started, a brief disclaimer. Please remember that information presented during this meeting is not intended to be a substitute for medical advice, diagnosis, or treatment. We are here today as a trusted source and friend provide you with information. Always seek the advice of your physician or other qualified health provider with questions concerning a medical condition.

Never disregard professional medical advice or delay seeking it based on information presented during an educational event. Throughout tonight's program, there will be medical images shared throughout the presentation. Please be advised. Alright. We are going to kick things off this evening by asking you to answer a quick question using the Zoom polling feature.

And we're gonna give it about thirty seconds for everyone to answer. So our opening

question is, please rank your understanding of how primary immunodeficiency affects your skin and causes dermatological problems. Alright. Thank you so much, everyone, for your answers. It looks like we have a good mix of levels of knowledge in the audience.

And hopefully, everyone gets a lot out of tonight's program. Alright. With that, I'm so pleased to introduce our two speakers for this evening. Alexandra Freeman is a senior clinician and director of the primary immune deficiency clinic at the National Institute of Allergy and Infectious Diseases at the National Institutes of Health. Dr.

Freeman works with individuals affected by complex primary immunodeficiencies and is recognized internationally for her work diagnosing and treating individuals with hyper IgE syndromes. I also want to give a huge thank you to Dr. Heidi Kong, for her contributions to tonight's program. Dr. Kong is a senior investigator at the National Institute of Arthritis and Musculoskeletal and skin disease.

Thank you so much for joining us. We're thrilled to have you both here for a discussion on dermatological issues in PI. Welcome.

**Dr. Freeman:** Thank you. Thank you so much. And I'm just pulling up my slides, and then I'll get going. Thank you so much Emma for the invitation to speak tonight about dermatology issues and inborn errors of immunity. So just so I'll know, I'm gonna do the first kind of bunch of slides and then Dr.

Kong will do some towards the end, and then we'll both be available for the question and answer session. Neither rest of any conflicts of interest or significant disclosures, but what we're speaking tonight is our own views and not necessarily those of the National Institutes of Health. So our objectives tonight are things we'll cover, are common dermatology conditions seen in inborn errors of immunity, and then general approaches two therapies of skin conditions. But as Emma was just saying, make sure that any advice we give is actually taken along with your actually treating team and that, you know, all of the charity's been by July's for you in your specific condition or your family members. Then we'll talk some about when to see a dermatologist and how to find one with with experience in primary immune deficiencies and some general guidelines for skin health.

Kind of through Avon at the end, we'll also talk about some of the ongoing research that is involved with dermatological conditions and and burden errors of immunity. And with that, I'm gonna start by talking about atopic dermatitis, which is a type of eczema. So, you know, and probably a lot of people actually know a fair amount about eczema, but this is something that I see very frequently in my own practice at NIH and that lots and lots of kids and adults have even outside of the world of important areas of immunity, more commonly actually outside of these individuals. So this is especially common in patients that have other allergies symptoms such as those with environmental allergies and asthma. And it's really characterized by having these dry and itchy patches of skin.

Some of the common areas are, as you can see in the picture, kind of the inside of the knees, you know, the on the back of the knees. The inside of the elbows, the hands, the face, especially in kind of these cold wintery months when you get the dry kind of itchy skin of your face in your hands. It often starts in childhood or infancy, but can also be triggered by other exposures. Like food or sometimes people are allergic to the nickel and belts and causes some kind of localized eczema rash with that. So in which inborn areas of immunity do we see atopic dermatitis.

And as I said, it is very common to see this without having any problem with your this without having a primary immune deficiency or a primary immune dysregulatory disorder. But we're here to talk about inborn errors of immunity. So these are some of the main ones where we see this. And but it really can be seen in all sorts of them. So my specialty is really the hyper IgE syndromes and and so we see that classically in that hyper IgE syndromes are characterized by both high IgE, that antibody, as well as these atopic dermatitis type rashes, as well as recurrent skin and lung infections.

And actually, the two pictures on the top there are taken of pictures that we of patients that we follow with autosomal dominant hyper IgE syndrome from SAT3 mutations. The rash in these individuals really starts in the newborn period. That's really classic for it. And you can see in the baby there on the left. Often in the face and the scalp.

It's often kind of these these patches with little kind of areas of little spots of pustules, some pustules underneath the little skin lesions. You know, and this is really a multisystem disease. The patients also get pneumonia, they have trouble with their teeth, with the baby teeth not coming out, the joints are flexible, they break, their bones more frequently have scoliosis. So those are some of the kind of hints to having the diagnosis of a hyper IgE syndrome. We also see very severe frequently atopic dermatitis and dock8 deficiency I'll show more slides later on at this as well.

This is a more of kind of a pure immune deficiency than I was talking about with a hyper IgE syndrome where all different organs and things like the bones are involved. This is really an immune deficiency where you can see, whatever degree of eczema can be very, very, very severe, as well as other types of allergy symptoms along with infections and other complications. This one's a little bit different and we'll talk about this more later and that we see many more viral skin infections such as warts and melasma. And the other two pictures that are shown here at the back of this individual with really significant eczema as well as these skin nodules, which was from long term eczema, are taken from individuals with [DOCK8] deficiency. Wiskott-Aldritch Syndrome is another inborn nerve immunity that usually also presents early in childhood, often with eczema.

This is seen in boys because it's an x linked disorder and associated also with low platelets. So these boys have trouble with bleeding as well, and often other kind of disease manifestation such as inflammatory bowel disease and intestinal issues. IPeX is immune

just regulation, polyendocrineopathy and neuropathy. It's also excellent, so it affects boys. And this is really an early onset inflammatory disease, you know, often presenting also an infant with really significant rashes, trouble with early onset diabetes or other endocrine issues.

And other signs of autoimmunity. Often there, you get inflammatory bowel disease as well. But there's many others that are associated with atopic dermatitis, and I just highlighted a few for this slide. So what are our treatment approaches for atopic dermatitis? So, you know, this is a disease that's associated with really, really dry skin and itchy skin, and it's really important then to really hydrate the skin.

So there's lots of different emollients, these creams and lotions can be used, and some are a little bit more greasy than others, and some patients sometimes prefer one or the other. But these are really important part of the treatment approach. And then another thing that we see both in people that have inbornary of immunity causing atopic dermatitis, but also in people that have eczema without having a specific premium deficiency is that there's an increased incidence of *Staphylococcus aureus* of staph on the skin and that can make the eczema worse and then the eczema causing little breaks from the skin and kinda you know, then interfering with that skin barrier can then make the staff infections worse. So often if you can decrease the amount of staff and some of the other bacteria on the skin, it actually can improve the eczema, the atopic dermatitis as well. So there's different ways to do that. What I often talk to my patients about is using different antiseptics. So some of them that we use are chlorhexidine. That can be used in washes. This one of the surgical soaps that people use as well, but, you know, you can use it in the shower, you can use it in newborns, even in infants, you know, in terms of a bathing. Also a dilute bleach bath, you know, where we use either I have a half a cup to a cup of bleach into a tub and you can soak there for ten or fifteen minutes.

It's good to then kind of rinse off the bleach and, you know, immediately put on one of the emollients so you don't dry out the skin too much. Swimming in coordinated pools is also, you know, a way of having a very, very big bleach bath since chlorine, you know, bleach is actually made from chlorine, so that can also decrease the amount of bacteria in the skin. And then, you know, for many individuals with primary immune deficiencies. They have trouble with recurrent infections, and we're worried about infections beyond just the skin. So the skin, you can decrease the amount of infections through using these different anti septics.

But, you know, for some of the people that we follow, they also have trouble with other infections like pneumonia. So many of these individuals are then on chronic antibiotics to decrease the amount of fat from the skin. Okay. Then another types of therapies that are used to treat atopic dermatitis are topical immune suppressions. So using, for instance, topical steroids, that's probably what people hear about the most, either ones like, hydro

cortisone or triamcinolone, It's really important to discuss the strength of the steroid with the treating team.

We try to have less strong steroids when we are using them on the face where the skin is thinner. Compared to for instance on the arms or legs or the trunk where you're able to use slightly stronger topical steroids. And then there's also steroids sparing agents because steroids can thin the skin some over time. So I listed a couple of them there like tacrolimus and pimecrolimus and Ruxolitinib. They're all kind of steroid sparing agents that also decrease the amount of inflammation that's on the skin.

More and more, we're seeing patients use different types of systemic therapies to treat isomodus dermatitis or atopic dermatitis. One of the ones that I'll kind of highlight in the next slide is dupilumab, you know, over the last five, six years, we've just seen this skyrocketing of the use of dupilumab. Many of my patients are on that and other patients are using it, and I'll talk more about that in a second, but the picture there on the slide is one of the patients that we see that has step three depression hyper IgE syndrome and that is showing the eczematoid rash on the top picture and then the response after being on dupilumab on the bottom. There's also increasing use of JAK inhibition, JAK inhibitors like Ruxolitinib, and I'll talk more about those later as well in terms of some of the side effects as well. And then, you know, We don't think about things like bone marrow transplant when we're thinking about just treating eczema.

But, you know, depending on the inborn error of immunity, you know, transplant might be the solution for Eczema. Again, not because of the eczema, but because of the disease association. It's eczema plus other infections and risk for instance, albumin malignancies. So again, I thought I would just highlight dupilumab a little bit more. It's being increasingly used in the treatment of atopic dermatitis in part because it is quite effective and also because it's usually very well tolerated.

So this is a monoclonal antibody. These are, you know, like, there's lots of different monoclonals that are used to affect them in system in different ways. This one binds to the IL-four receptor IL-four is an inflammatory cytokine that's involved with the lymphocytes, the T lymphocytes turning them along with IL-thirteen, which is another one to being Th2 skew. And we're saying that, this is kind of the different inflammatory milieus and how the T cells then grow up and learn to fight different types of infections. When they turn more into Th2 lymphocytes, they really then drive these allergy symptoms that you see in individuals that have things like anaphylaxis and urticaria that which is hyped or with eczema.

Anyway, so dupilumab is approved at a six months old for atopic dermatitis. I mean, this is, you know, really remarkable for systemic therapy. It's also used with kind of varying ages for asthma, eosinophilic esophagitis, which is when you get kind of some of these allergy cells in your esophagus that can react to different foods, as well as nasal polyps. You know, there's kind of increasing different entities that is being used for. It's usually dosed for most

individuals.

It's every two weeks, but that can vary. Sometimes it can even be four weeks where you're seeing a patient today who's on a four weeks for eczema, and it's given by injection. But it's usually very well tolerated. The most common side effect that we hear about is conjunctivitis. For whatever reason, I really see that extremely rarely in my patients.

But that's the most common reported side effect. And what we don't see is a lot of trouble with infections from this. Rarely there can be an allergic reaction. So especially if a patient is more allergy prone, I'll often have them have their first dose in a medical office. Okay.

So now I'm gonna change things and talk about different types of skin infections. So my training is actually not as a dermatologist and that's why we have doctor Kong here, but my training is actually an infectious diseases. So we will probably be a little bit more skewed in terms of infections because I tend to see those a lot. But that's what's important, you know, in terms of primary immune deficiencies, and we will talk about autoimmune India as well later, which is important for immune dose regulation syndromes. So one of the big issues when you have atopic dermatitis is that the skin then the skin kind of barrier, which keeps us kind of protected from different types of infection, is not as intact.

Right? You get little scratches in the skin, you get these little holes, and then different bacteria that normally line our skin, for instance, staff, can then get in and cause different infections. So the most common bacterial infections that we see in the skin are staff and Strep. And they can cause different things like impetigo, which is when you get just kind of little superficial infections of the skin. It can look like small blisters sometimes as well. You can see in the ear and the picture here, kind of this crusting this kind of honeycomb type of appearance. But there's some impetigo around that ear that actually has some eczema. You also can see follicularitis, which is the hair follicles. When they get infected, you can see that sometimes, you know, for instance, on the chest or on the back. You can see oils where you actually get a collection of pus under the skin, and you can see that in my top picture here, this is underneath someone's arm, that is a boil, and that is then full of pus as well as bacteria.

So to diagnose these, you know, often various medical care, you know, physicians are can actually do this just by looking at them. Like in the ear there, you can say, okay, that looks like impetigo. You know, and that might be enough and just give the individual either some topical therapies to use or systemic based on how widespread this is. But, you know, in my practice, I do like to actually obtain a culture to see what is the infection there. This is partly because if your initial kind of chosen therapy is not effective, then you have a culture where you can actually see, okay, exactly what bacteria is causing the problem.

And then from the bacteria, the microbiology lab can test different antibiotics to see which one would be the best to then treat it. You know, more and more both in clinics and emergency rooms and hospitals will actually do a PCR from MRSA. So some of you may

have heard of that. MRSA is a type of stuff where it is that's resistant to certain antibiotics. That doesn't mean that we don't have antibiotics treated.

We have, you know, we certainly have antibiotics that can treat MRSA, but it is resistant to some of the antibiotics like cephalexin for instance. Now when you do those PCR's, you can get an answer within, you know, a couple hours of whether or not MRSA is present and that will affect, you know, the antibiotic you chose, you choose. But, you know, for me, I'd like not just to have that PCR information because it's quick, but you actually want to have a culture. PCR is just kind of a quick DNA test and doesn't provide you the information about which antibiotics are best. And then as I mentioned, treatment, if it's just a small area, for instance, on the ear that's there, you know, you might consider just using a topical antibiotic like knee Pearson. But if you have a boil, like, in the top picture there, then you really want to open that up and let the puscom app because it's really hard for antibiotics to get into a pocket of pus when they're large like that.

And there's different systemic antibiotics we use as well. I put a couple examples there, cephalexin, that's a cephalosporin, which is kind of a cousin of penicillins, kind of a cousin of amoxicillin. They're usually very well tolerated. Doxacycline is another one. So one issue with cephalexin is that it's if the individual actually has MRSA, cephalaxan won't treat it. Doxociclib will cover some MRSA stuff as well as covering stuff. It's not MRSA and Strep can be quite effective as well and has good penetration into the skin. [trimethoprim-sulfamethoxazole], that has the brand name of Bactrim, that can also treat both some nurses as well as a regular step. It does not cover strep if your medical care provider is thinking about that. [clindamycin] is another antibiotic that covers some MRSA.

It's becoming increasingly resistant. It can have some stomach side effects for some people and linezolid is quite effective and great for the skin covers both MRSA stuff, regular stuff, really a great antibiotic. It has some long term side effects and is more expensive than the others I listed there. And I just thought one kind of study that we did that kind of highlighted kind of the importance of kind of interfering with staff and colonization with staff early in life was looking at some of the patients that we follow that have hyper IgE syndrome again from SAT3 mutation, and we started having the genetic diagnosis available in two thousand and seven when SAT3 was found to be the genetic ideology. And from that point on, if one of our patients had a child that was that could potentially be affected, we were able to genetically diagnose those babies, you know, within the first few months of life.

And when we made that genetic diagnosis in the first few months of life, then we would start those babies on the wash with the thoraxodyne, which we often started earlier because they would have these rashes. So we would start them on antiseptics to kind of try to interfere with the staff colonization of their skin, and then also start them on antibiotics early as well. And what we saw when we compared them to individuals, the babies that did

not have that family history, so we're not diagnosed often until there are a few years of life. And so they didn't get their early onset of antibiotics. Is that we saw, you know, this significant, Oopsie, sorry about that.

Decrease in the severity of the eczema, although most of the children still had some degree of eczema, you can see that there was less. This is kind of the p value of which is significant, less than point zero five. And we only had so many patients to look at that we saw less severe eczema and a lot less skin abscess, as well as some improvements in terms of the amount of pneumonias and other complications as well. So I wanted to also highlight an unusual infection, but it is important in case any of the people that are on tonight have X linked agammaglobulinemia or hear know about individuals with that. This is a rare infection, but one that is seen almost exclusively. So rarely you can see this outside of X-linked agammaglobulinemia.

So, but individuals with this mostly have trouble with, you know, lung infections and sinus infections and knee infections can do quite well on immunoglobulin replacement therapy. But, you know, but occasionally, and again, it's fairly rare, There can be these unusual infections with bacteria that usually just hang out in our stomachs and our intestines called helicobacter or campylobacter species. So *h pylori* people might know about because of its association with stomach ulcers. *Hilacobacter*. So that's *hilacobacter pylori*.

So these are cousins actually have *hilacobacter pylori*. There are other species and they can actually leave the stomach or intestines and enter the bloodstream and usually cause these rashes in the legs, you can see here kind of this redness, and then it can cause the sores in the legs. And this can go on and on and on. You know, it can often take months or even potentially over a year to make this diagnosis. Now, I think partly because a lot of people don't know about this infection, and then it's hard to grow.

These are bacteria that don't just kind of grow easily in the cultures like they do with *staph aureus*. So you need to really think about this and then your microbiology lab needs to either come up with different kind of special ways to culture this, sometimes that involves the CDC, or there's other kind of special microbiologic techniques that can make this diagnosis. And then once the diagnosis is made, then it requires really long term combination antibiotics to clear this up. And, you know, sometimes we can control the infection, but we don't think we're fully curing in, and so sometimes we'll even think about bone marrow transplant to fully cure this infection. Okay.

Now, I'm gonna talk about skin viral infections. So, again, viral infections can be common in kids and adults because viruses are what cause warts, that's human papillomavirus or molluscum, which are common infections in children. Herpes are also viruses that can cause both rashes, both in healthy children as well as in children and adults with inborn errors of immunity. So some of the common inborn errors of immunity that have trouble of viral skin infections where it's not just kind of these isolated events that you can see in

children and adults, are those that really affect the T lymphocytes for the most part. So examples are educate deficiency that I mentioned before and You'll see certain trends because there's also the diseases that I treat the most.

So I use them as examples a little bit more because I had those pictures. Got it too deficiency, which is more a disease in adolescence and adults. That is also studied at NIH. Severe combined immune deficiency skid, you know, most of those babies are diagnosis, babies with the newborn screening and transplanted right away. But every once in a while, there's a leaky scid mutation that does not get diagnosed right in the newborn period and can present, you know, a little bit later, like an early childhood or childhood for instance, we call that leaky scid, and there's some others like that one gain a function.

Disease. So HPV, again, is human papillomavirus that causes warts, kind of classic warts are the bumpy ones that you people know about because healthy individual get those as well. There's also flat warts. I have a picture I think on the next slide of flat warts. The picture on top there of my slide is an individual with that head decade deficiency and these are just lots and lots of warts.

Because this immune deficiency, particularly predisposition to that. And, you know, warts are something that people treat, you know, at home with over the counter type medications like salicylic acids. Or a dermatologist can treat it with those or with freezing them. There's also, you know, different kind of home techniques like putting duct tape around the warts and then removing that, you know, once or twice a week and kinda trying to soak the warts and file them down and then re putting on the duct tape. So there's different types of therapies that people use.

But if you don't have a good immune response against the warts, then you'll see them come back, and we'll talk about that more. Molluscum, Contagiosum, they're kinda like warts and that they're little bumps, but they look a little bit different. The picture here is also from an individual with dock8 deficiency showing these melasma. They have a central kind of umbilical. This kind of like pivot in the middle.

And there you can also either not be treated since children typically get these and they can last a while. But dermatologists have other techniques to treat this as well that can kampha or dins, which causes little blisters or freezing them or laser therapies. Herpes viruses, there's herpes simplex that can cause the cold sores or, you know, there's also the sexually transmitted herpes viruses as well. As well as zoster, which is causes either chickenpox or so, zoster or shingles. And people that also have problems with their t cells or with their natural killer and k cells, can have a lot of trouble with more frequent kind of recurrences of herpes simplex or with shingles or kind of severe chicken pox, or it can be more widespread than you would expect.

And these individuals should then be treated with antiviral. So I put some examples there, [acyclovir] and then for certain immune deficiencies that have a lot of trouble with this, or

for certain therapies that predispose of this, we will actually provide prophylaxis, kind of a chronic dose of those. And the picture at the bottom is actually a patient with a hyper IgE syndrome where we see a little bit of increase in the risk of zoster or shingles. And this is what it typically looks like. It's usually only on one side of the body, So it usually does not cross the midline if it's a classic case.

Now if there's a problem that means that sometimes you will see it kind of cross the midline and it causes these kind of little blisters that then eventually crossed over. But, you know, as I mentioned before, for some inborn errors of immunity, the warts of melasma may not improve until the immune system is improved, such as with bone marrow transplant. So, again, you know, sometimes we really worry about these when they get widespread and that they're not gonna resolve until there's a better immune system. So, as I said, these are common in children. So, when do you want to seek more care for these? You know, I know my own one of my own kids had melascom that I had thought, okay. You know, I ended up I never did take her to her dermatologist because they were covered by her clothes. And I knew, you know, she seemed healthy. And I was like, I know Meluscom can go on for a while. You know, they can go on for months, year, even two years. I think her Meluscom went on for two years. I'm finally, they fell off. Why the time when I was like, oh my gosh, I'm gonna have to take her through her dermatologist at some point. But, you know, they really can last a very, very long time. But, you know, it's that's why it's important to then bring it up with your doctor if you're concerned.

That there are either too many of these or they're going on too long. And a dermatologist can be extremely helpful in helping us think about whether or not the distribution, kinda like how widespread either the melasma words are. Is too much or, you know, they're treated and they come back and they're treated again and they come back. That can also be assigned that there's something wrong with the immune system. Also, kind of the appearance of them.

In the picture there, I have a patient that I saw a few months ago with flat warts these kind of they don't look like that typical bumpiness that you might think about with a typical wort, but instead they look kind of like these light spots, so they lose their pigment. And So they just they kind of look like, you can see a little bit of raise to them, but they're called flat warts and that's well, that picture is exactly what they look like. Another time we worry about viral skin infections is with when you keep having trouble with shingles, you know, there's a lot of different reasons that an individual can have shingles, but if you keep having it, you know, every few years or for some multiple parts of the body or, you know, not keep into that one stripe only on one side of the body. And then another time is when the herpes or the [] for shingles, if treating physician thinks that it needs IV therapy, we would think about the immune system. HPV, which causes warts, human papillomavirus, there's certain types of it.

There's all the different types of them. There's certain types that are associated with cancers. And so we think a little bit more about a problem in the immune system. When the warts, the HPV virus is causing cancers earlier than we would expect as well. Ideally, we would figure it out before there's a cancer though.

So as I said, you know, sometimes these warts and other viruses are a sign that there is a problem in the immune system and for some of these to get a response you need a bone marrow transplant. And kind of like I said with eczema, It's not like we say, okay, this person is egging out, let's do one more transplant to fix this. You know, warts can be very problematic, but a word itself is not a life threatening condition. The problem here is that warts can then lead to these cancers. And again, it's only certain types of warts and it's only in some cases when there's a issue with the immune system along with this.

But then, you know, we want to try to do these transplants four, these can turn into some sort of in brief before they can transform into a cancer. In this case, it would be a squamous cell cancer associated with HPV. So here are some examples of bone marrow transplants we've done for doc-eight deficiency. And you can see before and after of the legs, but the warts having disappeared and the fingers, but they disappear. And then then the individual at the bottom was molybdenum resolved as the immune system improved.

Again, just like I talked about with XLA, I'm gonna mention one rare type of viral infection that affects the skin, but it's good to be kind of aware of some of these since our diseases are rare, and these are Rubella associated granulomas. So RUBELA, that's one of the viruses. It was one of the viruses that you think about in MMR vaccine, measles mumps, RUBELA. These can be associated with either RUBELA virus or the vaccine strain, and they can cause these funny granuloma type skin conditions, and I have pictures from two patients that I follow there, that are seen mostly in combined immune deficiency. So these are mostly when there are T cell, usually cell with the combined with the b cell defects or in DNA will repair our defects.

You know, we mostly see these on the skin. Sometimes people can also have granulomas. It's kind of a funny type of inflammation that's not just on the skin. We seen that, for instance, someone who had them in the kidneys and in the liver. The diagnosis relies on a biopsy of these granulomas.

And, frequently, there has to be discussion with the CDC. They have some techniques to kind of make this diagnosis. Some other places are working on this as well. There's some research ongoing at NIH about this, and then also kids who live in at CHOP, you know, Philadelphia is also an expert in this. And a lot of treatments have been tried.

But, you know, viruses are very tricky to treat. And most viruses, we don't have good antivirus just like we don't have like we do, we have lots of antibiotics for bacteria, but we don't have as many antivirals for certain viruses. So, Rabela is tricky, and we don't really know whether or not we need to be targeting the virus or do we need to be targeting kind of

this funny immune response. So, You know, different things are tried. It's still work in progress, and transplant has been the most successful thing, but ongoing research to understand it.

And then finally, fungal infections of the skin. Then within fungus, we see yeast, we see mold, yeast, can cause in the mouth, Candida. It's often in kind of either dent like, moisture areas, warm areas kinda, you know, in folds such as under breath. And you can see in certain immune deficiencies, it can also affect the nails. You can see in this picture, of some of the hyper IgE syndrome.

Dermatocytes are ring worms, and they sometimes can be worse in immune deficiencies. And to diagnose those, dermatologists may do scrapings of the skin lesions and kind of look under the microscope of special stains and also can do fungal cultures. I put some of the different examples here as well. And the treatments can be topical for instance in the mouth. Sometimes people do, like, different rinses such as with nystatin.

Or for certain, like, a skin ringworm, dermatified infection, there sometimes we can use topical azal type antifungals or other antifungals. Or sometimes for people with terms of their immune system are depending on the location or the amount of fungal infection, we'll use systemic antifungals as well, which are typical typically azals like fluconazole, intracanalol one of those. Okay. So now we'll switch and talk a little bit about our immune skin conditions. You know, I think for many of the people on this audience, you know, immune deficiency is often paired with the immune system doing things we don't want it to do.

Right? Is why many are immune dysregulation syndromes, and we end up with autoimmunity as well as susceptibility to infections. And I put some examples there of different in membrane errors of immunity or types of immune deficiency. That are associated with more autoimmunity, such as common variable immunodeficiency CDID. These kind of leaky skids I mentioned before, set one and set three, gain of function, some CTLA four, which was initially kind of more like a CDID, but has a lot more autoimmunity or some secondary types of immune deficiency such as thymoma when you get a tumor in the thymus that can lead to autoimmunity.

So these can all be associated with different types of autoimmune problems in the skin as well. So some of the autoimmune skin conditions we see are lupus. So lupus can either cause a more primarily skin issue called discooid lupus and kind of in the far right here, there's a picture of a patient that I followed with some of the skin lesions that you see with this quite lupus, or there can be systemic lupus or a thromatosis, where you can often get this facial rash. You can see in the picture up here that you can see kind of a rash on the face as well as other manifestations in the body. Alopecia, which means hair loss, that can be associated with autoimmunity as well.

The picture here in the middle is an individual with [APECED] which we'll talk about a little

bit more. That's from mutations in a gene called AIRE, AIRE. Vitiligo is when you get the loss of pigment of the skin. You can see here an individual with one of these leaky scid, leaky scid, with brad deficiency. Again, you know, if it's not diagnosed and as a baby, there can be kind of these leakier mutations that lead to the presentation, either in childhood or sometimes even in adulthood.

And also, this isn't exactly out of our immune, but inflammatory skin conditions like cystic acne, which we can see in, for instance, conagrating lumitus disease. Just wanted to highlight one of the treatments that's being used for [APECED] again, that's from the mutations in AIRE. So some of the ongoing research at NIH has shown one particular type of inflammation that is frequently seen in [APECED] and treatment with JAK inhibitor called Ruxolitinib is actually seeing a really nice response to some of the autoimmunity here. And in these individuals, we've seen not only the improvement in the alopecia, so there's some really nice pictures here where you can see the lack of hair and then hair and as well as other autoimmune manifestations like thyroid and the stomach and nail distriate and even in some of the candidate infections that we see. We also see responses like this in individuals with cell lung gain function.

They can also have alopecia or other signs of outer immunity and actually see the hair growth after this treatment as well. Ruxolitinib is a JAK inhibitor and you know JAK inhibitors are being used a little bit more frequently and inborn errors of immunity. So I thought I would just mention that they they are immune suppressants. It is important prior to use that people are checked for tuberculosis and titus and some other infections. The main infection risk here is actually viral infections and shingles.

And so sometimes we'll think about people being on an antiviral like a acyclovir or [], depending on the [] deficiency. They can also be associated with lower blood counts, so we monitor that as well. And there's ongoing clinical research at NIAID kind of studying the response of these therapies for azapacid. I'm not going to talk a lot about this, but there is another disease that was actually described at NIH called adenosine DMNase two or data two, which is a little different than adenosine DMNase that's associated with one of the types of skin. That can actually present with kind of this lacy skin finding.

This is called libido, Rosimoza. And, you know, you see this. It almost looks like when you have sometimes if the laptop can cause if you have that on your lap too much in can cause this kind of funny skin findings. But these individuals can also present with lower blood counts and, you know, unfortunately, can also have strokes. So it's important to make this diagnosis to start therapy to prevent this.

I wanna mention that, you know, much as I love all the different antibiotics for my patients and I use them a lot, it is important that we realize that some of them are difficult for skin, and certain medications can make your skin much more sensitive to the sun, one of which is for commisol, that's an antifungal. I am extremely careful and try to avoid that if our

patients are out in the sun because of the burn that can cause. Another one is loxaciclib, which is also an antibiotic that can be used for instance, I mentioned it earlier for Saphne infections. You have to also be very careful. In the sun, you can see a picture here and someone that was actually hiking with hiking poles, so the top of their hands got the sunburn from that.

And then, you know, there are plenty of rashes that can be from antibiotics. This one is from amoxicillin and that picture. Penicillin sulfas and others can cause rashes as well and that's kind of a typical rash for that. These are some pictures from the vorre conizole. You know, the initial studies with vorre consult were under with patients that were undergoing bone marrow transplant, so we're not in the sun.

But, you know, the people that we follow, the people, you know, with the conditions that, you all are, you know, your family members may have may have to be on these medicines long term. And then you do go out in this and, you know, have these exposures, and it can cause some birds on long term can cause, you know, different types of skin issues related to the sun as well as even skin cancers. There are alternative anti fungals, I listed some here, plus aducanousol, atriConazol, atriConazol, that kind of mold activity. But for all the azals, there are drug interactions that people should be aware of, including with steroids, it can have some liver toxicity. And finally, I just wanted to mention that, you know, the immune system is very important in wound healing.

So neutrophils especially are really important how skin heals. And in case there's people here with or over the family member of chronic granulomatous disease that affects neutrophils and after surgery or when there are big wounds, there can really be this kind of abnormal exuberant inflammation. And sometimes you need to chill out that inflammation with like steroids or topical steroids to actually improve the skin healing, which sounds really counterintuitive to those of us that think of steroids as being really bad for wound healing. But in this case, then it can actually be helpful. Also, leukocyte adhesion deficiency, that's an immune disorder where the neutrophils stay in the blood.

They don't have the receptor to get out of the bloodstream to the site of the infection, and that often presents in the newborn period with the umbilical cord infections Vocal Cord actually won't fall off about those neutrophils helping and can have wound healing abnormalities. And I have a picture about some research with that in the next slide, but I also wanted to mention that you know, people with inborn errors of immunity that have increased staff infections around surgeries, sometimes we do give extra antibiotics just because, you know, it does take longer for these people to heal and they might be at more risk of infection. And this is actually a paper from NIAID, some from NIH, some research that's been ongoing, looking at leukocyte adhesion deficiency and one of the monoclonals against these two interleukins twelve and twenty three. It's a medication called vesikitinib and actually can improve some of the wound healing as well as some of the inflammation

that's seen in the mouth, also because of the issues with not having the proper neutrophils in the mouth. And now I'm going to hand it over to Dr.

Kong to talk to you a little bit about general skin health and finding a dermatologist and some of our research. And thank you, and then I'll be back on.

**Dr. Kong:** Absolutely. Thank you so much for having me today. As you can hear, Dr. Freeman sees so much skin disease that she knows how to manage. From a dermatologic perspective, a lot of the issues that are seen in airborne aerosol immunity. And so just highlighting, what are some of the general important concerns for protecting your skin? Protection is extremely important. Sometimes that's not just sunscreen and often remembering to apply it especially when you're going out and sweating at least once an hour, which seems like a lot and most people don't put enough on. It's it's should be somewhat uncomfortable in that you actually have a thick coating of sunscreen. But also physical modalities such as hats, long sleeves, and their clothing that are labeled, that have, sometimes they say, UPF on them, indicating that they are sun protective clothing. Another thing I like to tell patients is if you take a hat and you put it up to the sun and if you can see light coming through that, that means UV is coming through that hat or even that clothing.

And so vitamin D, there is a lot of talk about well. People need to have enough vitamin D. Vitamin D can also be obtained through other methods, not necessarily having to sit out in the sun and absorbing the UV rays. The other thing to think about is skin can be sensitive. And so certain soaps and lotions, it's not uncommon that people like a very fragrant or sometimes some younger children like the ones with glitter in them lotions.

And so using soaps and lotions that are mild. Usually, I tend to prefer ones that don't have a lot of fragrance just because it's adding additional contents into these soaps and emollients. The other thing to keep in mind is keeping cuts and wounds clean and dry.

That's very important. There are times where a dermatologist or wound care specialist, they say, okay, this wound actually needs to be kept covered and a little bit more moist.

So it just depends on what the wound is and potentially what the underlying immune deficiency is. So that's some of the things to think about. And that's why it is important to seek health medical care for some of these issues. Dr. Freeman just mentioned some of the side effects of some of the medications, sun sensitivity, especially something like doxycycline, or cortisol, those are the ones that we often think of very quickly when somebody says, what are some of the drugs that you are worried about that people can have exquisitely sensitive skin to sun on doxycycline, so that is something to be very careful of.

And then rashes such as potential allergies to some of these medications. And the other thing we like to talk about for these, for deficiencies, immune deficiencies is also just in

general keeping an eye out for new spots. If some patients have a lot of moles. And so it can be hard to figure out are these new, are these changing, and so often as individuals get a little bit older, is doing once month looking at your skin in front of a mirror and just making sure are all of these moles looking the same, turn around, look at the back, and just be familiar with what the spots are because it it can be important to say to a doctor that one particular spot on your skin appears to be changing. And those are important to point out to the doctor, especially a dermatologist who can take a look at that a little bit more carefully. Next slide. So how to find a dermatologist? It does take time to do a full full skin exam. And so often patients think, well, this is the only spot I'm worried about, so I don't need to change out of a gown. And so they'll say, well, I just I don't need to change.

I'm just gonna show you my one spot on my arm. The issue with that, particularly for thinking about moles, is that people tend to have a pattern of moles on their skin, for example. And that if we are only looking at that one spot, for example, one of my moles on somebody else may be looking problematic, but their my pattern or somebody else's wool on my skin may look different. So we have to look at the whole body to get a sense of what is this pattern, but also someone may not be aware that we are looking at something else on their back that they cannot see. And so we tend to have to understand what is going on with the whole skin surface to put the puzzle together sometimes.

And so you also want a dermatologist who is interested in understanding your underlying immune deficiency and is willing to connect with your inborn error or your IEI physician. One of the reasons why Dr. Freeman, when she was asked to do this, said, hey, would you be willing to join me since I am not a dermatologist. I said, sure, why? Because Dr.

Freeman and I have a long standing relationship over twenty years of working together because we see patients together because often we're having to work together to understand what is the immune deficiency and trying to understand what might be in a different way to manage a skin concern. And that is where understanding what is what are the treatments that you're getting for the IAI and understanding how that might integrate with skin directed treatments. The one thing to think about often when people are looking for dermatologists is to think about a local academic medical center. Generally those dermatologists may have a little bit more support, whether it's time wise, or individuals in the clinic to help address more complicated skin concerns. Definitely, there are many fabulous dermatologists out in the community what helps with an academic medical centers, they may be connected potentially with your IEI physician.

So that is one of the reasons why to that we often first look if we're having helping someone find a local dermatologist is to first look at the academic medical centers. And so also somebody that would be willing to work together again to collaborate with your doctors to make recommendation on what to do. And then also looking at what others in the, for example, the IDF or other individuals in your region who have I. E. Inborn errors of immunity,

who support a particular individual that said this particular dermatologist has been super helpful.

And so that's word-of-mouth can be helpful with that as well. So this is just a snapshot of one of the studies that we – Dr. Freeman and I work together with many other individuals. So you might have heard earlier from the Dock eight Deficiency. So normally what we see on healthy skin.

If you look under the right hand side of these bar charts, it says healthy volunteers, HVs. Normally, we see mostly green. And green indicates bacteria. So mostly bacterial microbes are exist on human skin. We all are covered in microbes.

We all have fungi on our skin. We all have some viruses, but we tend to have more bacteria than fungi and viruses. Whereas in the pre transplant on the far left, the purple, those are viruses. So, pretransplant in these patients with dock8 deficiency, we see many more viruses even in normal appearing skin. It might seem logical if they had warts that they would have viruses on the skin.

This was an even normal appearing skin. We were seeing many more viruses. And then over time, as you move to the right across these bar charts that have post transplant, These patients had transplants because they were at risk for developing malignancies, cancers, life threatening cancers, so they underwent transplant, HSCT, hematopoietic stem cell transplants. And then over time, their skin microbes tended to begin to look like what we see on the far right in healthy volunteers. So what this study really highlighted to us, even in normal appearing skin, we see that there is aboration in the communities, the microbial communities that exist on skin, and through the transplant process, we can see that that transitions.

This kind of this segues into the next slide, but for before I move there, some of these patients also had cancers that were, for example, most of these viruses were human papillomaviruses that we saw pictures of and described, Dr. Freeman described in other patients with cancers. And one of the cancers that one of the patients had was a vulvar cancer with stemming from an cancer related human papillomavirus. That by we could detect it on their skin, pre transplant, early post transplant, and then when they came to follow-up, later in transplant, we could not detect it, suggesting that this is a curative process. If for hematopoietic stem cell transplant for this particular patient population. Next slide, please. And so here is another example of a patient followed at the NIH who had [] deficiency and that predisposes patients to viral skin infections. And so on the left hand side is an invasive squamous cell cancer of the skin. And that was associated with a certain type of human papillomavirus. And it had actually been cut out before and it had recurred and cut out again And so what ended up happening was this patient also ended up having a hematopoietic cell transplantation.

And what we see here on the right hand side, this is post transplant. She had an excellent

outcome. And essentially was cured of this squamous cell because there was concern in some squamous cell carcinomas, cancers, particularly in a new deficiency can be quite aggressive. And so this is another story of where stem transplantation can do important things and resolve some of the skin problems, particularly the skin cancers that we've seen in some of these patients. Next slide.

So with that, hope we have a lot of questions that it looks like there might be some questions coming up. And so we look forward to the Q and A session. Thank you for listening.

**Emma Mertens:** Excellent. Well, thank you so much, Dr. Friedman and Dr. Kong. We are going to go ahead and transition to our Q and A here in just a moment.

There we go. Alright. So we just shared the ground rules for q and a in the chat, so we just ask that everybody respect the ground rules. And then we're gonna go ahead and get started with our first question. Alright.

So, this individual asks, if we are already on IVIG for our PI, does that provide any protection against skin infections, or do we still need to practice all the other recommendations that you outlined in your talk?

**Dr. Freeman:** I can take that. So that it's a really good question. The immune globulin replacement therapy is an IVIG. It actually has a lot of antibodies to a lot of different infections, but unfortunately, it doesn't really cover that many of the skin type of infections. There might be a little bit of activity against staff and in some studies, for instance, in hyper IgE syndrome, maybe decrease the amount of skin infection somewhat, but not as much as it impacted for instance the pneumonias where we do see more of an impact from immunoglobulin replacement therapy. So, and the same thing with the viral infections, unfortunately, the meanwhile IVIG doesn't have any impact on, for instance, HPV causing warts or herpes infections either. So, it does not have as much.

**Emma Mertens:** Sure. Thank you. Alright. Next question. So I know you touched on during your talk some great resources for locating a dermatologist who understands your PI, which is excellent.

And we're also wondering, what sort of recommendations do you have for enhancing communication that takes place between a dermatologist and say you're you're immunologist? Making sure everyone's on the same page.

**Dr. Kong:** That's a great question. It's a tough question because it's ideally one could encourage the your physician to say, would you be able to speak with my immunologist and confer with them about these medications that you might be recommending, or if this is ideal for my disease. And so that's where it does, unfortunately, because these are can be rare diseases. It's important for especially when you're developing the relationship, for

example, with your dermatologist that you have somebody who's willing to listen. I think that's what's really critical is somebody who's willing to listen.

And then in that case, this is someone that might be open to then communicating with the immunologist. And so that's it is is important to be an actively engaged in your care.

Because yes, physicians can be busy. They're seeing lots of patients, but there can be specific concerns. For immune deficiencies that need to be considered.

And so that's where it does help. If somebody is in an academic medical center because they are used to seeing a lot of the other physicians from other departments Mhmm.

Through different methods. Or through seminars or just even collaborating on different patients and they can develop that rapport and that can then help in future interactions for other patients. So that's where word-of-mouth on different physicians that are open to caring for patients with immunodeficiencies.

That can be really, really helpful. Howard

**Emma Mertens:** Bauchner: Alright, next question. This individual wants to know, do you know if PI can affect scarring They shared that their son had severe acne and she is worried long term about the healing process. Is there anything that can be done now to kind of set him up for success down the line?

**Dr. Freeman:** You want to take that one?

**Dr. Kong:** Yeah. So definitely, there are some and we see some of those patients that because of the specific immune deficiency, they may be at a higher risk for scarring. Scarring is tough because there are things that the, of course, when the lesion gets larger, it's likely to have more scarring. And so that's where if it's cystic acne, are there opportunities to use treatments to decrease the severity of the cystic acne so that just starting at the beginning and trying to minimize the actual lesion that happens as opposed to trying to after the lesion has already grown in multiple lesions, and then hoping that the scarring is minimized. It's really hard to, especially for cystic acne, to not have scarring because it's such a deep inflammation in the skin.

And so if there are way avenues or methods to just minimize how much one develops to begin with, that might be a more effective approach, if possible.

**Emma Mertens:** Howard Bauchner: Thank you. Alright, our next question. This person asks if I need antibiotics for skin infections, but I'm already on prophylactic antibiotics, will this cause resistance? Or is that not even an issue? Because if I'm already on the prophylactics, will they just not prescribe me an additional dose.

**Dr. Freeman:** Yeah. You know, that comes up a lot in my patients. They're on some sort of prophylaxis, and then they're seeing, like, an urgent care and they give them the exact same

antibiotic, which is really not helpful. This is where I think, you know, if you get a skin infection on top of your prophylaxis, this is when it's really helpful to get that culture so that you know what the resistance panel is to if it's stopped for instance. And then you can they should change the antibiotic if they think that it needs an antibiotic.

For instance, if they are on cephalexin, for instance Actually, let me do it the other way. Try Methampyr himself out, which is more commonly used as a prophylaxis, Then if you're seen, they can use something from a different class of antibiotics, so they can, for instance, use something like cephalexin, which wouldn't work if it was MRSA, but, you know, is a different class than the [trimethoprim-sulfamethoxazole]. So one of the reasons that I really like trimethorphan sofa for staff, prophylaxis and hyper IgE syndromes is it doesn't cause cross resistance if you end up with the antibiotic resistance. So if you have a staff that's resistant to the termithromyalgia, it's not going to then be resistant as well necessarily to cephalaxan or amarcicillin, covalent. So but why it's really important to get the culture because then within a couple days, you'll know which antibiotic is best.

**Emma Mertens:** Thank you so much. Alright. This next person is asking, my dermatologist wants to freeze off malayscom, but I'm worried about the open wounds getting infected. Is this done differently for someone who has an immune deficiency or is it typically the same process?

**Dr. Kong:** It's usually the same process. It is I think it's I completely understand it's a very good question that once you have a break in the skin barrier, does that put me at risk for developing other problems? In general, what we've seen is that that is not an issue. For the most part, for example, even when I do skin biopsies, the way I do skin biopsies for somebody who doesn't have immune deficiency and somebody who does have an immune deficiency, and I'm actually cutting through the skin. I manage them the same. I don't do anything particularly extensive with, you know, the surgical, you know, operating room type of cleaning and putting people in antibodies. I have excellent experience and we have for many, many decades of taking care of patients with immune deficiencies that we don't actually have to worry too much about doing something that breaks the skin. We aren't so worried about that. I think the only time I do pause is if somebody is about to go through transplant where they get the chemotherapy and that's wiping out their immune system and then they're going to be at particularly vulnerable, then if there is not a true need to do a biopsy in the week preceding the transplant, I say, let's put it off, or try to when we see patients before do the biopsy early enough, so I know that the skin is going to be healing before heading into the transplant That is the one time that I can think of where I'm a little bit more cautious about breaking the skin barrier.

**Emma Mertens:** Makes total sense. Thank you. Alright. This next individual wants to know Are there any skin medications that are absolutely off limits for someone who has PI? This particular person has CVID.

**Dr. Freeman:** I know I'm trying to think of any. You know, sometimes, I can't think it was for like a topical treatment. But you said, you said topical?

**Dr. Kong:** Yeah. I think it was a topical medication. I yeah,

**Dr. Freeman:** I could make viral infections worse some immune suppressants.

**Dr. Kong:** Right. So Sometimes we have had patients who have both the combination of eczema, which is often treated with steroids, and then somebody with and then that same patient can have problems with warts and melasma. And so if you Again, this is where I am a little bit cautious. I tend to not use as potent topical steroids as I would with somebody just with eczema. Because what happens is with the potent topical steroid, it suppresses the immune system in the skin, and then will make the viral infections worse.

So that's where the depending on what the whole story is, we have to put it into context and understand Is this person I you know, this is not uncommon that we'll see somebody with eczema and wart and warts and melasma. And that way, I end up not being as aggressive with the topical steroids because what will happen is they'll then tip over and then have many more melascom and that they're even more itchy because the melascom is are also itchy. So then it's, like, gone from one type of itchy to another type of itchy and I've caused that. So sometimes I it I have we have to assess the entire picture. And then because of what the underlying immune deficiency is, then make calculations.

I can't think for CBID, in particular, if there is anything that

**Dr. Freeman:** Yeah. I agree. I would

**Dr. Kong:** love to. Yeah. Not for that.

**Emma Mertens:** Thank you, both. That was a tough one. Alright. This next individual is asking about planter's words. So I know we touched on kind of the traditional words. We talked about the flat words. This individual wants to know if there's any connection between PI and planters warts.

**Dr. Kong:** So planters warts are fairly common. And they are extremely frustrating to treat because they don't like to go away. And so from that standpoint. It's a little bit hard to use that as a particular indicator. Now we have had in our experience at the NIH where they may have warts that cover the a lot of the bottom of the feet.

And that's when we start to get more concerned that it's not being contained in a region, but starting to affect toes and other parts of the foot. So that the extent of that may be

concerning. Now if you have planter warts and start and you have a history of multiple infections and other things. So again, looking at the holistic picture, that can be helpful. Alexandra, anything else that

**Dr. Freeman:** No. I agree. Like, plantar warts on their own wouldn't raise flax for me unless it's just kind of covering the whole foot. But isolated plantar warts not much.

**Emma Mertens:** Thank you both. Alright. This individual has has kind of a comment and a question. They shared they avoid allergens, but their eczema still doesn't improve. Is that because it's immune driven and not allergy driven?

**Dr. Kong:** Yes. Absolutely. I don't know that, yeah, Alexandra []

**Dr. Freeman:** No, no, no, not Coriant. Yeah.

**Dr. Kong:** So there are, so eczema is multifactorial, meaning that there are many potential contributors to the disease. Some often we see it run-in families. And so there may be some people who have a more allergic phenotype where maybe if they come into contact with, say, a pet, like a dog. They may have more rashes because they're allergic to the dog, where I remember a patient saying that every time they have chips, some way, cookies, they would break out more into a rash. You know, so clearly there's some tie there that they observe themselves.

Yet what is so frustrating about eczema is that sometimes you do everything the same that you thought was helping your eczema, and then it just rears its ugly head. And you didn't change anything and it just popped up again and flared. And so that's what's frustrating is that we like to say, oh, maybe I did x and that triggered it or maybe I did y and that's why I flared. But in reality, sometimes the eczema just starts to flare on its own. So it's And one of the reasons why we are beginning to see it is more There are yes allergic components. But a lot of the biologic agents that are being used currently in severe like atopic dermatitis and eczema are targeting different parts of the immune system and having some outstanding results. So that helps us understand that the immune system is really important in in eczema. Absolutely.

**Emma Mertens:** Thanks, Dr. Kong. And another question while we're on the topic of eczema, kind of a follow-up question. This person wants to know, how can we tell if the eczema is just flaring versus if it's actually infected? It always looks red and angry.

**Dr. Kong:** Yeah. So some of the things that I look for are is it yellow and crusty? Is it I completely agree, where it won't be, sometimes it's more oozy. You might say, risky is a concern for infection. What is it's interesting for me, especially if it's classically the types of eczema we have been seeing is that at having an antimicrobial component of the dilute bleach bands and the topical steroids that seem to be pretty effective for many, many

people.

So we are kind of targeting both. But if it starts to be a little bit more painful, more swollen, then those are the times that we begin to worry about or that yellow crusting that we sometimes see. Then we start to worry about more of a super infection, not just the eczema itself.

**Speaker 0:** Mhmm.

**Dr. Kong:** And the other one to think about is there is a risk with severe, more severe, moderate to severe eczema with herpes infections. And if it starts to become a little bit more ulcerated spread out very quickly and painful, then we do worry about that there is a secondary, like a spreading viral infection in the existing x So those are some things to think about as well. It should look different from then just a standard flare. There are some findings that can be helpful.

**Emma Mertens:** Dr. Freeman, did you wanna add something to that?

**Dr. Freeman:** I was just gonna add sometimes also, you know, for, like, for eczema, usually, if you use the topical steroids, it will usually improve things. So, you know, sometimes if you're having a difference in kind of your months to your typical therapies. I'll think about it more. Every once in a while, you know, for in certain mean deficiency, in certain locations, you know, there can also be a yeast that can be causing problems too. So You know, so and some of it's in the back of our head, but some of our patients will think about that too. But, yeah, that was my only other thought too. It's, you know, if you're putting topical steroids and it's worsening, then you'd be like, oh, am I missing an infection here?

**Dr. Kong:** Absolutely. I think that's really critical because what's important to think about what we often tell patients is that steroids actually feed fungal infections. It makes fungal infections worse. So that's where it is, that's a really key point Dr. Freeman brought up is if your standard treatment isn't working, that's – you need to think about what else might be happening.

**Emma Mertens:** Thank you both. All right, this next individual is wondering about kind of the intersection of dermatology and women's health. And PI. So I know during your talk, you touched on yeast a little bit. Are you aware of any connections between non lactating mastitis or infections such as BV in people with PI?

**Dr. Freeman:** I can talk a little bit about it for mastitis too. I do think, I'm not exactly sure how to turn it as much into dermatology too, but, you know, I think women's health, a lot of women's health issues have been, I think, you know, a little bit more recollected over the years. And I think in general, people with, from immunodeficiency, you know, we are having better therapies, we're having better recognition, people are living longer, and I think

Women's health issues are becoming something that we're looking at more strongly. So I know we've published about women's health and hyper IgE syndrome and, you know, mastitis and having breast abscesses are really in that disease. And the actual bacteria that are causing them can be a little bit different.

Like normally, we think about staff with the, you know, a lot of the abscesses there, but sometimes we will see a little bit different types of bacterial infections as well. And, you know, and, I mean, I feel like a lot of, I mean, deficiency immunologists work closely with dermatologists. It's a little bit lesser with the gynecologists. Right? So I think it's you know, it's kind of like these, you know, and I think the gynecologists are a little bit less used to working with the primary and inefficiency people.

So, you know, I think we're trying to deal with those barriers a little bit. But, you know, sometimes we have some issues by being like, you know, I am really worried that this is a mastitis from an infection in the patients. And same with thing with vaginal infections as well. Like, orphan glasses that are getting infected, for instance. We see epithersulcers in the mouth.

We see epithersulcers also, you know, in the vaginal tissue too. That can cause that can be really painful and are fairly common in some of the inmate Deficiencies we see. So the Clinical Immunology Society right now, one of the committees there is actually doing a study as well, looking at more issues in women's health I think pregnancy is the other one that comes up. But again, I'm going a little off topic with dermatology.

**Dr. Kong:** Yeah, that highlights again going back to how do you find the right doctor for each of these problems. And it's natural. It just tends to have more complex medical cases, tend to drift towards the academic medical center. And so that is a convergence of people a) that are physicians that are interested in more complicated or more complex medical problems, and then again because of the complexity of these issues that having doctors who are used to talking to each other. And so those are, again, the women's health physicians who tend to be at an academic medical center are again going to be more inclined to be potentially open to more unusual things or things that need some integration with other physicians.

**Emma Mertens:** Thank you both. All right. Next question. How would you define a mild soap or lotion? Are there certain obviously, I know you spoke about avoiding, like, sparkles in your sunscreen or, you know, super heavy perfumy smells.

Are there any particular chemicals or ingredients that people with maybe more sensitive or dermatological issues should avoid?

**Dr. Kong:** Yeah. So generally looking for the products that say that they are for sensitive skin or that they are for hypoallergenic hypoallergenic hypo. That's the an hypoallergenic. So

those types of they're they're many. There are many products that are out there on the market.

And also, you don't necessarily need to buy the name brand, that there can be generics that look that are often right next to the name brand one that can be, again, the ones that are for sensitive skin, the ones that are generally trying to avoid, like, fragrance free, you know, those are the ones that generally tend to be better for people who might have sensitive skin.

**Emma Mertens:** Thanks, Dr. Kong. Alright. Next question, are there any certain lifestyle changes, like diet, exercise, stress levels that affect skin health in folks who have primary immunodeficiency?

**Dr. Kong:** I think in general, stress can also always exacerbate skin disease. And particularly, I see it a lot in eczema more than potentially like trying to think of other ones, but definitely eczema where all of a sudden they're scratching more things are flaring because they're for excellent. There's an itch scratch cycle. The more you scratch, the more it rashes, and the more itches, so you more you scratch, and it just goes on and on. Diet more along the lines if it's very clear that somebody is sensitive to a particular food. I think that can be important. Sometimes if there are exercise it can be if there are deep skin folds and there's a lot of sweating and that sweat is retained in those skin folds. Sometimes you run the risk of maybe more fungal infections in those creases and folds. And so if one has extra folds and you're doing exercise, there are different types of clothing that maybe are sweat, you know, moisture wicking and, you know, making sure that one showers and dries those areas very carefully. So there are things that one could modify because these are important things to do for your for maintaining health. Especially mental health. Right? Some of these things are important. And so that's where it's important to do these things and it's just one may have to be a little bit more cautious about what might be irritating the skin if that makes sense.

**Emma Mertens:** Certainly. Thank you. So all the, you know, kind of the same things that would exacerbate any person just be cognizant of those and keep an eye out for those if you're someone who has PI as well. Alright. So I know you also touched on shingles a little bit, shingles and chicken pox in your talk.

This individual has a question about they they have CVID, and they were put on valtrex. But they're wondering if their primary immunodeficiency could contribute to them getting shingles again. And if they do get shingles again, how would that be treated the second time around?

**Dr. Freeman:** Yeah. You know, I think it that it's a little hard to tell because there's it really depends on kind of the specifics of the immune deficiency kinda in the risk of shingles. So

shingles is pretty common to have once in people in general, especially as people age and that's why the, you know, there's this shingles vaccine that is recommended for people now, you know, for middle aged people. And there is, in the past, there is only a live viral vaccine, there is now one that is an inactivated protein vaccine that would be available for people. But depending on the mean deficiency whether or not an individual respond is kinda a little bit, depends on the individual on their immune system.

Certain immune deficiencies predisposed to recurrent shingles or recurrent herpes infections. For people that have certain types of those immune deficiencies, you know, sometimes they will be placed on kind of long term valvulocycline or where you take it once a day or twice a day kind of long term. It's you know, for most people, it's a really safe medication without many side effects. But let's say this, if this person had taken it, stopped it, and then had shingles again, it's really, really rare for that to be resistant at that point. So the most likely treatment if it was a pretty standard case of shingles is to restart it.

It's just a question afterwards about prophylaxis or vaccine or things, but that really depends on the immune system. But I mean, it's very infrequent to become resistant.

Howard

**Emma Mertens:** Bauchner: Well, thank you so much, Dr. Kong and Dr. Freeman, I wanna be mindful of your time this evening, so we're going to wrap up the Q and A with that last question. But I just wanna thank you both so much for your time this evening and for your patience and your thoughtful answers to our Q and A questions and for putting together this wonderful presentation. We are so grateful.

And now we're gonna get ready to close out. I know you probably each have, you know, dinner you wanna get to or you wanna get to your family. So feel free to stick with us till the end or if you if you wanna go get back to your evening, so that's fine as well. But we are so grateful for your effort putting this awesome presentation together and I know our community is grateful as well, so thank you both so much.

**Dr. Freeman:** Thank you so much for having us.

**Dr. Kong:** Thank you.

**Dr. Freeman:** It's a

**Dr. Kong:** great question.

**Dr. Freeman:** Absolutely. Yeah.

**Emma Mertens:** Thank you both. Alright. So we're gonna get ready to wrap up here. Before I do, we're gonna share some upcoming events and some resources. So here we go.

Primary immune dot org is your go to website for additional resources, upcoming events, and more. All immune deficiency foundation materials are free to access, print, or have

mailed directly to you. If we didn't get to your questions tonight, you can contact our Ask IDF program. A team member will personally connect with you to tackle your questions and direct you to appropriate resources. You can even take the immune deficiency foundation on the road with our engaging podcast series.

You can find programs like bold conversations, undiagnosed, and chronic twenties by searching for the immune deficiency foundation podcast. We also have a YouTube channel where you can find recordings from all of our digital education events, including tonight's, which will be available in the coming weeks. Find a safe and supportive environment to link up with others impacted by PI through a get connect to groups. These groups are free virtual volunteer led opportunities to connect with others with PI all over the US. We offer location based groups, so in your city or state, diagnosis specific groups and nationwide groups, and because we meet virtually, you can join any group that works for you.

All upcoming meetings are listed on a calendar of events. Additionally, we offer facilitated support groups for young adults, parents and caregivers, spouses and partners and we also have a peer support option if you're looking for something more one on one. We're also very excited to share that we have revamped our idea of friends platform. It's a private online community, create created to provide you with all the best and latest resources for support. Connect with others in similar situations, share stories, ask questions, and find support. Our GetConnector groups will be moving to this platform this winter, and we cannot wait to connect with you in twenty twenty six. Tonight kicks off an exciting year of programming ahead here at the Immune Deficiency Foundation. And in case you missed it, registration is now open for our twenty twenty six national conference taking place this June in San Antonio, Texas. Scholarships are available and applications are open through March 31st. The Unique Efficiency Foundation is part of Walmart's Sparkgood round up campaign where customers can round up their purchases to the nearest dollar and donate the change to their favorite charity.

Simply visit [walmart.com/sparkgood](http://walmart.com/sparkgood), select the immune deficiency foundation, and sign in to your Walmart account. From there, you can donate spare change by automatically rounding up your orders to the nearest dollar at checkout. Alright. We're now going to launch our closing poll. Again, we'll give it about thirty seconds for everyone to answer, so that should pop up here.

Just in a minute. Our closing question is after tonight's program, please rank your understanding of how primary immunodeficiency affects your skin and causes dermatological problems. Alright. Thank you everyone for sharing. It seems like everyone's understanding has improved, and that's what we wanna see.

So thank you so much. Alright. And now is the time where we wanna hear from you. So we're going to invite you all to go ahead and share one new thing that you learned from tonight's program. If you can go ahead and put that in the Q and A box, And then I'll give it a

few moments and we'll read a couple out loud to go ahead and share that in the Q and A box.

Alright. Thank you everyone for sharing. We're getting lots of good comments about they learned a lot about warts, they learned a lot about egg eczema, the importance of paying attention to small skin changes, antibacterial baths. That was a new one that I learned about too. They people appreciated the advice to go to an academic center just people having aha moments about childhood eczema that maybe was the early indicator of their PI.

So this is great. So people learned a lot. So thank you so much, Dr. Freeman and Dr. Kong. This is awesome. Alright, everybody. Well, before we go, we do wanna give off heartfelt thank you to our amazing volunteers and supporters who make programs like this one possible. If tonight's presentation resonated with you, we do hope you'll consider supporting future programming. Your donation at any level helps us continue building community and delivering meaningful content.

So thank you so much for being here and being a part of our community. Alright, doctor Freeman and doctor Kong. Thank you again so much. We are so appreciative for you both leading this super important discussion. It's been such an honor hosting you for tonight's program.

Thank you both.