

The Fundamentals of Pemphigus Patient Education Webinar- February 16, 2023

Becky Strong: Hi, everybody! We're just gonna wait just a couple of seconds here and let's get everybody into the room, and then we will go ahead and start the Webinar. Thank you all for joining us today. We sincerely appreciate you taking the time out of your day to be here. Hope everybody is enjoying the weather and feeling well. Our numbers have stabilized a little bit. So welcome everybody. Our call is now being recorded. I'm Becky Strong, IPPF Outreach, Director and your host for today's webinar. Thank you for joining us. I'd like to thank each of you for joining us on the call and the support provided by sanofi and Regeneron for making today's call possible. Before we begin I'd just like to take a quick poll to see who we have with us today. So let us know what disease subtype you have. While you take a minute to answer the poll, I'd like to introduce our speaker for today. Dr. Brittany Schultz completed her undergraduate, medical school, and residency at the University of Minnesota. She is a graduate of the Combined Internal Medicine/Dermatology program, where she served as chief resident. She now works at the University of Minnesota as an Assistant Professor and at the Minneapolis Veterans Affairs Healthcare System as a Staff Dermatologist. She is Director of the Autoimmune Blistering Diseases Clinic at the University of Minnesota. Her clinical and research interests are complex medical dermatology and autoimmune blistering disorders. In her free time, she enjoys going on neighborhood walks with her husband and 2 sons. If we can show the results of the poll, it looks like an overwhelming percent of people, about 87% have pemphigus vulgaris, about 9% have pemphigus foliaceus and about 4% have IgA pemphigus. So thank you so much. So now I would like to go over a few housekeeping items... (Reviews Housekeeping Slides). Now it is my pleasure to introduce Dr. Schultz to discuss the Fundamentals of Pemphigus to better understand our disease and to answer your questions.

Dr. Schultz: Wonderful thanks for the introduction Becky, I'm really happy to be here today. This talk, as Becky said, is about the fundamentals of pemphigus. What it is, how our bodies react, a high level overview of some treatment. But really the focus of this talk is not so much about treatment, but just more about what is pemphigus itself, and some associations and other things. So there were many questions I received about treatment ahead of time. I apologize we're probably not going to cover many of those. But hopefully, I can still give you a short insight into some treatment. My overview today is what is pemphigus? What are the types of pemphigus? Why do I have it? How do you diagnose it? And what can I do about it? Which again is the very brief section. And then just one little miscellaneous slide, I couldn't quite fit nicely into my other sections, and then time for Q&A.

Dr. Schultz: So what is pemphigus? Pemphigus itself is a group of autoimmune blistering conditions. Let's dissect what that means. What does autoimmune mean? So normally your immune system protects you from infections. It fights bugs in you, infections, the flu, the cold, everything like that. When your immune system starts to fight yourself, that's what we call an autoimmune condition. So, instead of fighting just infections, it's fighting you too. Blistering, I don't have to tell you what blistering is, that's when you develop blisters on your skin. So all of the pemphigus conditions are autoimmune conditions that develop blisters. Why do we call it pemphigus? For any etymology buffs out there, pemphix is actually Greek for blister. That's why

it has this very strange word. As you know it can affect mucus membranes, the mouth, the eyes, the genital skin, the anal skin, esophagus and also your skin. It can be life-threatening. They're very different spectrums of involvement. Some people have more mild disease, some people have very severe disease, and then all kinds in the middle. No matter how severe it is, it significantly impacts quality of life, we know this. Even if you just have one blister that can have a huge impact on your quality of life, compared to someone who has many more blisters than just one, it still impacts you. Some of the pemphigus groups can be associated with other autoimmune diseases like thyroid disease or rheumatoid arthritis. So there can be other things that go along with it, too.

What is happening in pemphigus? Normally you have a nice framework for your skin. Pardon my rudimentary drawing there, but normally it's kind of like a brick wall of your skin. In pemphigus, there are antibodies that come along, which are normally again fighting bugs and infection, but they decide to fight you. So the antibodies come along and they attack the glue that holds the skin together and it attacks these connections. Then what happens is that these connections can't be maintained and they fall apart. You get this disruption of this brick wall in your skin. The skin is very fragile, and you get blisters and erosions, especially with trauma.

That results in what you see in the skin which you can see in the photos. You have blisters and then the top can come off and then you have open skin or what we call an erosion. An erosion is like when you skin your knee, you have that top layer of skin which is missing. So that is what is happening in pemphigus, that top layer of skin can't hold on so it gets disrupted and comes off. That also happens in the mouth. Same thing, the blisters get very easily disrupted, and then you get these erosions on the skin. For anyone interested in what it looks like under the microscope, which we'll talk about a little bit more in depth later.

This is a picture of your normal skin. This is a picture with a different stain, so it looks blue instead of pink. But that's just the difference in the stain. But so this is your normal skin. You have what's called your stratum corneum right on the top here, and then this middle layer is called the epidermis, and then this deeper layer is called the dermis. Normally these are all nice and tight together. In pemphigus you can see in this picture, on my right, that the top layer of the epidermis has come away from the bottom layer of the epidermis. So you get this little space in there, this little cleft and that's what on the skin looks like a blister. Then in the picture on my left, that top layer of skin is totally missing, and you can just see what's left of the bottom epidermis. So that's what your skin actually looks like under the microscope when this is happening. Instead of a nice epidermis next to a dermis, you've got an epidermis that is lifting up. The antibodies that are attacking the skin, the specific ones involved, depend on the type of pemphigus that you have.

There was a question I received about how is pemphigus different from pemphigoid? They're very similar. Antibodies are again attacking the glue that holds the skin together but compared to pemphigus, in pemphigoid the antibodies are deeper in the skin, so they're actually breaking apart that connection not within the epidermis, but the epidermis and the dermis. That results in

these deeper blisters that are often a little more sturdy or tense. They don't rupture as easily as they do in pemphigus, but they do still rupture.

The patients that we see pemphigoid in are a little bit older. They are classically very itchy. They don't always have to have blisters. You can see this person on my right has a lot of what we say, pink patches on the skin. It's kind of blotchy pink, not necessarily huge blisters. It less commonly involves the mucous membranes in pemphigoid but it can. Then like I said, there are different antibodies involved in pemphigoid as classically associated with neurologic diseases like strokes or dementia, things like that. So it's similar in many ways, but a little bit different. Then lastly, looking at the skin, you can see that the entire epidermis is lifted up away from the dermis, and there are big blisters in between. So in pemphigus the disruption was much higher within the epidermis. In pemphigoid it is deeper, it's below the surface of the skin, so that results in what we see clinically is those deeper, sturdier blisters.

Okay, moving on to types of pemphigus. The poll is very interesting, because, as we'll talk about pemphigus vulgaris is the most common subtype, followed by pemphigus foliaceus, and then paraneoplastic pemphigus and the IgA pemphigus are very much less common. So you yourselves are a very fitting representative of how common these conditions actually are. These are the four main types that we're going to talk about a little more detail.

Pemphigus vulgaris, which is the most common one, the most common type of pemphigus. You might wonder why it's called vulgaris. Again, that's for the etymology buffs that vulgar is latin for common. So it's just the most common pemphigus. In pemphigus vulgaris you have antibodies that are the IgG subtype. You have several different types of antibodies that float around in your blood. You have IgG, you have IgA, which we're going to talk about. You also have IgM, IgD, IgE. All these different types of antibodies that have different roles in the body that are involved in different areas of the immune response. But in specifically in pemphigus we're looking at IgG antibodies, and those are attacking the epidermis. So in pemphigus vulgaris the antibodies are IgG and the proteins they're specifically attacking in your skin are called desmoglein, which is abbreviated Dsg, you might see that throughout my presentation, desmoglein 3 and then some also have desmoglein 1. Those are antibodies that are living within the epidermis and attacking the connections between the cells. Essentially, every patient that has pemphigus vulgaris has involvement of the mucosa. The oral mucosa, the mouth is the most common, but it can also involve the eyes, esophagus, vaginal skin, anal skin, and anywhere you have a mucosal surface. One of the questions I received was, how common is it for the eyes to be involved? There are a few studies out there and it looks like about 14-17% of patients with pemphigus will have eye involvement. So it's much less common than the oral mucosa which again, is the most common. But it definitely can happen. Then about half of patients with pemphigus have skin involvement. It's really hard to know or predict who's going to develop what lesions on what location. There's no real way of knowing for sure. You might wonder, okay right now I just have it in my mouth and my skin but what am I going to have in a year? And it's just really hard to know. I will say that in my experience the patients I see in my clinic in general, by the time they arrive to me they've had their condition for usually at least a month, 2 months, 3 months, if not much longer. Usually by the time I see them, wherever they have the pemphigus is kind of where it

stays. It's less common for me to see someone who has it on their skin in their mouth and then the next time I see them it's also in the esophagus or also in the eyes. It's often kind of at the time of presentation, or shortly thereafter you kind of have all the sites that you're going to have. That doesn't mean you can't develop involvement elsewhere at some other time but in my experience it just is less common. Then in terms of why it affects mucosa versus skin, we do have a theory on that that I'll talk about a little bit later. We think the differences are related to which antibodies are present, so desmoglein 3 versus if you have 3 and 1. And again, I'll come back to that. Then, as many of you have experienced, this condition can be misdiagnosed for a very long time. It's more common for it to be misdiagnosed or undiagnosed when it doesn't involve the skin, and it just involves the mucosal surface. That's probably partly because this condition is very much in the dermatologist world. In dermatology we are very familiar with this condition. We see it, we treat it, we know about it. It's not as common for other specialties to know about it. Maybe this will resonate with you, but your dentist may never have heard of this condition. Your primary care doctor may never have heard of this condition. It's very rare, it's uncommon so there's less familiarity with it. If you don't have anything on your skin, the other doctors you're seeing might not think to send you to the dermatologist and we think this is often why it's undiagnosed or misdiagnosed. Unfortunately you're not finding the person who is most aware of the condition and most comfortable treating it. Just a shout out to the IPPF, that's one reason that they are so valuable. They do so much education with other specialties and reach out to promote awareness of this condition in dentistry, for example. A great service that the IPPF provides to hopefully reduce undiagnosis and misdiagnosis for a long time. So a little bit of a tangent there, but an important one. A little bit of a tangent there, but an important one.

What do we see on the mucosa and the skin? We see intact blisters but again, those blisters are so fragile, because that little top layer of epidermis is just so thin that often the blisters just break very quickly so then you just have the erosions left behind. You can see in these pictures that there's this bright redness on the gingiva, underneath the teeth. There's this redness up on the hard palate. There's redness on the skin. There's that crusting that develops because you know your skin gets oozy and drainage, and it gets crusty. I don't have to tell you that you know this can be very painful. You can have itchy, you can have burning. You have stinging. There's probably many other adjectives you could use to describe what you experience. But this is not comfortable, depending on where you have symptoms. You might have pain in your eyes, gritty eyes, dry eyes. You can have nose bleeds if it involves the nose. Pain with swallowing. Pain with urination, or bowel movement, pain with intercourse, if it affects the vaginal skin, and then you know, either while it's active or after you've had treatment there can be a lot of pigment change in the skin, so you can leave behind a lot of discoloration from prior involvement. Your nails can be affected and then there are 2 kinds of variants within Pemphigus vulgaris. One's called pemphigus vegetans. Essentially that's similar to Pemphigus Vulgaris, but patients that have kind of these cauliflower like lesions where the the skin kind of goes into hyper-drive trying to kind of heal things up. And so the lesion they're much more raised themselves, but it's still the same kind of process as Pemphigus Vulgaris. Then, herpetiform pemphigus is again essentially pemphigus vulgaris. But specifically the lesions are kind of herpes-like arrangements. So if you think of a cold sore it's kind of a group of blisters on your lip. And so you might have your Pemphigus vulgaris blisters are kind of grouped or like in circles. So they're essentially

Pemphigus vulgaris but just some different variants. That's Pemphigus Vulgaris, now moving on to Pemphigus Foliaceus or PF. Foliaceus is derived from a leaf in Latin, and so the idea being that some of the changes on the skin can almost look like little leaves. I guess this is very similar to Pemphigus vulgaris. It's again, an IgG antibody. But now, instead of desmoglein 3, plus or minus one. It's only desmoglein 1. So there's no desmoglein 3 involved. Desmoglein 1 is more superficial in the epidermis. And so these blisters are even more superficial than the ones you might see in pemphigus vulgaris. The skin is always involved, and the mucosa is not involved, and we'll talk a little bit later about why that is. But this condition does not affect the mouth. It's just the skin. I shouldn't say just the skin, but it's the skin alone, and it's often in the seborrheic areas or oil gland-like areas, So that's like your upper chest, your upper back, and the face. And again, the differences in the skin and Mucosa is related to the type of antibodies that are involved which we'll come back to.

So what does this look like in the skin? It can look very similar to pemphigus vulgaris. But again, it's on the skin alone. Nothing in the mouth. And so you see these erosions on the skin. You see a lot of scale. You see a lot of crusting, and then the symptoms are very similar to pemphigus vulgaris. This is not comfortable, either. There are several variants of Pemphigus foliaceus. There's a very interesting variant that's endemic in Brazil, meaning it's locally found in Brazil, and I actually think it might be related to this black fly that lives in an area. So maybe these patients are getting exposed or bitten by these black flies that somehow kind of revs up their immune system and has them develop this condition, and interestingly, as these areas are developed, they live in patients, live in better housing, not dirt floors. The incidence of this condition actually goes down, which is fascinating. Then there's also another variant called pemphigus erythematosus, and that you might recognize erythematosus from a condition called lupus. So lupus erythematosus. I guess that essentially is only happening in this area of malar rash or cheeks. So this is a variant of Pemphigus that essentially is only happening in this area that Lupus tends to attack or you can also have a drug induced variant.

This is maybe more than some of you will care to know about. It's a little nerdy, but it's very interesting. So this is why we think that some depend on your pemphigus vulgaris or foliaceus. Why you have your mouth or your skin involved, or why you might have both. So in your mouth you have a lot of a desmoglein 3. In your skin you have a lot of desmoglein 3. You still have desmoglein 1 and 3 in both places, but just lower quantities, and this is a little bit oversimplified version of it. But let's say you have Pemphigus Vulgaris, you knocked out a ton of desmoglein 3 in your mouth, and there's not enough desmoglein 1 to compensate. So you get blisters and involvement in your mouth. Versus on your skin there's so much desmoglein 1 there that even if you knock out desmoglein 3, you still have a lot of desmoglein 1. And so your skin is okay. In contrast to Pemphigus foliaceus when we knock out desmoglein 1, If you knock out desmoglein 1 in your mouth, your desmoglein 3 is fine. It's very happy. You don't have any blisters in your mouth, but if you knock out that desmoglein 1 in your skin, you don't have enough desmoglein 3 to compensate. So you get blisters on your skin. Then if you have pemphigus vulgaris, where you have both antibodies knocked out. Pemphigus 1 and 3, that's why you have involvement in your mouth and your skin. So maybe a little more than you wanted to know. But it's very interesting and it correlates very well how these changes in the antibodies result in the changes in your skin so it can be predictable in that way.

Moving on to the next subtype of Pemphigus, Paraneoplastic Pemphigus (PNP). This is very rare. It is associated with an underlying tumor. Now the tumor doesn't have to be cancerous. There can also be non cancerous tumors that can be associated with this. Most commonly it's either non Hodgkin's Lymphoma or CLL chronic lymphocytic leukemia. About 2 thirds of patients will have one of those blood cancers and then they also develop skin lesions similar to what is seen in pemphigus. It's pretty rare, so only about 3 to 5% of all Pemphigus cases will have Paraneoplastic pemphigus. Most patients will have already known that they have a cancer only about a third of patients kind of show up with pemphigus and then are later diagnosed with a with a cancer. Hearing this, you might be worried that if you have pemphigus, are you at risk to develop a cancer? It's very unlikely, much more likely that you would have had a cancer that we knew about, and then this develops. There was also different results in the blood and the skin that we'll talk about that tells your doctor which subtype you have, and this one looks very different than other types of pemphigus. So again it's IgG Antibodies, but now it's against a lot of different antibodies. So in Pemphigus Vulgaris and Foliaceus it's in desmoglein 3 and desmoglein 1 and it was just either one or a combo of those 2 in Paraneoplastic pemphigus there's many different antibodies called plakins and then that you can also have desmoglein 1 and 3, and then the bullous pemphigoid antibodies. So just to say, there's a lot of different antibodies, in addition to the antibodies you also have this other immune response that is caused by t cells. So it just adds an additional immune response that is unlike what we see in pemphigus. It can present very similarly to Pemphigus itself, pemphigus vulgaris mostly with the oral involvement, and then classically in Paraneoplastic pemphigus, the mouth is really really resistant to treatment, and it's very severe, and it's classically on the lips. So if someone has really severe lip involvement that doesn't mean you have Paraneoplastic pemphigus But in the patients that do have Paraneoplastic pemphigus we do see that severe lip involvement, and then the skin can look very different and can have very different skin presentations. It could look like pemphigus vulgaris or foliaceus. Other conditions are called erythema multiforme. So the skin can look kind of like anything. Importantly in this condition Paraneoplastic pemphigus can also involve your lungs, which can be very serious. Thankfully, that does not occur in Pemphigus vulgaris or foliaceus but it can involve the lungs in a condition called bronchiolitis obliterans and this can be more difficult to treat than pemphigus vulgaris or foliaceus. Kind of in the same family as Paraneoplastic pemphigus because they're kind of right now used interchangeably is called PAMS, Paraneoplastic autoimmune multiorgan syndrome is more of an inclusive term to capture all these other things that can happen like the lung involvement. So if you hear that term, it's also Paraneoplastic pemphigus.

This is kind of a different bucket. A different family of pemphigus. So this whole time we've been talking about IgG antibodies. In this case now we have IgA antibodies. So a little bit different antibody type. They are still attacking the connection in the epidermis. So they're still attacking this brick wall and your epidermis and making the cells fall apart. But again it's IgA that's doing it. There's 2 different types that are described. The names aren't extremely important. They're big mouthfuls, but you might hear them SPD type or IEN type. Maybe the SPD type is a little more superficial, and the IEN type is a little bit deeper. But again very similar. The antibodies are a little different. So we know an SPD it's a Desmocollin antibody in IEN. We're not quite sure what the antibody involved. Unfortunately, there's no test for desmocollin antibody. You can't

measure it like you can desmoglein, which we'll talk about. So this one is just harder to pinpoint exactly what antibodies involved. And then in IgA pemphigus there's usually no mucosal involvement. Maybe because these are less like desmocollin and the others are, or maybe less, of the main glue in your mouth, kind of like desmoglein one isn't as important in your mouth as desmoglein 3. So maybe desmocollin isn't as important to your mouth as desmoglein 3. This looks a little different on the skin. You still have blisters or vesicles, but they can often be a little more yellowish, or what are called pustules. So when there's a lot of cells called the neutrophil. That's an inflammatory cell. When that develops into a blister it creates more pus, and so the pus looks yellow and that's classic in this condition that they're more yellowy pustules, and then it loves what we call intertriginous areas which are areas in your neck, your armpits, your groin and kind of your skin folds, and then it likes to be in ring patterns or circular patterns or sunflower patterns. So this picture below kind of shows some of those like semi circles or rings, like patterns that can develop. This also could be extremely painful. Itchy, stinging, and burning exactly like Pemphigus Foliaceus or Vulgaris. And then, if anyone's ever heard of a very similar condition called Sneddon Wilkinson, or subcorneal pustular dermatosis. This looks identical to it, and really the only way you can distinguish from that condition is on blood work and biopsy. And so you don't need to remember the name of that condition. But if that was ever thrown around for you as a possible differential is because they can look identical on the skin.

And then last, I have one more one more nerdy topic. You know one of the questions that I received was about can you kind of move from one condition to the other? So if I have Pemphigus vulgaris can I go to Pemphigus Foliaceus? It's uncommon, but it has been reported specifically for those to pemphigus vulgaris and pemphigus Foliaceus. It would be much less common, rare. I don't want to say it's impossible. Nothing's ever impossible, but very very very rare to go from pemphigus vulgaris or pemphigus Foliaceus to Paraneoplastic pemphigus to vulgaris. That's just because those ones are just so much different from each other. But Pemphigus vulgaris and Foliaceus are a little more similar. And so there have been reports of people kind of going from one to the other, and what we think is happening is that it's kind of like your antibody response is kind of leading over to the other one. So we specifically call it epitope spreading. So an epitope is a part of your molecule in your body that antibodies are attacking. So you know it's attacking part of desmoglein one and it's attacking a part of desmoglein 3, and in epitope spreading it's spread to another similar molecule. So here's my very simplistic oversimplified picture that IgG is attacking desmoglein 3 and because desmoglein 1 looks so similar to desmoglein 3. Then your body also starts making an antibody to desmoglein 1. So again, it would be extremely rare to go to Paraneoplastic pemphigus or IgA pemphigus foliaceus. But you could go back and forth between the two because desmoglein 1 and 3 are so similar. So maybe a little again, too nerdy. But it's just very interesting how your body makes these changes and develops. So that's what we think is happening.

Moving on to the next section. Why do I have Pemphigus? Which I'm sure is on many of your minds. And unfortunately the answer is a little bit less satisfying than you might hope. So we don't really know. We think it's a combination of genetics and a combination of environmental factors. But we don't really know why a specific person will develop this condition. So, for example, the incidence of Pemphigus is 0.76, so less than one to 5 new cases per 1 million

people per year. But in people who have, for example, Ashkenazi, Jewish ancestry, there's 16 to 32 cases per 1 million people per year. So that's almost 3 to 6 times as common in patients with Ashkenazi Jewish ancestry. In most populations, Pemphigus vulgaris is the overwhelmingly more common subtype. But, Pemphigus Foliaceus can be more common in a few countries, such as Finland, Tunisia, and Brazil. It affects men and women equally in the usual age of onset is about 50 to 60 years old. There are genetics involved in this, but it's not one of the questions I received was about passing this on to children. It's not so much that you know, if you have a condition like cystic fibrosis or sickle cell anemia, or other neurofibromatosis, other genetic conditions that you know, you can calculate the percentage of chance that I'm passing this gene on to my child, and that doesn't really work like that in this instance. It's more like a tendency to develop an autoimmune condition. So I'd say it's much more common that my patient has pemphigus. Their grandma has rheumatoid arthritis. Their uncle has type one diabetes, their sister has vitiligo. It's much more that you're kind of inheriting a tendency towards autoimmune diseases. Not necessarily to develop Pemphigus itself. So thankfully, you know I wouldn't be worried that you're going to pass Pemphigus onto your children. But your children might have an increased risk of other autoimmune diseases, if that makes sense.

There have been certain triggers reported. I'm going to go on to the next slide, which is a very busy slide. I wish I could make this smaller, so you could see the very top. But you know these are a list of triggers that have been reported in pemphigus and I'll tell you that Some have much more evidence than others but they've definitely been reported. So here's medications, penicillin and cap to Prill, or probably the 2 that are most commonly reported vaccines have been reported to trigger pemphigus. We'll come back to that. There's been some reports of certain foods in the diet, like garlic or onions triggering pemphigus. It's hard to kind of prove triggers like that, because if you look at 2 people usually they're not exactly the same, except that one eats onion, and one doesn't eat any, so it's hard to say. Oh, yes, it was exactly the onion that caused it, but it's been reported. Sun exposure has been reported in some people to worsen pemphigus but not always.

So I usually tell my patients. You know it's hard again to kind of prove those triggers sometimes. But if you, as a patient, notice an association, you know you go out in the sun, you get a sunburn and it makes your skin worse. You're stressed and you're seeing it's worse, you know those are very real things. You eat an onion, and things are worse. You know those are very real things. So if those things are happening to you, then of course, avoid them when it's possible. But it's just hard to prove that you know, in these big studies that we are looking at, you know, many different people that have pemphigus. But triggers are definitely a real thing. It's just hard to know what was your trigger that actually brought this on? You know it's just hard to know. All right moving on to the next section of how do you diagnose Pemphigus? And this may be familiar to many of you of the test we're looking at, and you may interpret them with your doctor and kind of make treatment decisions based on some of them. So to first diagnose Pemphigus, you have likely all experienced this. You either need to get a biopsy of your skin or your mucosa. And then you really often need two biopsies. So first, if you're just looking at your skin under the microscope, you're just looking for what does the skin look like. Which is one important test. The second important test is, you look for those antibodies on the skin. So this is a test called direct

immunofluorescence or DIF, and so what you're looking at is you take a piece of your skin, and then you in the lab they put these antibodies on to the skin, and they see if any antibodies deposit in these areas. So if you had normal skin this, there would be no green here. It would look black. In Pemphigus you're getting all these antibodies deposited around these keratinocytes. So each little blob is a little skin cell and these antibodies are depositing all around the keratinocyte to the side of the skin cell. And so that's a positive test, and that tells us that you have in this instance. This is an example of Pemphigus. You also can look at the blood to look for those antibodies. So in the instance we were just talking about. We were looking at your skin, and you put antibodies on it. You also can draw your blood and then put your blood onto what we call substrate. So this is monkey esophagus and then you again look for the antibody pattern. So an indirect immunofluorescence is your blood. A direct immunofluorescence is your skin, and they both mean the same. You're looking for the same thing in both of them, the antibody deposition. Now it doesn't tell you what antibodies are depositing. It just tells you that there are antibodies there. So you can't necessarily say oh, Yes, there's desmoglein 1 or 3 or a plakoglobin or a desmocolin. Just all you can know is that there are antibodies there.

What the second blood test does, which is called an ELISA. That can tell you exactly what antibody is there, and how much of it you have, and that is extremely valuable, because in general, the higher your antibody level is the more activity you have on your skin. And so it can be very nice to monitor when you first came in your antibody level was a 100. We gave you our medications, and now it's down to 10. That's an amazing response. You know something like that, or oh is your disease starting to come back and flare. Your antibody level was 10, but now it's 50, so it's going back up. So when we know the antibody that's involved, and we can directly measure it, that can be extremely valuable.

We don't have this ELISA test, this antibody level test for all conditions. So, for example, we don't have it for desmocolin, we don't have it for all the plakoglobins. So it's helpful when we can use it, but we can't use it in every condition. And then, as I alluded to earlier, depending on the pattern we see in the combination of these 3 tests. The what's called the h and E under the microscope, what it looks like on its skin. The direct immunofluorescence, the indirect immunofluorescence. And then these ELISA antibody levels depending on the pattern of all those, it tells us what subtype of pemphigus you have, and then it can also distinguish between pemphigus and pemphigoid. And then, as we already talked about, diagnosis can be delayed, you know, sometimes it takes a while for people to think to do these subsequent tests or sometimes only one of them is positive, or 2 of 3 are positive, it can be difficult to get the diagnosis sometimes.

So what can you do about pemphigus? And again, the focus of this talk is not on treatment. So this is just a very brief, high level overview. But in general you know, your immune system is going haywire and attacking, it's supposed to be attacking bugs, but it's attacking you. So we kind of need to send a lightning bolt to the immune system and calm things down. So in Pemphigus Foliaceus and Pemphigus vulgaris. The most commonly used medications are ones like prednisone or Rituximab. We also use mycophenolate, azathioprine, IVIg, and others. But those are probably the most common ones. In Paraneoplastic pemphigus, it's most important to

treat whatever tumor or cancer, or non-cancerous tumor is driving it, but that oftentimes isn't completely enough. You usually also need to do a little bit of immunosuppression like, for example, Rituximab.

And then IgA Pemphigus is kind of again and it's other class, this IgA antibody that triggers these nutra fills. Those can actually respond really well to medicines that don't necessarily suppress the immune system. So those are medications you may have heard of like Dapsone or Colchicine. And then that really nice thing about those is, they don't suppress the immune system. And so for some patients you don't actually have to suppress your immune system to treat it. You're just attacking the cells that are causing the inflammation without affecting your ability to fight infection, which is nice. Now, some patients with IgA Pemphigus aren't going to respond to that and then they might need some of these other medications that I mentioned for the Pemphigus Vulgaris and Fallacious. but there is a subset of patients that respond really nicely to these medicines that don't suppress your immune system. And then, for all these conditions, we often are using topical steroids, because those are lower risk than pills you take, and can be a nice additional treatment.

And one of the questions I received. How do you know if the treatment you're using is working? The most important thing is that your skin or your mouth is improving. We also can again look at those blood levels of the antibody test when we have it available. So, For example, we don't have a for pemphigus or many of the antibodies for Paraneoplastic Pemphigus and for Pemphigus Vulgaris we can monitor that level and that is also another clue as to how well the treatment is working. And then, in addition to treating the condition, it's also very important to treat symptoms, so we want to help your skin heal. We want to avoid triggers. There's many different wound dressings. I put pictures on this slide of many different wound dressings that might look familiar to you. Things like saline spray, or eye drops taking care of yourself emotionally. This is a very devastating condition, and so, having peer support, family support, is crucial, and then also focusing on as best you can, good dental hygiene when it involves oral mucosa because as we know, poor dental hygiene will cause its own inflammation that can rev up the inflammation of Pemphigus. And again, this could be a whole talk in and of itself, but just a brief mention that we want to treat your condition- Pemphigus but we also want to treat all the symptoms you're dealing with.

And then you are likely seeing many different specialists. Dermatology is likely driving the most of your care. But you may also be seeing dentistry or a periodontist. If you've got eye involvement, ophthalmology, nose and throat, an ENT. Gastroenterologist, urology, gynecology, all these different specialties, mental health primary care, very crucial to have a good team on your side. This is another way. The IPPF helps you find a doctor resource where you can find specialists who are specifically interested, or have experience in treating conditions like pemphigus.

One of the questions I received, which was a great question is, what's the best way to keep all my doctors in the loop, especially what if you're seeing every single one of these and it and it can be really tricky. At an academic institution, for example, I work at the University of

Minnesota, so I can see notes from any other specialist in the University of Minnesota. So that's great if you're going to one place that has all your doctors in the same place. That's probably the easiest way to keep all your specialists in the loop, and they could easily talk to each other. But if that doesn't work out for you, depending on where you live or where your doctors are there are several electronic medical records that can talk to each other, and we can see each other's notes. If you don't have that, then there's still a good old telephone, and so you know, I've definitely called up doctors of my patients, and said, hey, this is what's going on. What do you think about this? This is my plan. Xyz: so it's definitely possible to keep doctors in loop, even if they're not of the same institution. It just might take a little more older forms of communication like a phone instead of the Internet. And then you know, very important also that you have a good primary care provider, because they can also be liaisons between many specialists. One thing I meant to mention with the multi-specialty care is now sometimes you'll see one of these specialists as kind of a screening like. Oh, you know I have trouble swallowing or I feel pain when I swallow. So you might go see a gastroenterologist, and they might look at your esophagus, they say, hey, everything's great. There's no pemphigus, Wonderful! You might not need to go back and see the gastroenterologist. Again, unless something else changes. So we sometimes have multi-specialty care just like a screening, because you have a symptom. I've got some pain in my eyes. Great. Let's have you see the eye doctor, but also help management, because, you know, I don't prescribe eye drops, or you know things in the throat nearly as much as I do on the skin. So the specialists are good for screening, and then also for treating those areas of involvement.

What are our goals of treatment? My goal is to get every patient in complete remission. What does remission mean? Clinically it means you have no lesions, and you're on no medication, so you know you wouldn't even know you have pemphigus because that is my goal for all of my patients.

There was a question I received about. You know, different study definitions or excuse me, different definitions of remission. And so we use these definitions and studies to kind of help quantify how well treatments work. So you know I don't necessarily think about these definitions when I'm seeing patients in a clinic, you know, complete remission on or off, there be partial remission on or off therapy and there's different specific definitions of those terms that we use and studies to again quantify how well medications work. But in my mind my goal is just. I want you to have no lesions on your skin, or very few, and be on no medications.

And in the studies that we have so far the highest rates of remission, are with Rituximab and Prednisone. Which is why maybe many of you, maybe not all of you. But maybe many of you have been treated with Rituximab and Prednisone. And then one more nerdy digression is that this is just very interesting to me that this is the study that led to the FDA approving Rituximab for Pemphigus treatment, which is just amazing. So in this study they had 90 patients with Pemphigus. Half of them got it Rituximab and Prednisone and half of them only got Prednisone or Rituximab and 2 years later 80% of the patients that received Rituximab and prednisone were in complete remission off therapy which is wonderful. So in 2 years, 8 out of 10 if you got Rituximab you were in complete remission of therapy versus if you did not get Rituximab and

just prednisone only 34% of patients were in complete remission. So this is an image from the article just showing the patients in blue who received Rituximab had a higher rate of remission essentially than the patients in red who only received Prednisone. So this is why the FDA said, Yes, we'll give Rituximab to people with Pemphigus. So that was very exciting for all of us. To just finally recap on the goals of treatment. So one question I received was, how do you know when it's time to stop my medications? I say, really, the treatment plan is individualized to each person, and in general our goal is to reduce medications as soon as possible without causing a flare in skin symptoms, but that really looks different for everyone. So in general, you're probably tapering medications as skin and mucosa clears. And then the mucosal surfaces improve. We can kind of taper medications, but really, how quickly that happens, looks very different for everyone and it's also hard to predict. So since we're using a lot of Rituximab to treat Pemphigus, I'll speak to that. But you know I tell my patients in general I expect you to need 2 rounds of treatment with Rituximab maybe 2 to 6 months apart. If I only have to do one. That's amazing. I love that. That's the best. If we have to do 2. That's very typical. If we have to do 3, 4, 5, 6, 7, that happens, but it can happen as quickly as one or 2 cycles as we talked about. It can take longer, It's just really hard to predict, and so our goal is to give you the least amount of medication possible to keep your skin clear.

Then this is the section I couldn't figure out where to put anywhere else. I have received a couple of questions about vaccines, which is a great question. So in general, you know, you have an autoimmune condition. Your immune system we have to kind of tamp and down that immune system that's attacking you. Well, that means we, as we've talked about. We reduce your body's ability to fight infection, and so, being on medicine that suppresses your immune system like rituximab, mycophenolate, azathioprine that increases your risk of other illnesses. And so it's really important, in all people, but especially people who have their immune system suppressed, that they receive vaccines to reduce the frequency of these conditions and the severity. So that's shingles, pneumonia, flu, and now, Covid. Importantly, rituximab and other medications, and the other medications reduce your body's ability to respond to vaccines. So it's ideal. If you already have received these vaccines even before you've ever received any treatment for your pemphigus. It doesn't always work out perfectly, because it might not be flu season, and then you develop pemphigus and have to start medicines before the flu check comes around so we know that's not always possible. But it's good to be up to date on vaccines. Get them when you can and then, if you're on medicine, that suppresses your immune system, like rituximab or mycophenolate or prednisone. There's different timings we use to try to give the vaccines in a way that your body can still respond to. So I should have listed some of the other medications that we use, like the prednisone and mycophenolate. In general, if you're going to get a vaccine, ask your doctor when they recommend you do get the vaccine. Just so you have the best chance of responding to it. And then, importantly, there have been reports of patients whose pemphigus flared after they received the Covid vaccine, or they never had pemphigus and then they developed it after receiving the Covid vaccine. The idea again being that when you get a vaccine it's revving up your immune system to respond to the vaccine. But then it can also rev up your immune system to give you a flare of your pemphigus or develop pemphigus. In general, we still say to get Covid vaccines or other vaccines. Even with this occurring, we don't really have any numbers on how frequent it is just because it's a newer occurrence. But

there's definitely reports of it happening, and what I tell my patients is if you get Covid. If you get the flu, shingles, pneumonia, etc., I'm unable to help treat that, and you can get very ill, and you could be in the hospital, or you could die from one of those infections. I can't help with that. What I can help with is, if you develop pemphigus or a flare of your Pemphigus. I know how to help treat that, and so just the benefit of protecting yourself from these infections, especially when you're immune suppressed, is so important that we do still recommend receiving these vaccines to try to protect you from that.

So that was a whirlwind about Pemphigus. I hope it was interesting, and I'm happy to answer any questions or give any clarifications. I know I talk a little fast, but I'd like to first acknowledge several people. So number one, the IPPF who has supported my career, and has just been a wonderful resource for myself and for all of my patients. Becky Strong, who is the reason I went into studying autoimmune blistering diseases. I went to her talk at a National Dermatology Conference many years ago. I have several mentors that you may see. And then, of course, I'd like to thank my patients who really make my job worthwhile. So thank you for your time and attention, and happy to move on to the Q and A portion of the talk.

Becky Strong: Dr. Schultz, Thank you very much. You gave us so much information, and I'm already getting emails and comments sent to me about what a great talk this was. We are getting a lot of questions. And we had some questions pre-submitted as well. One of the questions asked was- Can pemphigus affect the eyes and how do I know if it's affected my eyes?

Dr. Schultz: Great question! It definitely can. It's less common than other mucosal sites. I found two studies that looked at that and there was 14% to 17% of patients with Pemphigus had involvement in their eyes. So, between one or 2 and 10 of patients of Pemphigus had eye involvement. You would know if you had eye involvement with some eye symptoms. Now that symptom could be different for everybody. Pain in your eye, gritty eye, dry eye. I think probably the most convincing would be if you had blisters or erosions by your eyes. But I think more commonly, you're just gonna see maybe eye redness, eye pain, things like that. Now the eye I know much less about, and I know that dry eyes, gritty eyes, can be caused by lots of different things. So if you have those symptoms that does not mean you have pemphigus in your eye, but that does mean that's a great reason then to see the eye doctor, just for a screening, and say, hey, is there anything going on, or is it, you know, seasonal allergies, rosacea or other less worrisome things in the eye. Hopefully, so not to alarm anyone if you have any of those eye symptoms. But if you do, then I would definitely see an eye doctor, make sure you don't have it in your eyes.

Becky Strong: Great, thank you. We have another question from somebody who submitted, and said that they have thick scars where they have once had lesions, and what could be done to protect the skin, to decrease the amount of scarring? And are there any over the counter treatments that help or the silicone treatments are those helpful as well?

Dr. Schultz: It's so tough. I think we get really excited when patients don't have active lesions, that is, of course, what I'm shooting for is that people don't have blisters or sores but you are often left with a lot of other changes on your skin. So pigment changes, other scars, and then thick scars can definitely be one of them, and they're hard to treat. It is really hard to treat a scar. There are some patients who develop thick scars called keloids, and I don't know if that's what this person is referring to. But you know a keloid is when your body kind of scarred, kind of an overdrive, and it's very, very thick, and sometimes you can actually use steroid injections in the clinic with your doctor to kind of thin down that thick area. So that's one idea. Things like silicone are hard to know how well those work. If they were free, I'd say, yeah, give it a try. That's great, but they can be expensive. I think if you were interested in trying silicone for a scar. It probably works the best when the scar is kind of fresher. So a little more recent. Now you have to balance that. You don't want to flare up any of your pemphigus by putting on something irritating. So I guess I should take one step back and say: in general, we want your pemphigus to be totally controlled. Maybe before you start anything like this you're not getting new lesions and then, if you wanted to try something like silicone, I think you could, I don't think there's any studies looking at silicone specifically in pemphigus but for silicone and scars. We know they can help, and that silicone does help when the scar is earlier. But again it can be expensive. So I'd say if you wanted to give it a try, maybe pick like a test spot and try Silicone there and just see, and then report back to us at the IPPF, and you know, maybe that's something we need to study to see if it does help patients with pemphigus, but it's really tricky. I wish I had a good answer, I think for this person who has thick scars. I would see if you're a candidate for injections into the scar.

Becky Strong: Great, thank you. And this goes along with talking about healing. We've gotten a couple of questions about the use of using a hyperbaric chamber to help lesions to heal. Is that helpful? And then something else, I'm not familiar with, it's a Byoptron light therapy. Is that effective for pemphigus as well?

Dr. Schultz: So interesting. Well, I'm going to go to Google and look up what the Byoptron is because I'm not familiar with that either. The hyperbaric oxygen, we definitely have reports of hyperbaric oxygen helping wounds and other conditions. I did get an advance notice of this question. I went to the literature, and there's no studies on hyperbaric oxygen in Pemphigus, so I can't with any confidence say that it helps specifically in pemphigus but we do think it helps in wounds now. It probably helps the most in wounds that are much deeper in the skin. The hyperbaric oxygen is kind of a treatment that has like a lot of more to do associated with it. You have to go into this chamber and then another chamber. For example, University of Minnesota does not have hyperbaric oxygen but I think it could be considered if you had a very deep wound; and if your wounds weren't responding to other more typical treatments, but has not specifically been used in Pemphigus. And now, byoptron a specific optical unit. So, my guess is, it has not been studied in pemphigus. It doesn't mean it doesn't work. It just means it hasn't been studied yet?

Becky Strong: The question that we get very often is, are there any diets or nutrition believed to improve or trigger Pemphigus? For example, like the autoimmune protocols here definitely have been reports of certain food groups triggering Pemphigus.

Dr. Schultz: This is really tough. There definitely have been reports of certain food groups triggering pemphigus, kind of like the onion, the garlic, that kind of family of food. But it's definitely not definitive 100% But it's maybe been positive that could cause a pemphigus flare? We know that if you're eating something with citrus acidity pineapple, you know things like that. That's just going to inherently sting your mouth just because you have open sores in your mouth, not necessarily because we're seeing pemphigus but because it's just hurting your mouth because it's very acidic. So it's really hard, you know, to prove certain triggers. But what I tell people what I tell my patients is that if you eat something, it makes your pemphigus worse. That's very real. Whether or not I can prove it in a study that it was a trigger or not. So the same goes for things like a gluten free diet, autoimmune protocol diet. You know it's very hard to study those and prove that they help pemphigus. I don't have any evidence that that's definitely going to help all my patients with pemphigus. I think if you're interested in trying it just as another idea. I think it's very reasonable to do it, but I I don't have any evidence that it definitely helps Pemphigus. And me, I love Gluten so I would not want to try that. I'd want it to be a treatment of last resort. But you know, if I was looking for something else to try and it worked for my life, and I wanted to see if it helped. I think it's totally reasonable to try it. It's just again one of those things that I can't say. It definitely works in Pemphigus.

Becky Strong: Another question that has come across is, what is the relationship between pemphigus and an increased risk of cancer, and if there is a risk, what can be done to lower that?

Dr. Schultz: That's a good question. So you know it's a little bit tricky. So there's that paraneoplastic Pemphigus, we know, is associated with cancers. There's also a question that is pemphigus itself associated with cancer and it's really hard to to know for sure if it is. We know that pemphigus in addition to other conditions I treat on the skin like psoriasis for example, you have a lot of inflammation in your body, and we wonder if that kind of full body inflammation is then leading to the development of an increased risk of cancer. So I'll tell you that the association with cancers is unclear, not definitive, if that is, or isn't occurring, but it's possible. And so what I think is good for all patients is to have what we call age appropriate cancer screening. So you know, if making sure You're having your mammogram, Your colonoscopy, pap smears anything that you know CT Scans for your lungs if you've been a smoker, you know there are certain tests your primary care doctor is going to recommend to screen everyone for you know cancer is just with or with pemphigus, so it's just a really good idea to keep up with those. I don't routinely think about my patient. You have pemphigus and. I'm really worried about cancer. I usually don't think about that which is hopefully nice to hear. You know there's a question about it, but we don't have definitive evidence that it's really happening. And so it's just good to kind of be up to date on cancer screening just in case, but it usually doesn't mean we have to go hunting for cancer. You don't need a lot of CT scans or extra blood work or things like that.

Becky Strong: Great. Thank you. Another question that we have received. Is there any relation to pemphigus and infertility and my point B question to that is that if somebody with Pemphigus is considering pregnancy or conception, what advice do you have for that?

Dr. Schultz: This is a fascinating question, and it's actually a study that I'm working on at the University of Minnesota, that I hope to have published very soon. So there was one article that I think was 8 or 9 patients who had Pemphigus, who also had infertility. It was just a report of 8 patients who had pemphigus and infertility. There was no comment on whether this increased more than the general population? And so we don't really know if patients with pemphigus are at a higher risk of infertility. We don't really know. One thing that is also interesting is the Pemphigus we talked about. The main age of onset is kind of 50 to 60 years old. So by the time you have pemphigus most of my patients are past their childbearing age. Now, that doesn't mean that's everybody. You definitely can get pemphigus when you're younger. And so if I have a patient who is younger and is worried about childbearing or infertility, what I'd say is, I don't have any evidence that you're at a higher risk of infertility than the general world, you know you could have it, but that could maybe just be something that unfortunately, you have similar to the general population. But what becomes very important is treatment plans and recommendations. So certain medications we would not want to give you if you're actively trying to get pregnant. And so a long-winded way of saying, I don't have evidence that you have an increased risk of infertility. You still could have infertility if you're having trouble getting pregnant. I have a very low threshold too, you know. Have you seen a fertility specialist or the OBGYN team, and have us work together and if you are planning to have childbearing, then we really need to work together to figure out what treatment is best for you. But spoiler alert for the article I'm hoping to publish is, I don't think there's an increased risk of infertility and Pemphigus patients, which is great news to hear. But it hasn't been officially published yet.

Becky Strong: Great. Thank you so much for the inside scoop. Marissa is asking. Is there any relationship between hormonal changes and Pemphigus?

Dr. Schultz: That I mean, that is a fascinating question. I think it is report as one of the triggers, and isn't it fascinating that this is common in your fifties and sixties, you know, which is when a lot of women may be going through this is specific to women, maybe going through menopause, but certainly men are also having hormonal changes at that age in life. So again, it's not one that I can say definitively is associated. But there's definitely reports of it flaring around menopause or things like that. I might sound like a broken record. We think it's very possible, but it's just hard to prove, and so I think this is one of those ones that I think it's possible that it is playing a role, but it's hard to prove, and then it's also hard to do something about. I'm not going to give you estrogen, for example. which has other side effects to help prevent Pemphigus, and once you pemphigus I'll treat you differently. It's very academically interesting to think about what causes this. We all of course want to know why I get this? Why do I have this? It's a good theory, then it's just hard to know what you do with that information, if it ends up being that that was your trigger or your cause.

Becky Strong: Thank you. We're going to end kind of on an empowering question. I hope so. Dr. Schultz, the question is, what factors do you think contribute to a lack of understanding and stigma toward people with pemphigus within society. And how can we, as patients, address these challenges and kind of help, spread awareness.

Dr. Schultz: I love this question and it resonates with me as a dermatologist because I get a lot of comments when I say I'm a dermatologist like, oh botox, wrinkles, acne, things that don't matter which is so not true. This is a devastating condition. I don't have it so I can't speak from my personal experience, but I speak on behalf of my patients whose lives are upended, pain, misery, suffering. I know I don't have to tell everyone on this call. Then, I think there's also a lot of stigma, because patients who have sores on their skin have to wear funny dressings. You're probably wearing long sleeves to hide your arms. I mean there's a lot of stigma. Is this contagious? Am I going to catch this from you? You know things like that. And so I think it's on us in the dermatology world. It's on everyone involved in this condition to explain what this is to raise awareness. I think the IPPF is probably one of our most valuable resources. I love love love working with them. They are on Capitol Hill, raising awareness during Rare Disease week. We're outreaching to patients. I think you know you as a patient. If someone makes a comment, you know if you, if you want, feel free to say this is, you know this is not an infection. This is a really rare autoimmune condition and this is how it affects my life. I can't go swimming like I used to. I can't, in search however, it's affected your life. And if you feel up for sharing that with someone who really doesn't have any business knowing about it. But you know, if you feel like I want to share my story. You can do it in that venue. You can do it through the IPPF, you can work with the IPPF. Becky shared her story, which is how I got involved in treating patients with pemphigoid. So I think there's a lot of potential avenues to get involved, and I think the IPPF is just a wonderful, wonderful resource to kind of systemically address all of those. But I think it's a good question. I don't have the right answer. I think it's a tough question, because you're so right that there is a lot of you know lack of information about this condition and this is a very, very, very serious condition that I wish people have more awareness about. Hopefully, we, you, me, the IPPF hopefully will change that. I would actually also love to hear Becky's thoughts on that question. If I could ask if I'm allowed to ask her that question, what she thinks.

Becky Strong: So the easy answer for anybody who wants to make their voice heard right now. We just had the externally led patient-focused Drug Development meeting with the FDA and we need to write a voice of the patient report which the FDA will reference when drug approvals or devices come before them. So right now we are collecting patient statements. There is information on our website to be able to submit your story to be part of that. Again, there is a word limit and we are focusing on how the disease has affected your life, and how the treatments have affected or side effects are affecting. So I think that's a brilliant way right now, where you can really have your voice be heard and to amplify that. I think getting out and sharing your story. It's not for everybody. Sometimes it's as simple as talking to how you're feeling, or what you're experiencing to your friend or a friend group. It can be very small, rare disease day is coming up at the end of the month, and if you are feeling gutsy to talk to your city council to recognize where this disease is. To share your story that way. There are rare disease days going to be celebrated around the State in different States as well. Writing an article for our

Quarterly that will go out. Sharing your story on social media, hosting a fundraiser that talks about this, are all really wonderful ways kind of off the top of my head.

I just want to say thank you for joining us today. This has been a really quick time, and I think you've made it very easy to understand and get a basic primer about what pemphigus and the different subtypes are. And I really appreciate you joining us today to be on the panel. And I want to give a huge thank you to everybody else for joining us and listening in, and a big thank you to Sanofi and Regeneron for making today's call possible. Before we go, I do have a few announcements. We will be hosting our next patient education webinar on Thursday, March 9th to discuss the Regeneron Liberty BP Trial. We also have a couple of other webinars scheduled where we will be taking deep dives into treatments. We hope you will also join us on Thursday, April 6th with Dr. Annette Czernik to discuss the Fundamentals of Pemphigoid and Pemphigoid Treatments- Prednisone. Registration will be opening for this webinar soon. We also want to thank all of those who participated in the Externally Led Patient Focused Drug Development meeting that we hosted on January 25th. If you didn't get to speak and share your story we are still looking for people to submit written comments. Please submit your written comments to pfdd@pemphigus.org. Written comments should cover either Your disease and how it impacted your daily life or the treatments for your disease, the side effects of the treatments and how to improve them. Written comments should be no longer than 500 words. All writings will be published in our Voice of the Patient Report and shared with the FDA and industry partners and will be used for future decision making when developing drugs for our diseases. This year for #RareDiseaseDay, NORD and the IPPF are asking the pemphigus and pemphigoid Community to #ShowYourStripes by joining the IPPF Natural History Study Registry at www.pemphigus.iamrare.org

The Natural History Study is a patient registry sponsored by the National Organization for Rare Disorders (NORD) and the US Food and Drug Administration (FDA). Your information is private, the IPPF Natural History Study follows strict government guidelines to assure patient information is protected.

Your participation and the data will be used by the IPPF to help advance research, better understand the patient journey, find better treatments, and hopefully one day a cure. By sharing your journey and answering some questions, you directly have an effect on the future of all people affected by pemphigus and pemphigoid. So get involved today! Visit www.pemphigus.iamrare.org and show your strips for Rare Disease Day! If you are interested in continuing to help support the IPPF and allow us to continue to provide free programs and services like today's webinar, you can become a healing hero. Healing Heroes fund the future of the IPPF community by making sustaining, monthly gifts to support our mission of improving the quality of life for all those affected by pemphigus and pemphigoid. No amount is too small, even a \$5 or \$10 monthly donation goes a long way and continues to allow us to provide for the greater good of our community.

The IPPF has a number of upcoming virtual support groups across the country. If you are interested in attending a meeting, please check the IPPF's Event Page to register for a meeting.

Also, we are always looking to expand our support network. If you are interested in starting a support group in your region please contact Becky Strong at becky@pemphigus.org. It's easier than it sounds to start a support group and you can help connect others in your area with other patients.

This call recording will be sent out with the survey following this call. Thank you all for joining us.